Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

VKM Report 2017: 20

Assessment of selenium intake in relation to tolerable upper intake levels

Opinion of the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food Safety

Report from the Norwegian Scientific Committee for Food Safety (VKM) 2017: 20
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Assessment of selenium intake in relation to tolerable upper intake levels

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Assessed and approved

The opinion has been assessed by the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM). Kristin Holvik (chair), Livar Frøyland, Margaretha Haugen, Sigrun Henjum, Martinus Løvik, Tonje Holte Stea and Tor A. Strand.

(Panel members in alphabetical order after chair of the panel)

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Competence of VKM experts

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Summary

The Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) has, at the request of the Norwegian Food Safety Authority (Mattilsynet; NFSA), evaluated the intake of selenium in the Norwegian population. VKM has also conducted scenario calculations to illustrate the consequences of amending maximum limits for selenium to 50, 150 or 200 µg/day in food supplements. The existing maximum limit is 100 µg/day.

Selenium is a cofactor for enzymes and proteins with vital importance in antioxidant defence, thyroid hormone and insulin function and regulation of cell growth.

We reviewed four risk assessments undertaken by the Institute of Medicine (IOM), Scientific Committee on Food (SCF), Expert Committee on Vitamins and Minerals (EVM), and the Nordic Nutrition Recommendations (NNR). Because of limited evidence from human studies and due to the selection of a high uncertainty factor (UF), we decided to use the tolerable upper intake levels (ULs) set by the SCF (2000) and later adopted by NNR (2012).

Early signs of selenium toxicity are a garlic breath and a metallic taste. Severe selenosis results in fast hair loss and brittle nails, as well as other gastrointestinal symptoms such as nausea, vomiting, diarrhea, fatigue, irritability, and rash. Acute selenium intoxication and chronical overexposure may affect the nervous system and result in nerve damage.

The SCF established a UL for selenium at 300 µg/day for adults, including pregnant and lactating women. This UL was based on a no observed adverse effect level (NOAEL) of 850 µg/day for clinical selenosis applying a UF of 3, and was supported by three studies reporting no adverse effects for selenium intake between about 200 and 500 µg/day.

As there were no data to derive specific ULs for children, the SCF (2000) extrapolated the UL from adults to children based on reference body weights. The proposed UL values for children and adolescents ranged from 60 µg/day (1–3 years) to 250 µg selenium/day (15–17 years).

According to the scenario estimations in adults, the dietary selenium intake at the 95th percentile and additionally 150 µg selenium from food supplements will be below the UL while 200 µg selenium from food supplements will lead to exceedance of the UL for adults. For 13- and 9-year-olds, supplemental doses of 100 and 50 µg selenium per day, respectively, do not lead to exceedance of the ULs in these age groups. For 2- and 4-year-olds, all the suggested doses in food supplements will lead to exceedance of the ULs.

Key words: VKM, risk assessment, Norwegian Scientific Committee for Food Safety, selenium, food supplement, upper level, exposure.

Sammendrag på norsk

På oppdrag fra Mattilsynet har Vitenskapskomiteen for mattrygghet vurdert inntaket av selen i den norske befolkningen. VKM har også gjort scenarioberegninger for å illustrere konsekvenser av å endre maksimumsgrensen for selen til 50, 150 eller 200 µg/dag i kosttilskudd. Den eksisterende maksimumsgrensen er 100 µg/dag.

Selen inngår som kofaktor for enzymer og proteiner som er viktige for kroppens antioksidantfunksjon, tyroidhormoner og insulin samt regulering av cellevekst

Vi tok utgangspunkt i fire risikovurderinger som har blitt utført av Institute of Medicine (IOM), Scientific Committee on Food (SCF), Expert Committee on Vitamins and Minerals (EVM) og Nordic Nutrition Recommendations (NNR). På grunn av få humanstudier besluttet vi å bruke det øvre tolerable inntaksnivået (UL) fastsatt av SCF (2000) fordi denne har lagt til grunn den største usikkerhetsfaktoren (UF). Dette inntaksnivået ble også brukt i NNR (2012).

Tidlige tegn på selenforgiftning (selenose) er hvitløksånde og metallsmak. Alvorlig selenforgiftning gir hårtap og skjøre negler,mage- og tarmsymptomer som kvalme, oppkast, diare og også tretthet, irritabilitet samt utslett. Akutt selenforgiftning og kronisk forhøyet inntak av selen kan påvirke nervesystemet og føre til nerveskade.

SCF fastsatte en UL verdi på 300 µg/dag for voksne, inkludert gravide og ammende kvinner. Verdien ble satt på grunnlag av en «no observed adverse effect level» (NOAEL) på 850 µg/dag for klinisk selenose ved bruk av en usikkerhetsfaktor på 3. Konklusjonen ble støttet av tre studier som ikke fant bivirkninger ved seleninntak mellom 200 og 500 µg/dag.

Siden det ikke forelå data for å kunne utlede UL for barn, ekstrapolerte SCF (2000) UL fra voksne til barn på grunnlag av kroppsvekt. De foreslåtte UL-verdiene varierer fra 60 µg/dag (1-3 år) til 250 µg selen/dag (15-17 år).

