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Nutrient Reference Values for Australia and New Zealand  
Including Recommended Dietary Intakes

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## SELENIUM

### BACKGROUND

Selenium functions as an antioxidant and in redox reactions and thyroid metabolism. It exerts its effects as a constituent of several selenoproteins of which there are at least 30 in mammalian systems. The most important are the glutathione peroxidases (GP<sub>x</sub>s), selenoprotein P, iodothyronine 5'-deiodinases and thioredoxin reductases (TrxRs).

Different forms of GP<sub>x</sub> are found in the cytosol and membranes of cells in the gut, liver and colon and also in plasma. The cellular form (cGP<sub>x</sub>) is thought to regulate intracellular concentrations of hydroperoxides formed during metabolism and to have a role in cellular antioxidant systems. It may also perform a storage role for selenium (Holben & Smith 1999).

The function of plasma GP<sub>x</sub> is unknown. It may play an antioxidant role in kidney and be a secretory protein with antioxidant function in the extracellular space (Holben et al 1999). Gastrointestinal GP<sub>x</sub> is found in rat gastrointestinal cells and human liver and colon. It may play a role in protecting against the adverse effects of hydroperoxides formed in the gut and liver. Phospholipid hydroperoxide GP<sub>x</sub> reduces hydroperoxides formed in the metabolism of fatty acids, thereby reducing cell membrane peroxidation (Ursini et al 1985, Ursini & Bindoli 1987). It may also play a role in eicosanoid metabolism and regulation (Arthur & Beckett 1994).

Selenoprotein P is a selenocysteine-containing glycoprotein that may play an antioxidant role (Burk et al 1995) and a protective role against the endotoxin peroxynitrite (Mostert 2000). Iodothyronine 5'-deiodinases catalyse the conversion of thyroxine (T<sub>4</sub>) to its active metabolite, triiodothyronine (T<sub>3</sub>). Selenium deficiency increases plasma T<sub>4</sub> and decreases T<sub>3</sub>. Low dietary intakes also result in the production of these deiodinases in preference to GP<sub>x</sub> (Allan et al 1999). The TrxRs have a catalytic role in the NADPH-dependent reduction of thioredoxin (Mustacich & Powis 2000). They have a role as antioxidants and are important in a number of cellular functions including cell growth and transformation and recycling of ascorbic acid (vitamin C) from dehydroascorbic acid (Mustacich & Powis 2000). Several other selenium-containing enzymes have been identified in the muscle, sperm and prostate of animals, suggesting possible roles in muscle maintenance, fertility and protection against prostate cancer (Behne et al 1997, Calvin et al 1987, Vendeland et al 1993).

The potential role of selenium in cancer prevention has been assessed in humans. One prospective study of 34,000 men using a nested case-control study design showed that high selenium intakes were protective against prostate cancer (Yoshizawa et al 1998). However, few intervention studies have been done to date. One such study in China showed reduction in mortality from oesophageal cancer with a supplemental mixture of selenium, vitamin E and beta-carotene (Blot et al 1993).

A 10-year study of skin cancer in the US initially found no effect of supplemental selenium at 200 µg/day on basal cell or squamous cell skin cancer, but significant reduction in total cancer and cancers of the prostate, lung and colorectum (Clark et al 1996). However analyses of longer-term data showed that whilst selenium supplementation reduced total cancer incidence, it was not significantly associated with lung and colorectal cancer incidence (Duffield-Lillico et al 2002) and there was also an increase in squamous cell carcinoma and total non-melanoma skin cancer in supplemented subjects with relatively high baseline selenium (Duffield-Lillico et al 2003).

Selenium is found in a range of foods, the content of which varies with geographic sources of the food. Soil concentrations can range from <0.01 µg/g to >1,000 µg/g with plant food content reflecting this range. Variability of selenium levels is not so marked in animal foods. In Australia and New Zealand, the main dietary sources are seafood, poultry and eggs and, to a lesser extent, other muscle meats. The contribution of cereal products depends on the source. Much plant selenium is in the form of selenomethionine, selenocysteine or selenocysteine metabolites. Meats and seafood also contain selenoproteins with selenium in the form of selenocysteine. Low soil selenium levels in New Zealand mean that dietary intakes and selenium status are lower than in many other countries (Thomson 2004a).

