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NF03-580 Upper Safe Levels of Intake for Adults: Vitamins, Macrominerals, and Trace Minerals

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Upper Safe Levels of Intake for Adults: Vitamins, Macrominerals, and Trace Minerals

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Our bodies need vitamins and essential minerals; however, if taken in large amounts, they can adversely affect our health. In fact large amounts of many of the vitamins and minerals can be toxic.

Nutritional Status

Individuals can have deficient, adequate, or toxic intakes of any essential nutrient. A **deficiency** occurs when the intake of the essential nutrient is too low to meet a person's need for that specific nutrient. **Adequacy** occurs when a person gets enough but not too much of a nutrient. Nutrient **toxicity** occurs when a person gets an overdose of a given nutrient.

Dietary Reference Intakes

The National Academy of Sciences, Institute of Medicine, has established **Dietary Reference Intakes** (DRIs), which can be used in planning and assessing diets of the healthy general population, as well as for other purposes. The Dietary Reference Intakes are a set of nutrient-based reference values: the **Estimated Average Requirement** (EAR), the **Recommended Dietary Allowance** (RDA), the **Adequate Intake** (AI), and the **Tolerable Upper Intake Level** (UL). These terms are defined in *Table I*. An essential nutrient has either an EAR and RDA or an AI, for a specific gender:life stage group (such as female, 19 to 30 years) depending on whether sufficient data are available to set an EAR. If the data are insufficient an AI is given for that nutrient for a gender:life stage group. In that many individuals consume **fortified foods** (containing nutrients added during food processing) and **dietary supplements**, ULs have been set for many of the essential nutrients for a specific gender:life stage group. The UL is the highest level of daily nutrient intake that is considered to be safe for almost all individuals in a gender:life stage group. These ULs are based on intakes from food (including fortified food), water, and dietary supplements unless otherwise stated. The UL is for daily use over a long period of time. ULs are not available for all essential nutrients for each gender:life stage grouping as data regarding adverse effects are frequently limited.

Table I. Dietary Reference Intakes

Estimated Average Requirement (EAR): the average daily nutrient intake level estimated to meet the requirement of half the healthy individuals in a particular life stage and gender group.

Recommended Dietary Allowance (RDA): the average daily dietary nutrient intake level sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) healthy individuals in a particular life stage and gender group.

Adequate Intake (AI): the recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate — used when an RDA cannot be determined.

Tolerable Upper Intake Level (UL): the highest average daily intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase.

Directly quoted from Institute of Medicine, National Academy of Sciences, *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*, p. 3. Washington, DC: National Academy Press, 2000.

Nutrient Toxicity

The UL is calculated from hazard identification (primarily evidence of adverse effects) and dose-response data. The

appropriate critical adverse effect(s) for the nutrient is considered in setting the **no-observed-adverse-effect level** (NOAEL). The NOAEL is the highest intake or dose of a nutrient at which no adverse effects have been observed in individuals studied. If no adequate data are available to determine the NOAEL, then a **lowest-observed-adverse-effect level** (LOAEL) is used. The LOAEL is the lowest intake or dose at which an adverse effect(s) has been demonstrated.

The Tolerable Upper Intake Levels, or ULs, of Vitamins and Essential Macro- and Trace Minerals for Adults are given in *Table II*. DRIs for the electrolyte minerals (sodium, chloride, and potassium) have not yet been established. The reasons given by the Institute of Medicine, National Academy of Sciences, for the UL and the basis for the UL are listed in *Table II*.

The current RDAs or AIs as well as the Daily Values for these essential nutrients are also given in *Table II*. **Daily Values** are set by the Food and Drug Administration for use in nutritional labeling of food products and dietary supplements. RDAs or AIs are not the same as Daily Values. Information from older releases of the RDAs were used in setting the Daily Values. The RDAs or AIs and Daily Values for these essential nutrients were included in *Table II* so that the reader can compare these values to the ULs. These values are also useful in planning and evaluating diets, as diets should meet the RDAs or AIs for an essential nutrient without exceeding the ULs.

Diets for healthy individuals should not routinely exceed the UL for any essential nutrient; however, intakes above the UL may be appropriate for investigation within clinical research trials. Nutrient ULs are not meant to apply to individuals who may be given an essential nutrient under medical supervision.

References

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

Institute of Medicine, National Academy of Sciences, *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline*. Washington, DC: National Academy Press, 1998.

Institute of Medicine, National Academy of Sciences, *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. Washington, DC: National Academy Press, 2000.

Institute of Medicine, National Academy of Sciences, *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington, DC: National Academy Press, 2001.

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

U.S. Food and Drug Administration, *A Food Labeling Guide: Reference Values for Nutrition Labeling*. On-line http://vm.cfsan.fda.gov/~dms/flg-7a.html, accessed April 18, 2003.

Table II. Tolerable Upper Intake Levels (ULs) of Vitamins and Essential Macro- and Trace Minerals for Adults.

