Selenium

bw	body weight
CNS	Chinese Nutrition Society
CRN	Council for Responsible Nutrition
DRI	dietary reference intake
EC SCF	European Commission Scientific Committee on Food
EFSA	European Food Safety Authority
EVM	Expert Group on Vitamins and Minerals
ICMR-NIN	Indian Council of Medical Research - National Institute of Nutrition
IOM	Institute of Medicine
IU	international unit
JECFA	Joint FAO/WHO Expert Committee on Food Additives
KNS	Korean Nutrition Society
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NIH	National Institute of Health
NOAEL	no observed adverse effect level
NOEL	no observed effect level
RCT	randomized clinical trial
SUL	safe upper level
UF	uncertainty factor
UL	tolerable upper intake level

Introduction

Selenium is a trace element that is chemically similar to sulfur and replaces sulfur in the amino acid cysteine in certain enzymes (Levander and Burk 1994; Drake 2024). Selenium is essential for the function of 25 selenium-dependent enzymes (e.g., glutathione peroxidases, thioredoxin reductases, iodothyronine deiodinases) and is an element found in several amino acid analogs (e.g., selenocysteine and selenomethionine) (Drake 2024; EFSA 2024; Ren et al. 2024; NIH 2025). These amino acid analogs are incorporated into selenoproteins that have a role in DNA synthesis, reproduction, and thyroid hormone metabolism (NIH 2025). Selenium is also important

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to the cellular redox balance of biological systems (Drake 2024; NIH 2025).

Inorganic forms of selenium (e.g., selenites and selenates) are found in soil and ground water, and contribute minimally to dietary intake of selenium (EFSA 2023; Ren et al. 2024; NIH 2025). Plants can convert inorganic selenium to organic forms and methylated derivatives such as selenocysteine and selenomethionine, which are the primary dietary forms. Selenium is found in foods that are high in protein such as seafood, meat, poultry, organ meats, and Brazil nuts at concentrations ranging from 22-544 μg per serving. It is also in cereals, other grains and dairy products at concentrations up to 20 μg per serving (NIH 2025). Selenium can be incorporated into growing yeast, which then provides nutritionally useful forms of selenium (primarily selenomethionine) for animals and humans (NIH 2025). Common forms of selenium that are available in dietary supplements include (L-)selenomethionine, selenium-enriched yeast, sodium selenite, sodium hydrogen selenite, selenious acid, and sodium selenate at intake levels ranging from 2.5-400 μg per dose (EFSA 2023; NIH 2025).

Although toxic in large amounts, selenium is a necessary element for humans, and some populations suffer from low selenium. The first recognized sign of selenium deficiency, liver necrosis in laboratory animals, was discovered more than 40 years ago. In humans, selenium deficiency is associated with myopathies such as Keshan cardiomyopathy and Kashin-Beck osteoarthropathy, which occur in specific selenium deficient areas in Asia (Drake 2024). This deficiency results from the low selenium content of the soil in certain provinces and thus in the crops that are grown there. Selenium-deficient soils are not limited to China and have been identified in several other countries, including Finland, Ukraine, Germany, United States, the Congo, and New Zealand (Ren et al. 2024).

The current chapter focuses on the derivation of an UL value for supplemental selenium in adults.

Bioavailability

All forms of selenium are absorbed by the human body and selenium status does not affect absorption (EFSA 2024; NIH 2025). Dietary components can affect the absorption of selenium, with absorption ranging from 50-90% in humans (ATSDR 2003; EFSA 2024). Selenium-

containing amino acids or proteins need to first be digested to be absorbed through active transport. Selenomethionine is absorbed via intestinal methionine transporter proteins, whereas the absorption of selenocysteine is less known but expected to be absorbed in a similar manner. Selenite is absorbed via passive diffusion and is reduced to selenide in intestinal mucosa cells; thus, selenite is not expected to be in the blood. Selenate is absorbed via a carrier-mediated mechanism and appears in the blood unchanged. The different forms of selenium are further metabolized after transport to the liver, followed by distribution to organs and tissues (e.g., pancreas, nervous system, skin and hair, bone, skeletal and cardiac muscle, lungs and kidneys) (EFSA 2024). These selenium metabolites are primarily eliminated by urinary excretion but can also be eliminated in the feces (Hadrup and Ravn-Haren 2021; ATSDR 2003; EFSA 2024).