I henhold til scenarioberegninger, vil 200 µg selen fra kosttilskudd i tillegg til 95-percentilen fra kosten, føre til overskridelse av UL for voksne, mens en dose på 150 µg selen fra kosttilskudd vil gi et seleninntak under UL. For 13-åringer og 9-åringer vil doser i kosttilskudd på henholdsvis 100 og 50 µg/dag ikke føre til overskridelse av UL. For 2- og 4-åringer vil alle de foreslåtte dosene i kosttilskudd føre til overskridelse av UL.

Abbreviations and/or glossary

Abbreviations

AI – adequate intake
bw – body weight
DRV – dietary reference value
EFSA – European Food Safety Authority
EVM – Expert group on vitamins and minerals of the Food Standard Agency, UK
IOM – Institute of Medicine, USA
LOAEL – lowest observed adverse effect level
NFSA – Norwegian Food Safety Authority [*Norw.*: Mattilsynet]
NNR – Nordic Nutrition Recommendations
NOAEL – no observed adverse effect level
RI – recommended intake
SCF – Scientific Committee for Food
SUL – safe upper intake level
UF – uncertainty factor
UL – tolerable upper intake level
VKM – Norwegian Scientific Committee for Food Safety [*Norw.*: Vitenskapskomiteen for Mattrygghet]

Glossary

P5, P25, P50, P75 or P95-exposure is the calculated exposure at the 5, 25, 50, 75 or 95-percentile.

Percentile is a term for visualising the low, medium and high occurrences of a measurement by splitting the whole distribution into one hundred equal parts. A percentile is a statistical measure indicating the value below which a given percentage of the observations fall. E.g. the 95-percentile is the value (or score) below which 95 percent of the observations are found.

EFSA - Dietary Reference Values (DRVs) (EFSA, 2010)

Average Requirement (AR) is the level of intake of a defined group of individuals estimated to satisfy the physiological requirement of metabolic demand, as defined by a the specific criterion for adequacy for the nutrient, in half of the heathy individuals in a life stage or sex group, on the assumption that the supply of other nutrients and energy is adequate.

If an AR cannot be determined than an Adequate Intake is used.

Adequate Intake (AI) is defined as the average (median) daily level of intake based on observed, or experimentally determined approximations or estimates of a nutrient intake, by

a group (or groups) of apparently healthy people, and therefore assumed to be adequate. The practical implication of an AI is similar to that of a population reference intake, i.e. to describe the level of intake that is considered adequate for health reasons. The terminological distinction relates to the different ways in which these values are derived and to the resultant difference in the "firmness" of the value.

Population Reference Intake (PRI) is derived from AR of a defined group of individuals in an attempt to take into account the variation of requirements between individuals.

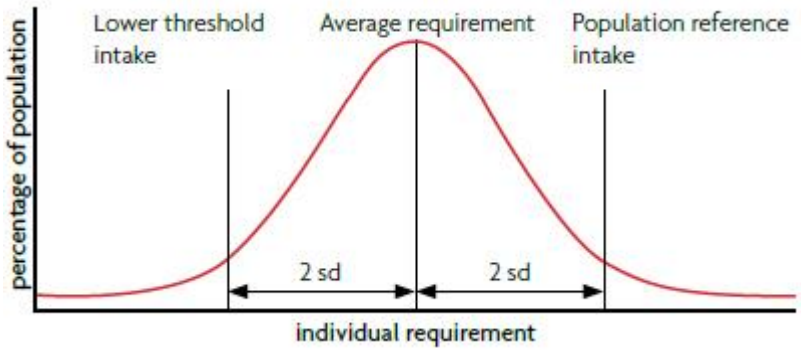

Figure 1: Population reference intake (PRI and average requirements (AR), if the requirement has a normal distribution and the inter-individual variation is known(EFSA, 2010).

Lower Threshold Intake (LTI) is the lowest estimate of requirement from the normal distribution curve, and is generally calculated on the basis of the AR minus twice its SD. This will meet the requirement of only 2.5% of the individuals in the population.

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.

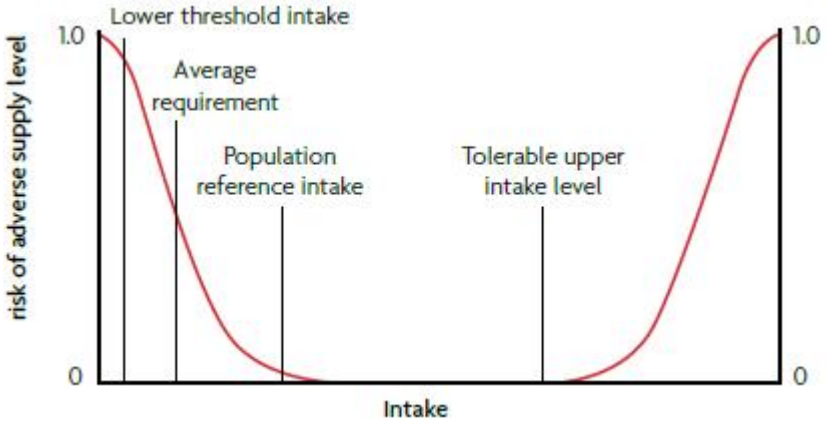

Figure 2: Relationship between individual intake and risk of adverse effects due to insufficient or excessive intake.

