

Adequate dosing of micronutrients for different age groups in the life cycle

Denise Bienz, Hector Cori, and Dietrich Hornig

Editors' Note

The Infant Research on Infant Supplementation (IRIS) protocol came out of the workshop in this series held in 1999 in Rio de Janeiro, Brazil. The concept was to provide interventions with either daily micronutrients as a single RDA dosage or weekly micronutrients as a two-fold multiple of the RDA. At the time, the only complete sets of daily intake recommendations based on human vitamin and mineral requirements dated to 1988 (WHO/FAO) and 1989 (10th Edition of the Recommended Dietary Allowances). The authors of this paper have made an exhaustive review and update of the emerging recommendations for nutrient intake throughout the life cycle coming out of the Dietary Reference Intakes deliberations in North America. These also introduced a systematic approach to recommending upper tolerable limits for regular micronutrient intake. The authors integrate the most up-to-date understanding of human micronutrient requirements in this review.

Abstract

Many studies of micronutrient supplementation in developing countries have used single-nutrient supplements with either vitamins or minerals. However, people in these countries often suffer from multiple, rather than single, micronutrient deficiencies. The objective of this paper is to discuss the factors that go into determining the adequate dosing of vitamins and/or minerals for people of different ages. To elaborate on the adequacy of micronutrient doses in supplements, a model described by the US FNB was used, which calculates the difference between the mean observed intake for an individual and

the estimated average requirement for a life stage and gender group. This model allows estimating the degree of confidence that a certain nutrient intake (from supplements and diet) is adequate. The US/Canadian DRI values have been used as the basis for these calculations, from which it can be concluded that a daily supplement of one RDA of each micronutrient is adequate to cover the personal requirements of all individuals in each respective age and gender group of the population, provided that 20 to 40% of an RDA is supplied by the diet—likely a realistic value for developing countries.

DRI values vary significantly between different age groups, reflecting changing needs over a life cycle. With the objective of a supplement to be adequate and safe, the design of a one-for-all supplement covering all age groups is not realistic. Such a supplement would either underscore or surpass the required intake of some of the age groups. Additionally the dosage of certain micronutrients might exceed the upper level of intake for lower age groups. Therefore, it is suggested that three different supplements following the one RDA concept for all micronutrients be developed for research use in developing countries for the following age groups: 1 to 3 years, 4 to 13 years, and females >14 years (excluding during pregnancy).

Key words: Deficiency, dosage, intervention, micronutrients, requirement, supplementation, vitamin/mineral

Introduction

Ideally, a sufficient and balanced diet should meet all of a person's micronutrient requirements. Unfortunately, large groups of people in deprived populations, such as in developing countries and in certain segments of industrialized countries, do not meet their requirements through diet. This may result in suboptimal intake of certain vitamins and minerals as well as severe clinical nutrient deficiencies [1]. Insufficient

Denise Bienz, Hector Cori, and Dietrich Hornig are affiliated with the Micronutrient Intervention Project, Roche Vitamins Ltd. in Basel, Switzerland. Address for correspondence: Denise Bienz, Roche Vitamins Ltd., CH-4070 Basel, Switzerland; phone: +41 64 688 5448; email: denise.bienz@roche.com.

food supply and/or food availability in many developing countries is strongly associated with micronutrient deficiencies. In addition, traditional and cultural variations as well as the wide variety of food patterns across countries and regions may be contributing factors.

Current research in industrialized countries is exploring the potential role of vitamins and minerals reducing risk for chronic, degenerative diseases such as cardiovascular disease, certain type of cancer, and eye diseases. These studies generally use single-entity vitamin supplements and study measurable endpoints, such as mortality or incidence of disease events. In developing countries, however, the main public health problem remains micronutrient undernutrition and deficiency. In these areas, the focus of research is to develop and implement strategies to provide adequate nutrition and micronutrients to the population. The observation that eliminating micronutrient deficiency will not only alleviate overt deficiency symptoms, but also will generally improve morbidity and reduce mortality of these populations was a major breakthrough. For example, correction of vitamin A deficiency in infants was demonstrated to not only prevent blindness but also to reduce significantly mortality in vitamin A-treated infants [2]. Similarly, elimination of iodine and iron deficiencies was shown to normalize overall development of infants and children [3, 4].