Absorption of selenium – mostly selenomethionine and selenocysteine – from food is about 55–70% (Whanger 1998). Selenomethionine is absorbed mainly in the duodenum in the same way as methionine and is unaffected by selenium status. It is transported round the body in plasma albumin and red cell haemoglobin. Selenomethionine from food enters the methionine pool in the body and shares the fate of methionine until catabolised. The resulting free selenocysteine is further broken down to liberate a reduced form called selenide. Less is known about the absorption of other forms of selenium, although it is thought that both selenocysteine and selenate are well absorbed. Ingested selenate, selenocysteine and selenite are all metabolised directly to selenide. The selenide can be metabolised to selenophosphate, the precursor of selenocysteine in selenoproteins, or converted to excretory metabolites.

Excess selenium intake from selenate, selenite or selenocysteine is excreted in urine. The kidneys account for 50–60% of total excretion of selenium. There is also some faecal excretion of unabsorbed selenium and losses through skin, hair and, at high intakes, expired air.

Frank selenium deficiency results in a condition called Keshan Disease, an endemic cardiomyopathy occurring in low selenium areas of China that is responsive to sodium selenite supplementation (Keshan Disease Research Group 1979a,b). Keshan Disease results in cardiac enlargement, heart failure, arrhythmias and premature death. It is associated with low selenium intake, low blood and hair levels and affects mostly children and women of childbearing age. Keshan Disease may occur at intakes of selenium of 20 µg/day or less, however, some features of the disease cannot be explained solely on the basis of low selenium status, so Keshan Disease is thought to depend on the presence of additional factors such as a virus, mineral imbalance or environmental toxins (Ge et al 1983, Yang & Xia 1995).

Other conditions such as Kashin-Beck disease, a cartilage condition, also occur in selenium-deficient areas (Yang et al 1988) although it has not been shown to respond to selenium supplementation. Selenium deficiency in conjunction with iodine-deficiency has also been reported to increase the risk of cretinism (Vanderpas et al 1992).

Indicators that have been used for assessing requirements include the existence of Keshan Disease, selenium in hair, nails and blood or GP<sub>x</sub> and selenoproteins in blood. Whilst some countries base their minimum requirements on levels at which no Keshan Disease is evident in susceptible populations, most use measures of GP<sub>x</sub> and other blood measures in response to varying intakes of selenium (Thomson 2004b).

1 mmol selenium = 79 mg selenium
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## RECOMMENDATIONS BY LIFE STAGE AND GENDER

<i>Infants</i>	<b>AI</b>	<b>Selenium</b>
<b>0–6 months</b>	<b>12 µg/day</b>	
<b>7–12 months</b>	<b>15 µg/day</b>	

**Rationale:** The AI for 0–6 months was calculated by multiplying together the average intake of breast milk (0.78 L/day) and the average concentration of selenium in breast milk of 15 µg/L based on the New Zealand and Australian studies of Cumming et al (1992), Daniels et al (2000) and Dolamore et al (1992), and rounding. The AI for 7–12 months was extrapolated from that of the younger infants on a metabolic weight basis.

<i>Children &amp; adolescents</i>	<b>EAR</b>	<b>RDI</b>	<b>Selenium</b>
<b>All</b>			
1–3 yr	20 µg/day	25 µg/day	
4–8 yr	25 µg/day	30 µg/day	
<b>Boys</b>			
9–13 yr	40 µg/day	50 µg/day	
14–18 yr	60 µg/day	70 µg/day	
<b>Girls</b>			
9–13 yr	40 µg/day	50 µg/day	
14–18 yr	50 µg/day	60 µg/day	

**Rationale:** The EAR for children was extrapolated from the adult data on a metabolic body weight basis, and rounded to the nearest 5 µg. The RDI was derived assuming a CV of 10% for the EAR. EARs and RDIs were estimated using the absolute data but rounded up to the nearest 5 µg for the final recommendations.

<i>Adults</i>	<b>EAR</b>	<b>RDI</b>	<b>Selenium</b>
<b>Men</b>			
19–30 yr	60 µg/day	70 µg/day	
31–50 yr	60 µg/day	70 µg/day	
51–70 yr	60 µg/day	70 µg/day	
>70 yr	60 µg/day	70 µg/day	
<b>Women</b>			
19–30 yr	50 µg/day	60 µg/day	
31–50 yr	50 µg/day	60 µg/day	
51–70 yr	50 µg/day	60 µg/day	
>70 yr	50 µg/day	60 µg/day	

**Rationale:** The EARs for adults were based on the experimental data of Duffield et al (1999) and Xia et al (2005) assessing GP<sub>x</sub> activity at various supplemental selenium intakes. The findings were corrected to the reference adult body weights. The RDI was set assuming a CV for the EAR of 10%. Both the EAR and RDI were rounded up to the nearest 5 µg for the final figure but the unrounded EAR was used to estimate the RDI before rounding.