IOM - Dietary Reference Intakes (DRIs) (IOM, 2000b)

Estimated Average Requirement (EAR) is a nutrient intake value that is estimated to meet the requirement of half the healthy individuals in a life stage and gender group.

Recommended Dietary Allowances (RDA) is the dietary intake level that is sufficient to meet the nutrient requirement of nearly all (97 to 98 percent) healthy individuals in a particular life stage and gender group. RDA = EAR + 2 SD_{EAR} or if insufficient data to calculate SD a factor of 1.2 is used to calculate RDA; RDA = 1.2*EAR

Adequate Intake (AI) is the recommended intake value based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of healthy people that are assumed to be adequate – used when an RDA cannot be determined

Tolerable Upper Intake Level (UL) is the highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population.

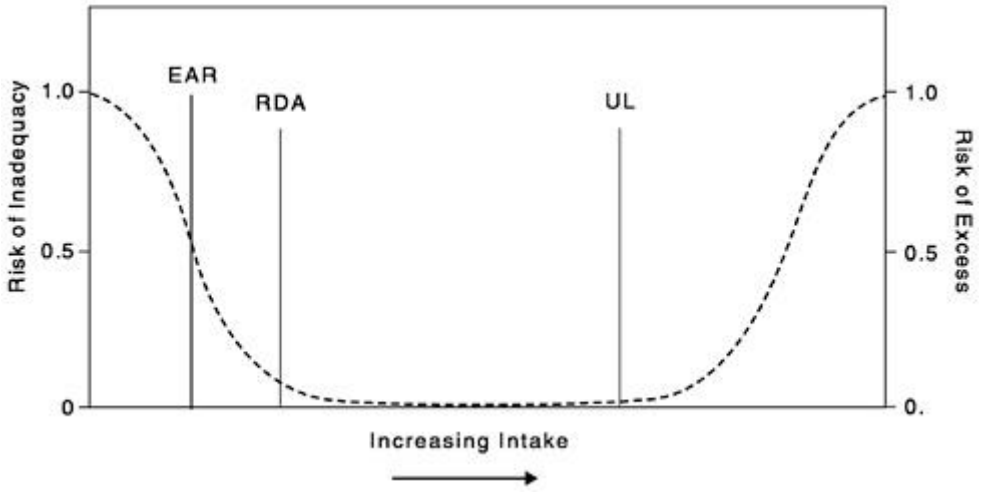

Figure 3: Dietary reference intakes.

NNR -Recommended Intake (NNR Project Group, 2012)

Average Requirement (AR) is defined as the lowest long-term intake level of a nutrient that will maintain a defined level of nutritional status in an individual i.e. the level of a nutrient that is sufficient to cover the requirement for half of a defined group of individuals provided that there is a normal distribution of the requirement.

$AR_{NNR} = EAR_{IOM} = AR_{EFSA}$

Recommended Intake (RI) is defined as the amount of a nutrient that meets the known requirement and maintains good nutritional status among practically all healthy individuals in a particular life stage or gender group. RI= AR + $2SD_{AR.}$

RI_{NNR} = RDA_{IOM} = PRI_{EFSA}

Upper Intake Level (UL) is defined as the maximum level of long-term (months or years) daily nutrient intake that is unlikely to pose a risk of adverse health effects in humans.

UL_{NNR} =UL_{IOM} = UL_{EFSA}

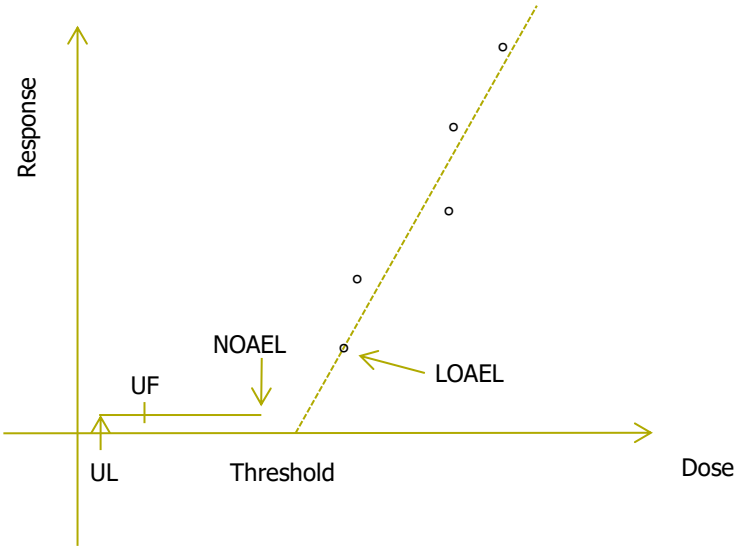

Figure 4: Derivation of Upper Intake Level (UL)

UF: Uncertainty factor

Expert group on vitamins and minerals (EVM), UK (EVM, 2003)

Safe Upper Intake Level (SUL): EVM used SUL instead of UL and defined SUL as the determination of doses of vitamins and minerals that potentially susceptible individuals could take daily on a life-long basis, without medical supervision in reasonable safety. The setting of these levels provided a framework within which the consumer could make an informed decision about intake, having confidence that harm should not ensue. The levels so set will therefore tend to be conservative.