Many studies of micronutrient supplementation in developing countries have used single-nutrient supplements with either vitamins or minerals. But the people in these countries often suffer from multiple, rather than single, micronutrient deficiencies [5]. Additionally, it is well known that micronutrients act in concert and that many physiologic interactions exist between vitamins and minerals. To obtain maximum benefit, it is therefore necessary to supplement a balanced array of vitamins and minerals in an adequate combination. This makes multiple-micronutrient intervention the strategy of choice. A workshop convened by UNICEF/WHO/UNU has taken a similar approach previously and has made recommendations for the composition of a multi-micronutrient supplement to be used in pilot programs treating pregnant women in developing countries [6].

Various strategies have been developed and are currently in use to provide micronutrients to populations suffering from undernutrition. One strategy that has been shown to be successful in many instances is the fortification of staple foods, such as sugar, flour, or vegetable oil. This paper discusses another effective intervention strategy—supplementation with multivitamin/multimineral supplements. The objective of this paper is to discuss the factors that go into determining the adequate dosing of vitamins and/or minerals for people of different ages. The possibility of a “one-for-all” supplement, which includes multiple micronutrients, for use in research programs in

developing countries will also be considered. Such a supplement would streamline operational strategies and distribution systems and perhaps lower costs, compared with programs using single-micronutrient supplements.

The most vulnerable groups within the life cycle are infants, small children (through adolescence), and women of childbearing age. Unfortunately, the scientific database particularly for the young age groups is insufficient and the knowledge of the daily requirements to prevent vitamin and mineral deficiencies is limited. Important factors to be considered in determining appropriate dosage levels are upper levels of intake and potential adverse effects related to supplementation in these age groups. In addition, the form of delivery (chewable tablet, tablet, capsule, syrup) and its impact on compliance and bioavailability must be considered.

Scientific basis for determination of dose

The US Food and Nutrition Board (FNB) of the Institute of Medicine, National Academy of Sciences, has recently developed a comprehensive set of reference values for dietary micronutrient intakes for all age and gender groups in a healthy population. All of the respective panel reports have been published or are available in pre-publication format [7–10]. Dietary reference intakes (DRI) are reference values that can be used for assessing and planning diets for healthy populations and for many other purposes. DRIs encompass the estimated average requirement (EAR), the recommended dietary allowances (RDA), the adequate intake (AI), and the tolerable upper level of intake (UL).

EAR is the nutrient intake that meets the requirement determined by a specified functional parameter in 50% of the individuals in a life stage and gender group, with the other 50% not meeting their micronutrient requirement. It is important to recognize that the EAR includes an adjustment for an assumed bioavailability of the respective nutrient.

The RDA is the average daily intake level that is sufficient to meet the nutrient requirement of 97% to 98% of individuals in a life stage and gender group and applies, therefore, to individuals. RDAs are calculated from the EAR using a coefficient of variation of mostly 10% (niacin 15%, vitamin A 20%), because data on variability in requirements are insufficient for most micronutrients.

The AI can be considered a surrogate for the RDA if insufficient scientific evidence is available to evaluate an EAR and to calculate a RDA. This is generally the case for infants up to one year of age and some children. AIs were also set for all age groups for several vitamins and minerals, including calcium, fluoride, vitamin D, vitamin K, pantothenic acid, and biotin. The AI is to

be used as a goal for the nutrient intake of individuals. Both the RDA and AI are micronutrient intake levels that should decrease the risk of developing a condition associated with a negative functional outcome, such as nutrient malnutrition or clinical nutrient deficiency state. However, intakes at the level of the RDA or AI replete undernourished individuals only over a longer period of time.