Nutrient	***UL***[a] (per day)	***Reasons given by the Institute of Medicine, National Academy of Sciences, for UL***	***Basis for UL*** (NOAEL or LOAEL[b] per day)	***RDA or AI***[c] (per day) ***Men/Women***	***Daily Value***[d] (per day)
Vitamin A (preformed)	3,000 mcg	The critical adverse effect is liver abnormalities except for women of childbearing age in which it is teratogenic. Other adverse effects include nausea, vomiting, headache, increased cerebrospinal fluid pressure, vertigo, blurred vision, muscular incoordination, bulging, fontanel in infants, nervous system changes, and bone and skin abnormalities.	LOAEL = 14,000 mcg, except for women of childbearing age, NOAEL = 3,000 mcg	900/700 mcg	5000 IU (1500 mcg preformed vitamin A)
Vitamin D	50 mcg	The critical adverse effect is hypercalcemia. Other adverse effects include anorexia, nausea, vomiting, increased thirst and urination, metastatic calcification of soft tissues (kidneys, blood vessels, heart, lungs), and renal disorders.	NOAEL = 60 mcg	5, 10, or 15 mcg[e]	400 IU or 10 mcg
Vitamin E[f,g]	1,000 mg α-tocopherol	No adverse effects from consumption of vitamin E naturally occurring in foods. The critical adverse effect of high intakes from fortified foods, dietary supplements, or pharmacologic agents is increased tendency to hemorrhage. Adults deficient in vitamin K, including those taking coumarin drugs, have increased risk of coagulation defects.	LAOEL = 500 mg/kg	15/15 mg α-tocopherol	30 IU (22 mg of natural d-α-tocopherol acetate[h])
Vitamin K	ND[i]	No adverse effects from consumption from foods or dietary supplements.	NE[j]	120/90 mcg	80 mcg

Nutrient	*UL*[a] (per day)	*Reasons given by the Institute of Medicine, National Academy of Sciences, for UL*	*Basis for UL* (NOAEL or LOAEL[b] per day)	*RDA or AI*[c] (per day) *Men/Women*	*Daily Value*[d] (per day)
Vitamin C	2,000 mg	The critical adverse effects are osmotic diarrhea and gastrointestinal disturbances. Other possible effects include increased oxalate excretion and kidney stone formation, uric acid excretion, pro-oxidant effects, rebound scurvy, increased iron absorption leading to iron overload, reduced vitamin B_{12} and copper status, increased oxygen demand, and erosion of dental enamel.	LAOEL = 3000 mg	90/75 mg	60 mg
Thiamin (vitamin B_1)	ND	No adverse effects from consumption from foods or dietary supplements. There have been occasional reports of anaphylaxis to parenteral thiamin as well as pruritus due to allergic sensitivity to thiamin injection.	NE	1.2/1.1 mg	1.5 mg
Riboflavin (vitamin B_2)	ND	No adverse effects from consumption from foods or dietary supplements.	NE	1.3/1.1 mg	1.7 mg
Niacin[g] (nicotinic acid & nicotinamide)	35 mg	No adverse effects from consumption of naturally occurring niacin in foods. The UL for nicotinic acid is based on vasodilation (flushing). Nicotinamide appears not to be associated with the flushing effects. There are gastrointestinal effects for patients treated with nicotinic acid. Hepatic toxicity has been reported in patients treated medically with the vitamin.	LOAEL = 50 mg	16/14 mg	20 mg
Vitamin B_6	100 mg	No adverse effects from consumption from food sources. The critical adverse effect from high intake is neuropathy.	NOAEL = 200 mg	1.3, 1.5, or 1.7 mg[k]	2.0 mg
Folate[g]	1,000 mcg	No adverse effects have been associated with the consumption of folate levels in foods or fortified foods. Excess folate may precipitate or exacerbate the neurological damage of vitamin B_{12} deficiency.	LOAEL = 5 mg	400/400 mcg[l]	400 mcg
Vitamin B_{12}	ND	No adverse effects from consumption from foods or dietary supplements.	NE	2.4/2.4 mcg[m]	6.0 mcg
Pantothenic Acid	ND	No adverse effects have been associated with high intakes.	NE	5/5 mg	10 mg
Biotin	ND	No adverse effects from foods or dietary supplements.	NE	30/30 mcg	300 mcg
Choline	3.5 g	The critical effect is hypotension and fishy body odor is a secondary consideration. Also nausea and diarrhea.	LOAEL = 7.5 mg	550/425 mg	NE
Calcium	2.5 g	The critical effect is kidney stone formation or milk-alkali syndrome (hypercalcemia and renal insufficiency). Also affects absorption of iron, zinc, magnesium, and phosphorus.	LOAEL = 5000 mg	1,000 or 1,200 mg[n]	1,000 mg
Phosphorus	3 or 4 g[o]	The critical effect is hyperphosphatemia. Other effects include hypocalcemia, adjustments in calcium-regulating hormones, and calcification of nonskeletal tissues (especially kidneys).	NOAEL = 10,200 mg	700/700 mg	1,000 mg
Magnesium	350 mg	Adverse effects are from nonfood sources, such as magnesium salts used for pharmacologic purposes. The critical effect is osmotic diarrhea. Other effects include nausea, abdominal cramping, serious neurological and cardiac symptoms, and death.	LOAEL = 360 mg	310, 320, 400, or 420 mg[p]	400 mg
Fluoride	10 mg	The critical effects are enamel fluorosis and skeletal fluorosis.	NOAEL = 10 mg	4/3 mg	NE