Background as provided by the Norwegian Food Safety Authority

Directive 2002/46/EC on food supplements was implemented in Norwegian law in 2004 in Regulation 20 May 2004 No. 755 on food supplements. Pursuant to Directive 2002/46/EC, common maximum and minimum levels of vitamins and minerals in food supplements shall be set in the EU.

National maximum limits for vitamins and minerals were established in the former vitamin and mineral supplements regulation from 1986 and were continued in the 2004 regulation.

The European Commission started establishing common limits in 2006, but the work was temporarily put on standstill in 2009. The time frame for the further work is not known.

Maximum limits for levels of vitamins and minerals in food supplements shall be set on the basis of the following criteria, pursuant to article 5 in Directive 2002/46/EC:

- Upper safe levels of vitamins and minerals established by scientific risk assessment based on generally accepted scientific data, taking into account, as appropriate, the varying degrees of sensitivity of different consumer groups
- Intake of vitamins and minerals from other dietary sources

When the maximum levels are set, due account should also be taken of reference intakes of vitamins and minerals for the population.

Pending establishment of common maximums limits in the EU, the Norwegian Food Safety Authority is evaluating the national maximum limits for vitamins and minerals in food supplements.

Assessment of selenium

The Norwegian Food Safety Authority will evaluate the national maximum limits for selenium in the food supplement regulation. The minimum and maximum limits for the content of vitamins and minerals in food supplements are listed in Annex 1 to the food supplement regulation:

Background Table: Minimum and maximum limits for selenium in the food supplement regulation (October 2015).

	Minimum amount per recommended daily dose	Maximum amount per recommended daily dose
Selenium, µg	10	100

Permitted selenium substances which may be used in the manufacture of food supplements are listed in "Forskrift om kosttilskudd 2012", http://www.lovdata.no/cgi-wift/ldles?doc=/sf/sf/sf-20040520-0755.html.

Terms of reference as provided by the Norwegian Food Safety Authority

The Norwegian Food Safety Authority (NFSA, Mattilsynet) requests the Norwegian Scientific Committee for Food Safety (VKM) to assess the intake of selenium from the diet, including fortified products, in all age groups in the population above 1 year (mean intakes, median, P5, P95).

VKM is also requested to conduct scenario estimations to illustrate the consequences of amending maximum limits for selenium (to 50, 150 or 200 µg/day, as examples) in food supplements, and to evaluate these scenarios against already established tolerable upper intake levels.

Assessment selenium

1 Introduction

Selenium is an essential micronutrient and is particularly important for the production and action of thyroid hormones. It is needed for the production of selenoproteins, which are antioxidants protecting the cells from free radical damage. Selenium is also necessary for normal function of the immune system.

The concentration of selenium in foods is greatly dependent on the Se content of the soil in which plants are grown and the seleniume content in animal feed. Seafood and liver are the most selenium-rich foods (400-1500 µg/kg), meat (100-400 µg/kg) and grains contain less, and fruits and vegetables very little (Kohlmeier, 2015).

Selenium deficiency is uncommon and usually a result of a severe gastrointestinal disease. Poor selenium status can lead to heart disease, hypothyroidism, and a weakened immune system.

Early signs of selenium toxicity are a garlic breath and a metallic taste. Severe selenosis results in hair loss and brittle nails, as well as other gastrointestinal symptoms such as nausea, vomiting, diarrhea, fatigue, irritability, and rash. Acute selenium intoxication and chronical overexposure may affect the nervous system and result in nerve damage. Immediate adverse effects include lethargy, dizziness, motor weakness, and paraesthesia. An increased risk of amyotrophic lateral sclerosis has also been described in people with high selenium exposure.

Acute and chronic selenium toxicity have been shown in a wide variety of animals and humans. Soluble selenium salts (in cases of supplementation) may be acutely more toxic than organic bound selenium from food. Organic forms may be more toxic than inorganic during long-term consumption due to incorporation into proteins rather than excretion. Despite old (from the 1930s) reports of increased susceptibility of cancer in populations with high selenium exposure, experimental data do not indicate that inorganic selenium salts or organic selenium compounds relevant in food and nutrition are carcinogenic.

1.1 Requirements and recommended intakes

The recommended intakes of selenium are given in Tables 1.1-1 and 1.1-2.

Table 1.1-1 Recommended intakes of selenium in Norway, both sexes (Helsedirektoratet, 2014).

Age	µg/day	
	Men	Women
6-11 mo.	15	15
1-2 years	20	20
2-5 years	25	25
6-9 years	30	30
10-13 years	40	40
14->75 years	60	50
Pregnant	-	60
Lactating	-	60

The Norwegian recommendations are based on the NNR (2012) recommendations.

Table 1.1-2 EFSA's Adequate Intakes (AIs) for selenium intakes, both sexes (EFSA, 2014).

Age, both sexes	Adequate intake µg/day
7-11 mo.	15
1-3 years	15
4-6 years	20
7-10 years	35
11-14 years	55
15-17 years	70
≥ 18 years	70
Pregnant	70
Lactating	85

2 Tolerable upper intake levels

Institute of Medicine (IOM, 2000a), USA

The (IOM, 2000a) set the lowest-observed-adverse-effect-level (LOAEL) of selenium intake at 900 µg/day, and the no-observed-adverse-effect level (NOAEL) at 800 µg/day. They characterised the adverse health effects observed at the LOAEL as not severe, but likely not readily reversible, which they used to justify an uncertainty factor (UF) of 2. Dividing the NOAEL (800 µg/day) by this UF, the IOM concluded that 400 µg/day is the tolerable upper intake level (UL) of selenium from food and supplements.