Safety Considerations

Chronic Selenium Toxicity (Chronic Selenosis)

Chronic selenium toxicity, known as chronic selenosis, occurs following chronic ingestion of excess selenium from the diet and/or other sources, such as dietary supplements. Symptoms primarily include effects on keratinized epithelia, such as alopecia (hair loss, brittleness) and nail changes (dry, thickened, brittle, discolored). Other side effects due to high intakes of selenium can include skin irritation (cutaneous eruptions), garlic odor in the breath, nausea, diarrhea, fatigue, irritability, and nervous system abnormalities (Rayman et al. 2018; EFSA 2023; Drake 2024; NIH 2025). For example, one episode of human poisoning by selenium involved a manufacturing error that resulted in a dietary supplement product containing approximately 200 times the amount of selenium declared on the label (MacFarquhar et al. 2010; Aldosary et al. 2012). Adverse effects occurred within a few weeks and included changes in the hair, nails, and liver.

The UL values established previously by the UK EVM (2003), EC SCF (2002), and IOM (2000) were based on cross-sectional data demonstrating human selenium poisoning in a high-selenium area of China that also produced adverse effects on the nails, skin, nervous system, and teeth (Yang et al. 1983; see *Official Reviews* section for additional UL information). Application of regression methods to these data later identified a LOAEL of 910 µg per day and a NOAEL of

approximately 850 µg per day in the Chinese adult of 55 kg weight (Yang, Zhou, et al. 1989; Yang, Yin, et al. 1989; Combs 1994; Poirier 1994). In affected individuals, symptoms were shown to fully reverse following reductions in dietary selenium (Yang and Zhou 1994). Based on these data, UL values for total intake were derived ranging from 255 to 400 µg selenium per day (UK EV 2003; EC SCF 2002; IOM 2000) (see *Official Reviews* for more details). CRN previously based its supplemental UL on a clinical trial by Clark and colleagues (Clark et al. 1996a, 1996b; Combs and Clark 1997), in which no adverse effects were observed at daily supplemental intakes of 200 µg selenium (i.e., NOAEL) in yeast for a mean of 4.5 years (follow up for a total of 8-10 years).

More recently, the EFSA (2023) reviewed available clinical, cross-sectional, and case report data and determined that symptoms of selenium toxicity can occur below the previous NOAEL of 850 µg per day identified by the EC SCF (2002). The EFSA Panel reviewed five RCTs with selenium that provided data specifically on symptoms of selenium toxicity. Four of these studies did not demonstrate an increased risk of alopecia or other symptoms of selenium toxicity at doses ranging from 200 to 600 µg selenium per day. However, despite the long duration of most of these studies, the EFSA noted that they were smaller in size or had limitations in recording methodology (Algotar et al. 2013b; Winther et al. 2015; Thompson et al. 2016; Fairris et al. 1989). The Negative Biopsy Trial (NBT) administered 0, 200, or 400 µg selenium per day for a mean of 2.9 years (Algotar et al. 2013), the Danish Prevention of Cancer by Intervention with Selenium (PRECISE) study administered 0, 100, 200, or 300 µg per day for 5 years (Wintham et al. 2015)[1], and the Selenium and Celecoxib (Sel/Cel) trial administered 0 or 200 µg per day for a mean of 3 years (Thompson et al. 2016).

The EFSA (2023) also reviewed data from the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which investigated the effect of selenium on prevention of prostate cancer in 8,752 healthy men (Lippman et al. 2009).[2] The study methods included specific queries regarding occurrence of alopecia, dermatitis, fatigue, halitosis, nail changes, and nausea. The authors

[1] Winther et al. (2015) reported the outcome of PRECISE trial that also includes publications by Perri et al. (2022), Cold et al. (2015), and Rayman et al. (2018). Perri et al. (2022) was identified in the updated literature search for this chapter described on the next page.

[2] Lippman et al. (2009) was reviewed in the 3rd edition of this chapter with regard to cancer outcomes; however, data on symptoms of selenosis were not described.

concluded that the only statistically significant differences ($p<0.01$) in these symptoms were an increase in alopecia and dermatitis (grades 1 to 2) in the selenium group. In its review of this study, the EFSA (2023) noted that "that this study shows an increased risk of developing alopecia at selenium intakes of around 330 µg/day compared with selenium intakes of 130 µg/day." However, the Panel also noted that the incidence of alopecia in the SELECT study indicates that the NOAEL "might not be far from the LOAEL" of 330 µg per day.

Data from cross-sectional studies reviewed by the EFSA (2023) demonstrated inconsistent results regarding increased risk of symptoms of selenosis. Based on evidence from the SELECT study (Lippman et al. 2009) and some cross-sectional studies, the EFSA Panel identified a LOAEL of 330 µg per day (130 µg per day from baseline diet plus 200 µg per day supplementation) from Lippman et al. (2009). (See *Official Reviews* section for additional information).