<i>Pregnancy</i>	<b>EAR</b>	<b>RDI</b>	<b>Selenium</b>
14–18 yr	55 µg/day	65 µg/day	
19–30 yr	55 µg/day	65 µg/day	
31–50 yr	55 µg/day	65 µg/day	

**Rationale:** Estimates from studies in New Zealand, Germany and Poland show additional requirements for fetal needs from 1–2 µg/day (Casey et al 1982, FAO:WHO 2001, Oster 1988, Zachara 2001). One US study indicated higher requirements in the order of 3–4 µg/day (Schroeder et al 1970) based on measures of skeletal muscle selenium, but this may reflect non-selective deposition of excess selenium in muscle tissues in a population with high selenium intake rather than skeletal muscle needs. Several countries assume that any additional requirement in pregnancy can be met by an adaptive increase in absorption (Netherlands Food and Nutrition Council 1989, Scientific Committee for Food EU 1993,

Department of Health 1991). An additional 2 µg/day was added to the EAR of adult women and rounded up to the nearest 5 µg. The RDI was set on the unrounded EAR assuming a CV of 10% and rounded up.

<b>Lactation</b>	<b>EAR</b>	<b>RDI</b>	<b>Selenium</b>
14–18 yr	65 µg/day	75 µg/day	
19–30 yr	65 µg/day	75 µg/day	
31–50 yr	65 µg/day	75 µg/day	

**Rationale:** The EAR for lactation includes an allowance of 12 µg/day for selenium secreted in breast milk which is added to the mother's requirement. The RDI was set assuming a CV of 10% for the EAR. The EARs and RDIs were estimated using the absolute data but rounded up to the nearest 5 µg for the final recommendations.

## UPPER LEVEL OF INTAKE - SELENIUM

### Infants

0–6 months	45 µg/day
7–12 months	60 µg/day

### Children and adolescents

1–3 yr	90 µg/day
4–8 yr	150 µg/day
9–13 yr	280 µg/day
14–18 yr	400 µg/day

### Adults 19+ yr

Men	400 µg/day
Women	400 µg/day

### Pregnancy

14–18 yr	400 µg/day
19–50 yr	400 µg/day

### Lactation

14–18 yr	400 µg/day
19–50 yr	400 µg/day

**Rationale:** The UL relates to intakes from food and supplements. There are limited data about toxicity in humans but the most common outcomes are brittleness and loss of hair and nails (Yang et al 1983) as well as gastrointestinal disturbance, skin rash, fatigue, irritability and nervous system abnormalities (CDC 1984, Helzlsouer et al 1985, Yang et al 1983, 1989a). Studies from China (Yang et al 1983, 1989b, Yang & Zhou 1994) give a NOAEL for adults of 800 µg/day which was consistent with one US study (Longnecker et al 1991).

The Nutritional Prevention of Cancer Trial (Duffield-Lillico et al 2003) showed an increase in the risk of squamous cell carcinoma and total non-melanoma skin cancer with supplements of 200 µg/day among individuals at high risk of non-melanoma skin cancer. It is not known how this would relate to risk for the general public.

An UF of 2 is applied (FNB:IOM 2000) to protect sensitive individuals because of gaps in data and incomplete knowledge, bearing in mind that the toxic effect of selenium is not severe but may be irreversible. The UL is therefore set at 400 µg/day for all adults, as there are no data to suggest increased susceptibility during pregnancy and lactation.

The UL for young infants was based on the studies of Shearer & Hadjimarkos (1975) showing that a human milk concentration of 60 µg/L was not associated with adverse effects. This gives a NOAEL of 47 µg/day (7 µg/kg body weight). A UF of 1 was applied, as there is no evidence that maternal intakes associated with human milk in this range cause toxicity for mothers or infants.

As there is no evidence of increased toxicity in older children and adolescents, the ULs for these groups were estimated on a body weight basis from the younger infant data using the level of 7 µg/kg body weight.

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