Hair and nail brittleness and loss were selected as the critical endpoints on which to base the UL as these effects have been reported more frequently than other signs and symptoms of chronic selenosis. Data from Chinese investigators (Yang and Zhou, 1994 cited in IOM, 2000a) from a re-examination (in 1992) of five patients previously found to have overt signs of selenosis (hair loss and nail sloughing) was used. The same five patients were studied over time while consuming different levels of selenium. Blood levels of selenium were compared, and dietary intakes were inferred from blood selenium concentrations. By examining the relation between intake, plasma concentrations and symptoms, they arrived on the above mentioned LOAEL and NOAEL.

The findings from the Chinese data was supported by a study by Longnecker et al (1991) cited in IOM (2000a) in 142 ranchers in Wyoming and South Dakota who, based on the occurrence of selenosis in livestock raised in that region, were suspected to have high selenium intakes. Average selenium intake was 239 µg/day. It was noted that selenium intake exceeded 400 µg/day in 12 subjects, with the highest intake being 724 µg/day. Since 724 µg/day was 3.4 standard deviations above the mean intake, intakes this high was expected to be very rare. Dietary intake and selenium in body tissues (whole blood, serum, urine, toenails) were highly correlated. Blood selenium concentrations in this western U.S. population were related to selenium intake in a similar manner to that found in other studies. No evidence of selenosis was reported, nor were there any alterations in enzyme activities, prothrombin times, or haematology that could be attributed to selenium intake. The UL based on the Chinese studies was therefore considered to be relevant for the population in the United States and Canada.

Table 2.2-1 Tolerable upper intake levels for selenium in different age groups adjusted by body weight suggested by the Institute of Medicine (IOM, 2000a).

Age (years)	UL µg/day
1-3	90
4-8	150
9-13	280
14-18	400
19 and older	400

Scientific Committee for Food (SCF, 2000), EU

The UL established by the Scientific Committee for Food (SCF, 2000) is mainly based on the same studies as the UL established by IOM.

In this report, it was discussed that high selenium intake previously was considered potentially carcinogenic (Smith and Westfall, 1937 cited in SCF, 2000), however the more recent Chinese studies of endemic selenium toxicity in humans (Yang et al., 1983; Yang et al., 1989a; Yang et al., 1989b; Yang and Zhou, 1994 cited in SCF, 2000) and the 1991 American study (Longnecker et al., 1991 cited in SCF, 2000), could not demonstrate an increased risk of cancer from chronic selenium toxicity. Based on the Chinese studies (Yang et al., 1989a; Yang et al., 1989b; Yang and Zhou, 1994 cited in SCF, 2000), the dietary intake sufficient to cause symptoms of selenosis (i.e., hair or nail loss, nail abnormalities, mottled teeth, skin lesions and changes in peripheral nerves) was set to about 1200 µg/day (range: 913-1907 µg Se). The LOAEL for clinical symptoms of selenosis was about 900-1000 µg/day. No clinical signs of selenosis had been recorded in individuals with blood selenium below 1000 µg/l, corresponding to an intake of about 850 µg/day, which was selected as a NOAEL for clinical selenosis. The SCF used data from the five Chinese individuals (described above) who recovered from selenosis as justification for a NOAEL of approximately 850 µg/day. However, SCF used a UF of 3 "to allow for the remaining uncertainties of the studies used in deriving an upper level". A UL of 300 µg selenium per day was therefore derived for adults. The UL covers selenium intake from all sources of food and supplements. This UL was supported by a supplementation study (Clark et al 1996) where they did not observe any signs of selenosis in the supplemented group (selenium enriched yeast), having an estimated mean total intake of about 300 µg selenium/day. The study in US rangers (Longnecker et al., 1991) and a study of lactating women from Venezuela (Brätter and Negreti de Brätter, 1996 cited in SCF, 2000) further supported this UL. Data is limited and there was no data available to suggest that other life-stage groups have increased susceptibility to adverse effects of high selenium intake. Therefore, the UL of 300 µg /day was considered to apply also to pregnant and lactating women. There are no reports of adverse effects on infants born from mothers with high intakes of selenium or adverse effects on lactating women with dietary selenium intakes below the UL for adults. Therefore, the UL for pregnant and lactating women is the same as for non-pregnant and non-lactating women. There are no data to support a derivation of ULs for children, and the ULs for children were extrapolated from the UL for adults on the basis of reference body weights. The proposed UL values ranged from 60 µg/day (1-3 years) to 250 µg selenium/day (15-17 years).

Table 2.2-2 Tolerable upper intake levels for selenium in different age groups adjusted for body weights suggested by the Scientific Committee for Food (SCF, 2000).