The UL is defined as the highest level of daily total chronic intake for a vitamin or mineral from food, fortified foods, and supplements that is likely to pose no risks of adverse health effects to almost all individuals in the general population. With high probability this intake level is biologically well tolerated and is therefore considered a safe intake. If adverse effects have been associated with intakes from fortified foods or supplements only, the UL is based on intake from those sources only. For some of the vitamins and minerals there are insufficient data available to set a UL, or no adverse effects have been described. In this case, no UL has been set. A UL was not determinable for infants up to 12 months of age due to lack of data on adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Also data to derive a UL for infants and adolescents were considered insufficient and in many cases a UL was extrapolated from those established for adults.

Recently, WHO has recognized that substantial segments of the population in developing countries are in a rapid transition toward considerable physical inactivity, overweight, and unbalanced nutrition contributing significantly to the current rise in chronic diseases. At the same time, control of undernutrition remains an unfinished work. Recognizing this development, the 53rd World Health Assembly (2000) adopted resolution WHA53.17 on the prevention and control of non-communicable diseases, requesting WHO to continue to give this area high priority. WHO is taking steps to implement this global strategy.

Therefore, the US/Canadian DRI values have been used as the basis for this publication, because these values encompass the concept of micronutrient deficiency as well as risk reduction of chronic diseases by micronutrients.

Dosing of an appropriate supplement

Annex I gives an overview of the US/Canadian DRIs, subdivided by age groups and gender. The question arises if using one RDA for a daily multivitamin/multimineral supplement for populations in developing countries is the adequate dosing to meet the requirements of at least 97% of the population, or if an adjustment to a multiple or a fraction of the RDA would be more appropriate. This section elaborates on that question.

Considering that, even within a well-defined population, individuals vary greatly in their metabolism, activity level, and response to environmental exposures, it is obvious that their individual nutrient requirements may vary significantly. The fundamental question, therefore, is whether a person's diet is meeting his or her individual micronutrient requirements (defined as the lowest intake level to maintain a level of nutrition for a given criterion of nutritional adequacy). Figure 1 shows the assumed distribution of requirement and of intake of a particular micronutrient in a given population with the RDA covering the requirement of 97% to 98% of the individuals in that group. The more these two curves overlap, the higher the probability that an increasing number of individuals may no longer meet their personal requirements and that insufficient intakes cause micronutrient undernutrition or deficiency. Consequently, the objective of any micronutrient intervention strategy should be to shift the intake curve to sufficient high intakes, which also cover the variation of individual requirements. However, the requirement of an individual is mostly not known. Likewise, the individual's usual intake (average intake of a nutrient over a long period) is often not available or can only be determined by tedious procedures.

An approach that could be used to determine how large the difference (D) is between mean observed intake for an individual (y) and the requirement (EAR) for a life stage and gender group is described by the US FNB [11]. It gives the basis to conclude with a sufficient degree of confidence that the unobservable usual intake exceeds the unobservable actual requirement.

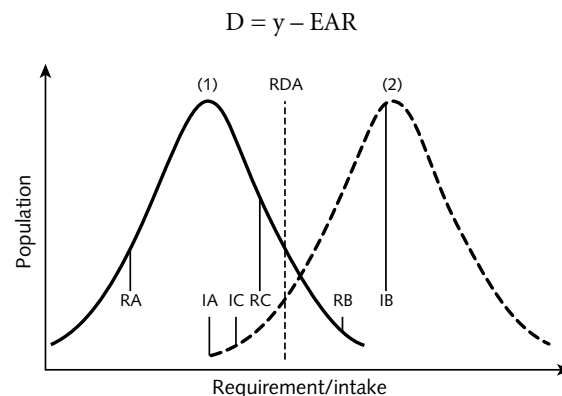


FIG. 1. Assumed (1) distribution of the requirement for a micronutrient in a population group and (2) distribution of intake for the same micronutrient in the same group. Requirement and intake of three hypothetical individuals are shown.