Nutrient	*UL*[a] (per day)	*Reasons given by the Institute of Medicine, National Academy of Sciences, for UL*	*Basis for UL* (NOAEL or LOAEL[b] per day)	*RDA or AI*[c] (per day) *Men/Women*	*Daily Value*[d] (per day)
Selenium	400 mcg	The critical effects are hair and nail brittleness and loss. Other effects include gastrointestinal disturbances, skin rash, garlic breath odor, fatigue, irritability, and nervous system disorders.	NOAEL = 800 mcg	55/55 mcg	70 mcg
Iron	45 mg	The critical adverse effect is gastrointestinal side effects. Other effects include impaired zinc absorption, increased risk for vascular disease and cancer, and systemic iron overload.	LOAEL = 70 mg	8 or 18 mg[q]	18 mg
Copper	10 mg	The critical adverse effect is liver damage. Other effects include abdominal pain, cramps, nausea, diarrhea, and vomiting.	NOAEL = 10 mg	900/900 mcg	2.0 mg
Zinc	40 mg	No adverse effects from consumption from foods. The critical adverse effect is the influence of excess zinc on copper metabolism. Other effects include epigastric pain, nausea, vomiting, loss of appetite, abdominal cramps, diarrhea, headaches, and immune response impairment.	LOAEL = 60 mg	11/8 mg	15 mg
Iodine	1,100 mcg	The critical adverse effect is elevated serum thyroid stimulation hormone concentrations. Acute responses include burning of mouth, throat, and stomach, abdominal pain, fever, nausea, vomiting, diarrhea, weak pulse, cardiac irritability, coma, and cyanosis. Also can produce goiter, increased risk of thyroid papillary cancer, and iodermia.	LOAEL = 1,700 mcg	150/150 mcg	150 mcg
Manganese	11 mg	The critical adverse effects are elevated blood magnesium concentration and neurotoxicity.	NOAEL = 11 mg	2.3/1.8 mg	2.0 mg
Chromium	ND	No adverse effects have been convincingly associated with excess intake of chromium from food or dietary supplements.	NE	20, 25, 30, or 35 mcg[r]	120 mcg
Molybdenum	2 mg	The UL is based upon impaired reproduction and fetal development in rats and mice. Molybdenum compounds appear to have low toxicity in humans, but inadequate data are available.	NOAEL = 0.9 mg/kg (from rat data)	45/45 mcg	75 mcg

[a]UL = The maximum level of daily nutrient intake that is likely to pose no risk of adverse effects.
[b]NOAEL = No-observed-adverse-effect level; LOAEL = Lowest-observed-adverse-effect level.
[c]RDA = Recommended Dietary Allowance; AI = Adequate Intake.
[d]The Daily Value is used in nutritional labeling of food products and dietary supplements. The values given are for individuals age 4 years and above.
[e]5 mcg vitamin D for 31-50 year olds, 10 mcg for 51-70 year olds, and 15 mcg for those above 70 years.
[f]As α-tocopherol; applies to any form of supplemental α-tocopherol.
[g]The ULs for vitamin E, niacin, and folate apply to synthetic forms from supplements, fortified foods, or a combination of supplements and fortified foods.
[h]The conversion of IUs to mg α-tocopherol depends on the form.
[i]ND = Not determinable due to lack of data of adverse effects.
[j]NE = Not established.
[k]1.3 mg vitamin B_6 for 19-50 year olds, 1.5 mg for women age 51 and above, and 1.7 mg for men age 51 and above.
[l]All women capable of becoming pregnant should consume 400 mcg from supplements or fortified foods in addition to intake of food folate from a varied diet.
[m]Adults over 50 years are advised to meet their RDA mainly by consuming foods fortified with vitamin B_{12} or a supplement containing vitamin B_{12}.
[n]1,000 mg calcium for 19-50 year olds and 1,200 mg for those 51 years and older.
[o]4 g phosphorus for adults 19-70 years old and 3 g for those above 70 years.
[p]310 mg magnesium for women 19-30 years, 320 mg for women 31 years and above, 400 mg for men 19-30 years, and 420 mg for men 31 years and above.
[q]8 mg for men and for women 51 years and older and 18 mg for women 19-50 years.
[r]20 mcg for women 31 years old and above, 25 mcg for women 19-30 years old, 30 mcg for men 31 years old and above, and 35 mcg for men 19-30 years old.

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