Age (years)	UL µg/day
1-3	60
4-6	90
7-10	130
11-14	200
15-17	250
Adults	300

Expert Group on Vitamins and Minerals (EVM 2003), UK

The Expert Group on Vitamins and Minerals (EVM) used the same data as the SCF and IOM reports described above and arrived at the same NOAEL and LOAEL. In their risk assessment, they concluded that "Selenium has a variety of toxic endpoints in both animals and humans. In man, the first signs of chronic toxicity appear to be pathological changes to the hair and nails, followed by adverse effects on the nervous system. Changes in biochemical parameters have also been reported. The available studies indicate the development of selenosis is associated with selenium intakes in excess of 0.85 mg/day (0.014 mg/kg bw for a 60 kg adult). Supplementation studies in humans indicate that up to 0.3 mg/day additional selenium is not associated with overt adverse effects over a short period of time, although specific symptoms have not always been investigated. However, the study by Clark et al., (1996) cited in EVM, 2003, which specifically considered symptoms of selenosis, indicated that 0.2 mg/day additional selenium for up to 10 years did not result in symptoms of selenosis."

EVM established a UL at 450 µg/day for adults using UF=2 because they extrapolated a LOAEL at 900 µg/day to a NOAEL and stated that because the LOAEL was based on a population study, a UF for inter-individual variation was not required.

Nordic Nutrition Recommendations (NNR Project Group, 2012)

In this report, it was concluded that: "Selenium toxicity is rare in humans but well known in animals. Acute toxicity has been observed after consumption of a large (250 mg) single dose or after multiple doses of ~30 mg. The symptoms include nausea, vomiting, and garlic-like breath odour. Other symptoms of toxicity are nail and hair deformities and, in severe cases, peripheral nerve damage and liver damage. Because of the risk of toxicity, high doses of selenium are not recommended. A NOAEL for clinical signs of selenium toxicity and a threshold of 850 µg/d for inhibited prothrombin synthesis were found in Chinese studies. The EU SCF derived an upper level of 300 µg/d using a factor of three to allow for uncertainties in different studies."

2.1.1 Summary tolerable upper intake levels

The established ULs for selenium range from 300-450 µg/day. They are mostly based on the same studies, but various UFs have been applied. An overview is given in Table 2.1.1-1.

Table 2.2.1-1 Overview of ULs for selenium in adults set by various authorities.

	UL/SUL µg/day	Based on	NOAEL	LOAEL	UF
IOM, 2000	400	Clinical studies	800 µg/day		2
SCF, 2000	300	Clinical studies	850 µg/day		3
EVM, 2003	450	Clinical studies		910 µg/dag	2
NNR, 2012	300	SCF			3

The SCF (2000) adopted the value of 300 µg/day as a UL for adults including pregnant and lactating women. This UL was based on a NOAEL of 850 µg/day for clinical selenosis and applying an uncertainty factor of 3 and was supported by three studies reporting no adverse effects for selenium intake between about 200 and 500 µg/day. As there were no data to support a derivation of ULs for children, the SCF (2000) extrapolated the UL from adults to children on the basis of reference body weights. The proposed UL values range from 60 µg/day (1–3 years) to 250 µg selenium/day (15–17 years).

Because there are limited evidence from human studies, we decided to use the ULs set by the SCF (2000) and later adopted by NNR (2012) as it has the largest UF of the approaches described above.

3 Intakes and scenarios selenium

3.1 Short description of the Norwegian dietary surveys

The estimated intakes of selenium presented in this opinion are based on data from the national dietary surveys in young children (2-year-olds), children and adolescents (4-, 9- and 13-year-olds) and adults (aged 18 to 70 years). The national dietary surveys were conducted by the Department of Nutrition, University of Oslo in collaboration with the Directorate of Health, the Norwegian Food Safety Authority and the Norwegian Institute of Public Health. Different methodologies were used in the different surveys and thus direct comparisons between the age groups may be misleading.

A description of the dietary surveys and the different methodologies used is given below.

Adults: "Norkost 3" is based on two 24-hour recalls by telephone at least one month apart. Food amounts were presented in household measures or estimated from photographs (Totland et al., 2012). The study was conducted in 2010/2011, and 1787 adults (925 women and 862 men) aged 18-70 participated.

9- and 13-year-old children/adolescents: "Ungkost 3" is based on a 4-day food intake registration with a web based food diary. All food items in the diary were linked to photographs for portion estimation (Hansen et al., 2016). The study was conducted in 2015 and 636 9-year-old children and 687 13-year-old adolescents participated.

4-year-old children: "Ungkost 3" is based on a 4-day food intake registration with a web based food diary. All food items in the diary were linked to photographs for portion estimation (Hansen et al., 2017). The study was conducted in 2016, and 399 4-year-olds participated.

2-year-old children: "Småbarnskost 2007" is based on a semi-quantitative food frequency questionnaire. In addition to predefined household units, food amounts were also estimated from photographs. The study was conducted in 2007, and a total of 1674 2-year-olds participated (Kristiansen et al., 2009).

3.2 Dietary intakes of selenium in the Norwegian population

Intake of selenium in the various age groups and in groups of users of selenium supplements are presented in tables in Appendix 1. The tables in Appendix 1 also include estimates for P25 and P75. Selenium intake from fortified products is not included in the calculations, but are however, evaluated to be very low.

Adults (n=1787)

The mean intake of selenium from the diet alone is 57.2 µg/day (median 50.0 µg/day) in adults (n=1787). The P5 intake is 21.0 µg/day and the P95 intake is 117.0 µg/day.

In Norkost 3, 267 (15%) participants reported use of selenium-containing supplements. Their mean total intake of selenium including that from food supplements is 95.1 µg/day (median 84.0 µg/day). The P5 intake is 41.4 µg/day and the P95 intake is 197.6 µg/day.