A: Intake is lower than the recommended intake ($IA < RDA$), but the requirement for this individual (RA) is covered.

B: Requirement is greater than the recommended intake ($RB > RDA$), but the intake is covered because $IB > RB$.

C: Requirement is below the recommended intake ($RC < RDA$), but because the intake is even lower than the requirement ($IC < RC$), this individual is at great risk for deficiency of this micronutrient.

To solve this question, one must know the following: (1) the variability of D (SD_D), (2) the standard deviation of the requirement (SD_{EAR} , assumed to be 10% for most nutrients), and (3) the within-person standard deviation (SD_{within}) of day-to-day intakes that can be estimated from large surveys of similar populations. The probability whether the intake is above (sufficient intake) or below (insufficient intake) the requirement can be determined by examining the ratio of $D:SD_D$.

To evaluate the adequate dosing for a supplement for malnourished populations, some assumptions are introduced. Because the population to be supplemented has a limited unknown micronutrient intake that will be mostly below or, at the most, close to the median requirement (EAR) as judged by the observed undernutrition, the dietary intake will not be taken into account. It will only be evaluated whether supplementation with, for example, one RDA (or AI) would be sufficient to cover the individual variation in requirement under consideration of the respective standard deviations. An example is given below for vitamin C:

Male adolescent, 13 years; duration of supplementation 180 days; EAR: 39 mg/day; $SD_{EAR} = 3.9$ mg/day; RDA: 45 mg/day; day-to-day variation in that age group (taken from Continuing Survey of Food Intakes by Individuals [CSFII]): 81 mg/day.

By using the formula

$$SD_D = \sqrt{V_{EAR} + V_{within} / n}$$

$$[V_{EAR} = (SD_{EAR})^2; V_{within} = (\text{within SD})^2; n = \text{duration of supplementation}],$$

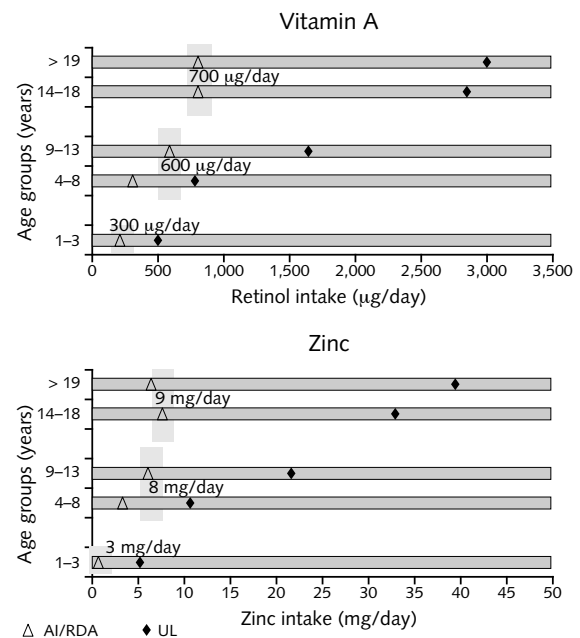
the SD_D yields 7.1 mg/day, and the ratio $D:SD_D = (45-39)/7.1 = 0.45$. That value implies a probability for a correct conclusion of 70% to 85% based on calculations by Snedecor and Cochran [12]. Thus, an intake of approximately 53 to 64 mg/day would be necessary to have confidence that intake is fully adequate. Because this model does not consider the ordinary dietary intake, one can assume that supplementation with one RDA is sufficient under this assumption, and that approximately 20% to 40% of the RDA (about 10 to 20 mg/day) is being consumed from the diet, in addition to the supplement. A similar calculation with 2 RDA will result in a $D:SD_D$ of 7.1, implying 99% confidence that the chosen intake would be adequate. Adding only 50% of a RDA under the same assumptions will result in a $D:SD_D$ of -2.3, implying that supplementation with only half the RDA is inadequate, and it would be uncertain whether the dietary intake could cover the difference.