A large volume of human intervention studies published since the 3rd edition of this chapter were identified with potential relevance to this update (approximately 130). Given that the EFSA Panel (2023) conducted a comprehensive review of available RCTs and carried forward markers of selenium toxicity as the basis for deriving an UL value, the date of the EFSA's comprehensive literature search used to support its evaluation (i.e., February 2021) was selected as the publication date for CRN's screening approach. Therefore, while titles and abstracts of all identified studies since 2014 were screened, only studies published between 2021 (February) and 2025 were reviewed in detail for the purposes of this update. Thirty-three publications starting in 2021 were identified that met the inclusion criteria for the current update.[3] A full literature review is outside the scope of this chapter; however, an overview of the information reviewed is summarized below.

Of the studies identified, two open-label trials concluded chronic, high doses of selenium to be "safe and well tolerated"; however, both studies reported alopecia and nail changes in participants (Vivash et al. 2021, 2022; Dilcher et al. 2022; Moses et al. 2022).[4] No placebo

[3] Literature search conducted September 2025. Thirty-three publications representing 31 unique RCTs were identified. One study was an additional publication of the PRECISE pilot study and is discussed in the corresponding section above.

[4] Four publications covering two studies

groups were employed. Vivash et al. (2021; Moses et al. 2022) administered 12,540 µg selenium per day (10 mg sodium selenate three times a day) for a period of 6 to 23 months to Alzheimer's disease patients. The authors reported that alopecia and nail changes occurred in 21% and 32% of patients, respectively, which resolved prior to or upon cessation of the intervention. The incidences of effects were higher in behavioral variant frontotemporal dementia patients receiving 18,810 µg selenium per day (15 mg sodium selenate three times a day) for a year (Vivash et al. 2022; Dilcher et al. 2022). In this study, alopecia and nail changes occurred in 42% and 58% of patients, respectively, but decreased as patients were titrated to lower doses of selenium. All symptoms were resolved at 6,270 µg selenium per day.

No serious adverse effects or effects related to potential selenium toxicity (e.g., alopecia, nail changes) were reported in any other study identified as part of this update; however, not all studies included monitoring for such in the methodology. For example, no adverse effects were noted in a study published by Meherpooya et al. (2023), in which rheumatoid arthritis patients were given selenium at doses of 400 µg per day (200 µg twice per day) for 12 weeks. This study stated that "22 patients were excluded from the study due to drug side effects such as nausea or lack of referral" but did not provide any specific information on what the side effects were or if the occurrence of such differed between treatment and placebo groups. Twenty-six clinical trials were identified that tested selenium at 200 µg per day for durations ranging from 4 weeks to 5 years. Two studies reported data specifically on incidence of side effects related to potential selenium toxicity, such as alopecia, nail changes, skin reactions, and/or breath odor (Potita et al. 2024; Okunade et al. 2021), while four additional studies provided summary conclusions on these specific side effects (Dehghani et al 2021; Salimian et al. 2022; Walsh et al. 2021; Hu et al. 2021). Ten additional studies reported that there were no side effects associated with selenium intervention but did not clarify if such effects specific to selenium toxicity were assessed (Roshanravan et al. 2022; Yigit et al. 2024; Walsh et al. 2021; Zamani et al. 2024; Jamal et al. 2022; Balali et al. 2024; Assarzadeh et al. 2022; Mesdaghinia et al. 2023; Rahimi et al. 2024; Almanza-Monterrubio et al. 2021).

Type 2 Diabetes Mellitus

As briefly reviewed in the 3rd edition, available evidence is mixed regarding the effect of selenium

intake on type 2 diabetes (also reviewed in Drake 2024). For example, the study conducted by Bleys et al. (2007) was discussed, which examined data from the Third National Health and Nutrition Examination Survey and found that adults with diabetes had very slightly higher serum selenium concentrations compared with nondiabetics. Before the data were adjusted for a number of factors (gender, age, ethnicity, etc.), the differences were very small and nonsignificant. After adjustment, the mean serum selenium concentrations of selenium were as follows: diabetics 126.8 ng per ml, and nondiabetics 124.7 ng per ml. Because of the large number of persons evaluated, this small difference was labeled as "significant" ($P = 0.02$). However, a lack of biological plausibility associated with the observed effects was noted, as it is unlikely that such small differences in selenium concentrations would have a causal relationship to diabetes. In addition, there was no evidence of a dose-response relationship in this study.