Mean intake of selenium from supplements alone in adults reporting use of selenium-containing supplements is 38.6 µg/day (median 25.0 µg/day). The P5 intake is 8.0 µg/day and the P95 intake is 90.6 µg/day.

In 13-year-olds (n=687)

The mean intake of selenium from the diet alone is 35.1 µg/day (median 32 µg/day) in 13-year-olds. The P5 intake is 15 µg/day and the P95 intake is 61.6 µg/day.

In Ungkost 3, 23 (3%) participants reported use of selenium-containing supplements. Their mean total intake of selenium including that from food supplements is 53.8 µg/day (median 53.0 µg/day).

Mean intake of selenium from supplements alone in 13-year-olds reporting use of selenium-containing supplements is 17.1 µg/day (median 15.0 µg/day).

In 9-year-olds (n=636)

The mean intake of selenium from the diet alone is 33.7 µg/day (median 31.5 µg/day) in 9-year-olds. The P5 intake is 17.0 µg/day and the P95 intake is 58.0 µg/day.

In Ungkost 3, 19 (3%) participants reported use of selenium-containing supplements. Their mean total intake of selenium including that from food supplements is 52.3 µg/day (median 48.0 µg/day).

Mean intake of selenium from supplements alone in 9-year-olds reporting use of selenium-containing supplements is 35.1 µg/day (median 31.0 µg/day).

In 4-year-olds (n=399)

The mean intake of selenium from the diet alone is 30.5 µg/day (29.0 µg/day) in 4-year-olds. The P5 intake is 16.0 µg/day and the P95 intake is 50.0 µg/day.

In Ungkost 3, 20 (5%) participants reported use of selenium-containing supplements. Their mean total intake of selenium including that from food supplements is 45.0 µg/day (median 41.5 µg/day).

Mean intake of selenium from supplements alone in 4-year-olds reporting use of selenium-containing supplements is 15.6 µg/day (median 12.0 µg/day).

In 2-year-olds (1674)

The mean intake of selenium from the diet alone is 26.2 µg/day (median 25.0 µg/day) in 2-year-olds. The P5 intake is 14.0 µg/day and the P95 intake is 42.0 µg/day.

In Småbarnskost 2007 3, 75 (5%) participants reported use of selenium-containing supplements. Their mean total intake of selenium including that from food supplements is 39.5 µg/day (median 37.0 µg/day). The P5 intake is 25.0 µg/day and the P95 intake is 55.2 µg/day.

Mean intake of selenium from supplements alone in 4-year-olds reporting use of selenium-containing supplements is 12.6 µg/day (median 15.0 µg/day). The P5 intake is 4.0 µg/day and the P95 intake is 30.0 µg/day.

3.3 Scenario calculations for selenium

For scenario calculations VKM used the intake groups below P5 and above P95 from food alone to calculate selenium intake and added the suggested supplementation levels from NFSA (50, 150 or 200 µg selenium per day). The existing maximum limit for selenium in food supplements (100 µg) has also been included, see Tables 3.3-1 and 3.3-2.

Table 3.3-1 Calculated total selenium intakes for various age groups in scenarios with 50, 150 or 200 µg as supplements added to the P5 of intake from food alone (µg/day).

Age group	P5 from food	Including 50 µg from suppl	Including 100 µg from suppl	Including 150 µg from suppl	Including 200 µg from suppl
Adults	21.0	71.0	121.0	171.0	221.0
13 years	15.0	65.0	115.0	165.0	215.0
9 years	17.0	67.0	117.0	167.0	217.0
4 years	16.0	66.0	116.0	166.0	216.0
2 years	14.0	64.0	114.0	164.0	214.0

Table 3.3-2 Calculated total selenium intakes for various age groups in scenarios with 50, 100, 150 or 200 µg as supplements added to the P95 of intake from food alone (µg/day).

Age group	P95 from food	Including 50 µg from suppl	Including 100 µg from suppl	Including 150 µg from suppl	Including 200 µg from suppl
Adults	117.0	167.0	217.0	267.0	317.0
13 years	61.6	111.6	161.6	211.6	261.6
9 years	58.0	105.0	158.0	205.0	258.0
4 years	50.0	100.0	150.0	200.0	250.0
2 years	42.0	92.0	142.0	192.0	242.0

4 Assessment of the intakes of selenium

4.1 Evaluation of selenium intakes, including scenarios with supplementation

Dietary calculations have been performed for intake in P5, P25, mean, P50, P75 and P95 in children (2-, 4 and 9-year-olds), adolescents (13-year-olds) and in adult men and women. The 95th percentile intake is lower than the UL for all of the age groups while the 5th percentile is somewhat lower than the RI for all age groups.

Table 4.1-1 Recommended intakes (RI) from Norway, ULs from SCF (2000), and 5th and 95th percentiles of selenium intakes from food alone in various age groups (µg/day).