This approach has several limitations. It does not take into account individual dietary intake, because it is unknown. The basis for the within-person standard deviation of intake is derived from the CSFII [12], which is conducted in the United States and may not be

representative of individuals in micronutrient-deficient populations. In these groups, the within-subject variation might be much larger, leading to a lower $D:SD_D$ ratio, indicating reduced confidence that the intake is adequate. Based on the above argumentation and calculations, it can be concluded that a supplement of one RDA of each micronutrient daily will mean that all individuals in each respective age group of the population will meet their personal requirements, if at least 20% to 40% of an RDA for the US/Canadian population is provided by dietary intake. This seems to be a realistic value for developing countries.

Feasibility of a "one-for-all" supplement

The availability of a one-for-all supplement in a life cycle group would provide significant logistic and programmatic advantages in research programs in developing countries. However, as demonstrated in Annex I, the recommended intake (RDA) and the upper level of intake (UL) vary substantially across different age groups. Figure 2 illustrates this for vitamin A and zinc, respectively. It also implies that a one-for-all supplement suitable for ages 1 to 13 years and >14 years (females, excluding pregnancy) either will



FIGS. 2a, 2b. RDA/AI (Δ) and UL (\blacklozenge) values according to age groups for vitamin A and zinc, respectively [10]. The vertical axis represents age groups for females. Vertical bars indicate the suggested dosages for the life cycle-specific supplements for age groups 1 to 3 years (vitamin A 300 μ g retinol/day; zinc 3 mg/day), 4 to 13 years (vitamin A 600 μ g retinol/day; zinc 8 mg/day), and >14 years (females, excluding pregnancy; vitamin A 700 μ g retinol/day; zinc 9 mg/day).

underscore or surpass the required intake. Additionally, the dosage of certain micronutrients may exceed the upper level of intake (UL) for lower age groups where such an intake level has been defined. It is therefore suggested that three different supplements containing vitamins and minerals be developed for the life cycle groups 1 to 3 years, 4 to 13 years, and >14 years (females, excluding pregnancy). In order to assure the highest probability that the personal requirements of all individuals in a life cycle group are covered, the RDA of the age group with the highest requirement was selected. The composition of micronutrients in these supplements is based on the results of the UNICEF/WHO/UNU workshop [6] and a more recent workshop organized by the Ministry of Health, Brazil, and UNICEF in Rio de Janeiro [13]. In addition to these recommendations, it is suggested that vitamin K be included in such a supplement based on emerging results on the importance of this vitamin in bone health [14]. Table 1 summarizes the recommended dosage for these age-specific supplements suggested to be used in micronutrient research programs in developing countries.

Safety considerations

Supplementation with one RDA of micronutrients is not expected to create a nutrient imbalance. On the contrary, it is generally accepted that health protection could be achieved by establishing a better micronutrient status in a specific population. Several large

intervention trials of micronutrient supplementation in the range of one RDA have demonstrated the overall safety of vitamins and minerals [15–17]. Nevertheless, safety considerations must be a specific component in each trial protocol and mechanisms must be in place to monitor any potential adverse effects during a trial. The US FNB has defined the UL as that daily chronic intake of a micronutrient that does not show any risk of adverse effect in the most sensitive part of a gender and age group. In fact, because the UL is derived in most cases from its NOAEL (no observed-adverse-effect-level) or for some micronutrients from its LOAEL (lowest-observed adverse-effect-level) it has already built in a margin of uncertainty regarding the strength of the overall data determining the NOAEL (or LOAEL). Defined as such, the UL is a safe intake. When compared with the RDA intake level, the UL is for most micronutrients a multiple of a RDA or AI (see Annex I). The FNB panels have used the National Health and Nutrition Examination Survey (NHANES) III data to elaborate on the likelihood of overconsumption due to supplementation of any content as available on the market in the United States and has recognized that no discernible portion of people consumed more than the UL. Therefore, in an undernourished population the risk for overconsumption of micronutrients is rather limited, even when supplemented with one RDA over longer periods of time. However, due to the often limited scientific data to derive the UL for several of the micronutrients for infants and children, these subjects should be closely monitored for any potential adverse effects during supplementation trials.