Age (years)	RDI, µg/day		Age (years)	P5 µg/day	P95 µg/day		Age (years)	UL µg/day
1-2	20		2	14	42		1-3	60
2-5	25		4	16	50		4-6	90
6-9	30		9	17	58		7-10	130
10-13	40		13	15	62		11-14	200
							15-17	250
14- >75	50		Adults	21	117		Adults	300
Pregnancy	60			-	-			
Lactation	60			-	-			

5 Uncertainties

It should be noted that the intakes have been calculated based on various dietary surveys for the different age categories and a comparison of calculations across age groups can be misleading. The calculated intakes in the higher and lower percentiles are always associated with a higher degree of uncertainty than mean or median intakes.

Thus, the percentile estimates of dietary intake are prone to random error due to the limited number of participants in the dietary surveys. The degree of uncertainty is largest in the estimated percentiles for 4-year-olds with a sample size of n=399, corresponding to about 20 observations below the 5-percentile and above the 95-percentile, respectively.

Another issue is that low participation limit the representativeness of the participants compared with the general background population in Norway. The participation among 13-, 9- and 4-year-olds in the dietary surveys were 53%, 55% and only 20%, respectively, while they were 37% in adults and 56% in 2-year-olds. In general, participants had considerably higher education level than the background population, and are expected to represent a health-conscious subgroup of the population. Some population subgroups are not covered, e.g. ethnic minorities.

For the determinations of the ULs for selenium, EFSA, IOM and EVM have not reached the same conclusions, indicating uncertainty regarding establishment of these ULs both for adults, and even more for children and adolescents.

The terms of reference has been to assess the intake in Norway in relation to already established tolerable upper intake levels which were established between 2000 and 2012. No literature search has been conducted for this VKM assessment and relevant recent evidence may accordingly not have been included.

6 Answers to the terms of reference

The Norwegian Food Safety Authority (NFSA, Mattilsynet) has requested the Norwegian Scientific Committee for Food Safety (VKM) to assess the intake of selenium from the diet, including fortified products, in all age groups in the population above 1 year in relation to tolerable upper intake levels (ULs).

VKM is also requested to conduct scenario estimations to illustrate the consequences of amending maximum limits for selenium to 50, 150 or 200 µg/day in food supplements. The existing maximum limit is 100 µg/day.

In the assessment of selenium, VKM uses the tolerable upper intake level established by the SCF at 300 µg/day for adults.

According to the scenario estimations in adults, the dietary selenium intake at the 95th percentile and additionally 150 µg selenium from food supplements will be below the UL while 200 µg selenium from food supplements will lead to exceedance of the UL for adults. For 13- and 9-year-olds, supplemental doses of 100 and 50 µg selenium per day, respectively, do not lead to exceedance of the ULs in these age groups. For 2- and 4-year-olds, all the suggested doses in food supplements will lead to exceedance of the ULs. Selenium intake from fortified products is not included in the calculations, but are however, assumed to be very low.

An overview of the conclusions is presented in Table 6-1.

Table 6-1 An overview of the conclusions for selenium according to doses in supplements.
Green: No exceedance of the UL.
Red: Exceedance of the UL.

Doses in supplements / Age group	50 µg/day	100 µg/day	150 µg/day	200 µg/day
Adults				
13 years				
9 years				
4 years				
2 years				

7 Data gaps

More age groups should be included in dietary surveys in addition to subgroups like different ethnical groups. Evidence from RCTs with long follow-up with adequate registration of adverse effects is needed.

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Appendix I

Summary tables of selenium intake for all age groups

Intakes of selenium in the various age groups are presented in the tables below. The tables summarise intakes from the diet alone, selenium-containing supplements alone (users only) and total intakes from both diet and supplements (Tables 1 and 2).

Table 1 Selenium intakes from diet alone in various age groups (µg/day).

	Adults (n=1787)	13 years (n= 687)	9 years (n=636)	4 years (n=399)	2 years (n=1674)
Selenium from diet alone, mean	57.2	35.2	33.7	30.5	26.2
Selenium from diet alone, median	50.0	32.0	31.5	29.0	25.0
Selenium from diet alone, P5	21.0	15.0	17.0	16.0	14.0
Selenium from diet alone, P25	36.0	25.0	25.0	23.0	20.0
Selenium from diet alone, P75	69.0	42.0	40.0	37.0	31.0
Selenium from diet alone, P95	117.0	61.6	58.0	50.0	42.0

Table 2 Selenium supplement users intake of total selenium from diet and supplements, and from supplements alone (users only), in various age groups (µg/day).

	Adults (n=267)	13 years (n=23)	9 years (n=19)	4 years (n=20)	2 years (n=75)
Total selenium from diet and supplements, mean	95.1	53.8	52.3	45.0	39.5
Total selenium from diet and supplements, median	84.0	53.0	48.0	41.5	37.0
Total selenium from diet and supplements, P5	41.4	-	-	-	25.0
Total selenium from diet and supplements, P25	63.0	-	-	-	34.0
Total selenium from diet and supplements, P75	108.0	-	-	-	46.0
Total selenium rom diet and supplements, P95	197.6	-	-	-	55.2
Selenium from supplements alone, mean	38.6	17.1	17.2	15.6	12.6
Selenium from supplements alone, median	25.0	15.0	15.0	12.0	15.0
Selenium from supplements alone, P5	8.0	-	-	-	4.0
Selenium from supplements alone, P25	25.0	-	-	-	6.0
Selenium from supplements alone, P75	50.0	-	-	-	15.0
Selenium from supplements alone, P95	90.6	-	-	-	30.0