TABLE 1. Recommended dosages for 3 life-cycle specific supplements for age groups 1 to 3 years, 4 to 13 years, and > 14 years (females, excluding pregnancy) suggested to be used in micronutrient research programs in developing countries

Micronutrient	1 to 3 years	4 to 13 years	> 14 years
Vitamin A (μg)	300	600	700
Vitamin D (μg)	5	5	5
Vitamin E (mg)	6	11	15
Vitamin C (mg)	15	45	75
Vitamin K (μg)	30	60	90
Iron (mg)	7	10	18
Zinc (mg)	3	8	9
Copper (μg)	340	700	900
Iodine (μg)	90	120	150
Thiamine (mg)	0.5	0.9	1.1
Riboflavin (mg)	0.5	0.9	1.1
Vitamin B ₆ (mg)	0.5	1.0	1.3
Niacin (mg)	6	12	14
Folate (μg DFE)	150	300	400
Vitamin B ₁₂ (μg)	0.9	1.8	2.4

Conclusion

Interventions of multiple-micronutrient supplements, rather than single-nutrient supplements, may be the strategy of choice to be pursued in selected age and gender groups, such as young children and adolescents, to combat micronutrient undernutrition or deficiency states in developing countries. In this context, the question of composition and adequate dosing of vitamins and/or minerals for different age groups in the life cycle arises. Optimally, a “one-for-all” supplement preparation should be designed for general use in research programs in developing countries. It should include the following nutrients: vitamins A, D, E, B₁, B₂, B₆, B₁₂, C, folic acid, and niacin; and minerals iron, zinc, copper, and iodine. More recent research has indicated that vitamin K should also be included.

For the determination of adequate dosing, two main approaches were used: (1) The US FNB's new DRIs were an excellent and most recent scientific compilation for intake recommendations (RDA/AI) and for upper levels of intake (UL), and (2) The personal requirements and dietary intakes of individuals

within a specific population were considered when these reference values were applied in the design of an adequate supplement. Unfortunately, in most cases, neither the personal requirement of an individual for a micronutrient nor his or her usual intake was known. By using a model recently described by the US FNB and by employing standard deviations of requirement and within-person standard deviations, one can determine with a high degree of confidence whether supplementation with one RDA is sufficient to secure that all individuals in these populations will meet their personal requirements. Based on these calculations, it can be concluded that a multivitamin/multimineral supplement containing one RDA of each micronutrient is adequate to cover the individual requirements of a population, provided that 20% to 40% of the RDA is supplied by the diet—likely a realistic value for developing countries.

DRI values vary significantly between different age groups, reflecting the changing needs over a life cycle. The overall objective of a supplement is to be adequate and safe. Consequently, the design of a one-for-all supplement for covering all age groups is not realistic and would either underscore or surpass the required intake. Therefore, it is suggested that three different supplements following the one-RDA concept for all micronutrients be developed for use in research in developing countries for the following age groups: 1 to 3 years, 4 to 13 years, and females >14 years (excluding pregnancy). The UL can be used to estimate the likelihood of potential adverse effects of micronutrients. Because the UL is a multiple of the RDA or AI for most micronutrients, the risk for overconsumption is rather limited in an undernourished population, even when supplementation with one RDA over longer periods of time occurs.

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ANNEX I: DRI values (Calcium Panel Report 1997; B-Vitamins and Choline Panel Report 1998; Dietary Antioxidant Panel Report 2000; Vitamin A, Vitamin K, Trace Elements Panel Report 2001). Indicated are ranges depending on gender and age.

Nutrient	RDA	AI	UL
Children (1–3 years)			
Vitamin B ₁	0.5 mg	—	None
Vitamin B ₂	0.5 mg	—	None
Niacin	6 mg NE	—	10 mg NE
Vitamin B ₆	0.5 mg	—	30 mg
Folate	150 µg DFE*	—	300 µg folic acid, none for folate from food
Vitamin B ₁₂	0.9 µg	—	None
Vitamin C	15 mg	—	400 mg
Pantothenic Acid	None	2 mg	None
Biotin	None	8 µg	None
Vitamin A	300 µg	—	600 µg
Vitamin D	None	5 µg (200 IU)	50 µg (2000 IU)
Vitamin E	6 mg**	—	200 mg***
Vitamin K	—	30 µg	None
Calcium	None	500 mg	2500 mg
Phosphorus	460 mg	—	3.0 g
Magnesium	80 mg	—	65 mg****
Fluoride	None	0.7 mg	1.3 mg
Copper	340 µg	—	1000 µg
Iodine	90 µg	—	200 µg
Iron	7 mg	—	40 mg
Zinc	3 mg	—	7 mg
Selenium	20 µg	—	90 µg
Children (4–8 years)			
Vitamin B ₁	0.6 mg	—	None
Vitamin B ₂	0.6 mg	—	None
Niacin	8 mg NE	—	15 mg NE
Vitamin B ₆	0.6 mg	—	40 mg
Folate	200 µg DFE*	—	400 µg folic acid, none for folate from food
Vitamin B ₁₂	1.2 µg	—	None
Vitamin C	25 mg	—	650 mg
Pantothenic Acid	None	3 mg	None
Biotin	None	12 µg	None
Vitamin A	400 µg	—	900 µg
Vitamin D	None	5 µg (200 IU)	50 µg (2000 IU)
Vitamin E	7 mg **	—	300 mg***
Vitamin K	—	55 µg	None
Calcium	None	800 mg	2500 mg
Phosphorus	500 mg	—	3.0 g
Magnesium	130 mg	—	110 mg****
Fluoride	None	1.0 mg	2.2 mg
Copper	440 µg	—	3000 µg
Iodine	90 µg	—	300 µg
Iron	10 mg	—	40 mg
Zinc	5 mg	—	12 mg
Selenium	30 µg	—	150 µg

continued

ANNEX I: DRI values (Calcium Panel Report 1997; B-Vitamins and Choline Panel Report 1998; Dietary Antioxidant Panel Report 2000; Vitamin A, Vitamin K, Trace Elements Panel Report 2001). Indicated are ranges depending on gender and age. (*continued*)

Nutrient	RDA	AI	UL
Children (9–13 years)			
Vitamin B ₁	0.9 mg	—	None
Vitamin B ₂	0.9 mg	—	None
Niacin	12 mg NE	—	20 mg NE
Vitamin B ₆	1.0 mg	—	60 mg
Folate	300 µg DFE*	—	600 µg folic acid, none for folate from food
Vitamin B ₁₂	1.8 µg	—	None
Vitamin C	45 mg	—	1200 mg
Pantothenic Acid	None	4 mg	None
Biotin	None	20 µg	None
Vitamin A	600 µg	—	1700 µg
Vitamin D	None	5 µg (200 IU)	50 µg (2000 IU)
Vitamin E	11 mg**	—	600 mg***
Vitamin K	-	60 µg	None
Calcium	None	1300 mg	2500 mg
Phosphorus	1250 mg	—	4.0 g
Magnesium	240 mg	—	110 mg****
Fluoride	None	2.0 mg	10 mg
Copper	700 µg	—	5000 µg
Iodine	120 µg	—	600 µg
Iron	8 mg	—	40 mg
Zinc	8 mg	—	23 mg
Selenium	40 µg	—	280 µg
Adolescents (14–18 years)			
Vitamin B ₁	1.2 / 1.0 mg°	—	None
Vitamin B ₂	1.3 / 1.0 mg°	—	None
Niacin	16 / 14 mg NE°	—	30 mg NE
Vitamin B ₆	1.3 / 1.2 mg°	—	80 mg
Folate	400 µg DFE*	—	800 µg folic acid, none for folate from food
Vitamin B ₁₂	2.4 µg	—	None
Vitamin C	75 mg / 65 mg	—	1800 mg
Pantothenic Acid	None	5 mg	None
Biotin	None	25 µg	None
Vitamin A	900 / 700 µg°	—	2800 µg
Vitamin D	None	5 µg (200 IU)	50 µg (2000 IU)
Vitamin E	15 mg **	—	800 mg***
Vitamin K	—	75 µg	None
Calcium	None	1300 mg	2500 mg
Phosphorus	1250 mg	—	4.0 g
Magnesium	410 / 360 mg°	—	350 mg****
Fluoride	None	3.0 mg	10 mg
Copper	890 µg	—	8000 µg
Iodine	150 µg	—	900 µg
Iron	11 / 15 mg°	—	45 mg
Zinc	11 / 9 mg°	—	34 mg
Selenium	55 µg	—	400 µg

continued

ANNEX I: DRI values (Calcium Panel Report 1997; B-Vitamins and Choline Panel Report 1998; Dietary Antioxidant Panel Report 2000; Vitamin A, Vitamin K, Trace Elements Panel Report 2001). Indicated are ranges depending on gender and age. (*continued*)

Nutrient	RDA	AI	UL
Adults (19–50 years)			
Vitamin B ₁	1.2 / 1.1 mg ^o	—	None
Vitamin B ₂	1.3 / 1.1 mg ^o	—	None
Niacin	16 / 14 mg NE ^o	—	35 mg NE
Vitamin B ₆	1.3 / 1.3 mg ^o	—	100 mg
Folate	400 µg DFE ⁺ ; 600 µg DFE* (pregnancy) ⁺	—	1,000 µg (synth.), none for folate from food
Vitamin B ₁₂	2.4 µg ⁺⁺	—	None
Vitamin C	90 mg / 75 mg	—	2000 mg
Pantothenic Acid	None	5 mg	None
Biotin	None	30 µg	None
Vitamin A	900 / 700 µg ^o	—	3000 µg
Vitamin D (19–50 y)	None	5 µg (200 IU)	50 µg (2,000 IU)
Vitamin E	15 mg ^{**}	—	1,000 mg ^{***}
Vitamin K	—	120 / 90 µg ^o	None
Calcium	None	1000 mg	2,500 mg
Phosphorus	700 mg	—	4.0 g
Magnesium (19–30 y; >31 y)	400 / 310 mg ^o ; 420 / 320 mg ^o	—	350 mg (non-food only)
Fluoride	None	4 / 3 mg ^o	10 mg
Copper	900 µg	—	10,000 µg
Iodine	150 µg	—	1100 µg
Iron	8 / 18 mg ^o	—	45 mg
Zinc	11 / 8 mg ^o	—	40 mg
Selenium	55 µg	—	400 µg

* DFE = dietary folate equivalents = 1 µg food folate = 0.5 µg synthetic folic acid on empty stomach = 0.6 µg synthetic folic acid with meals

** vitamin E activity of α -tocopherol is defined to be limited to the naturally occurring form RRR- and the other 3 synthetic 2R-stereoisomer forms RSR-, RRS-, and RSS- of α -tocopherol

*** of any form of supplementary α -tocopherol

**** supplementary magnesium

+ in addition to dietary folate 400 µg of folic acid as supplement is recommended for women capable of becoming pregnant to reduce the risk of neural tube defects

++ adults > 51 years are advised to obtain most of this amount by taking foods fortified with vitamin B₁₂ or vitamin B₁₂-containing supplements

o males / females