Recently, the EFSA (2023) reviewed the available human clinical trial data on incidence of type 2 diabetes, stating that the body of evidence suggests a positive relationship between selenium intake and incidence of diabetes. The level of certainty in a positive and causal relationship was determined to be moderate. However, the Panel concluded that the increased risk of type 2 diabetes observed from supplementation studies is not supported by the results of studies reporting on measures of glucose tolerance, indices of insulin sensitivity/resistance, or measures of blood glucose control. While observational data were also found by the Panel to suggest a positive relationship with type 2 diabetes, the probability of a positive and causal relationship was found to be low, due to uncertainties in the data. In addition, the Panel determined that a mechanism of action for the proposed effect has not been established. Thus, the Panel concluded that observational studies and information regarding the mode of action could not be used to modify the level of certainty regarding the relationship identified from clinical studies. The Panel noted that the UL of 255 µg per day derived in its assessment based on signs of selenium toxicity (see *Official Reviews* section) is lower than the mean selenium intake levels associated with an increased number of type 2 diabetes cases in intervention studies; therefore, type 2 diabetes was not identified by the EFSA as a critical effect for deriving the UL. Of note, some analyses suggest the relationship between selenium intake and risk of type 2 diabetes to be non-linear, indicating a potential U-shaped relationship with both low and high intakes increasing risk (Vinceti et al. 2018; Wang et al. 2023). However, the dose-response meta-analysis conducted by the EFSA (2023) concluded that departures from non-linearity could not be consistently

identified in the range of concentrations available in the dataset, noting a lack of data points at the higher serum ranges (e.g., >120 µg per L).

No RCTs were identified in the literature search for this chapter update that provide additional data relevant to the evaluation of diabetes risk following interventional selenium. One study in infertile women undergoing *in vitro* fertilization reported that 200 µg per day for 8 weeks resulted in "beneficial effects" on glycemic control as measured by fasting plasma glucose, serum insulin, and lipoproteins levels (Zadeh Modarres et al. 2022).

Official Reviews

IOM (2000). The IOM used the dose response data for selenium intakes reexamined by Yang and Zhou (1994) to identify a NOAEL for selenium of 800 µg per day, based on nail and hair brittleness and loss as the critical endpoint (i.e., selenosis). An UF of 2 was selected to provide protection for sensitive individuals, noting that the effect is not severe but "may not be readily reversible," resulting in a UL of 400 µg selenium per day for adults for total oral intake from all sources. The IOM did not express an opinion on safe levels for selenium supplementation.

Expert Group on Vitamins and Minerals (EVM 2003). The UK's EVM did not identify a NOAEL but considered the studies of Yang and colleagues (Yang, Yin, et al. 1989; Yang, Zhou, et al. 1989) to support a LOAEL of 910 µg per day based on symptom of selenosis (nail, hair, and skin lesions). The EVM applied an UF of 2 to a LOAEL for LOAEL to NOAEL extrapolation, deriving an SUL for selenium of 450 µg per day. The EVM noted that a margin of 350 µg per day "is available for supplementation or other additional intake", assuming that dietary intake is a maximum of 100 µg per day from food.

European Food Safety Authority (EFSA 2023). Previously, the EC SCF (2002) considered the data of Yang, Yin, and colleagues (1989) sufficient to identify a NOAEL of 850 µg per day. An UL of 300 µg per day was derived from this NOAEL by application of a UF of 3. More recently, the EFSA (2023) published its *Scientific Opinion on the Tolerable Upper Intake level for Selenium*. The Panel identified alopecia as the critical effect, given that it is a "well-established adverse effect of excess selenium exposure," and noting that such effects on hair,

nails, and skin are a result of altered protein metabolism. A LOAEL of 330 µg per day from the SELECT study (Lippman et al. 2009) was identified by the EFSA, noting that this average intake was comprised of approximately 130 µg per day from the diet and 200 µg per day from supplements. In its discussion of the uncertainties, the Panel stated that data on the steepness of the dose-response curve are limited but concluded that the available data suggest the NOAEL "might not be far from the LOAEL." Based on this uncertainty and considering that the alopecia observed in the Lippman et al. (2009) study is an early sign of selenium toxicity, a mild effect, and likely reversible, an UF of 1.3 was applied to yield an UL of 255 µg per day for adults from all sources for selenium.

Other potential adverse health effects in adults were evaluated by the EFSA (2023) Panel, with the following conclusions:

- The Panel concluded the available data do not suggest a positive relationship between dietary intake of selenium and risks of hypertension, Alzheimer's dementia, amyotrophic lateral sclerosis, thyroid diseases, prostate cancer, skin cancer, or all-cause mortality.
- The Panel concluded that there is a moderate level of certainty (50-75%) that data from RCTs support a positive and causal relationship between dietary intake of selenium and risk of type 2 diabetes. However, the level of certainty could not be modified based on evidence from observational studies and information on mode of action. See *Type 2 Diabetes Mellitus* section for more details.

Chinese Nutrition Society (CNS 2023). The CNS derived an UL of 400 µg per day for adults, including pregnant and lactating individuals.

Indian Council of Medical Research - National Institute of Nutrition (ICMR-NIN 2020). The ICMR-NIN did not derive an UL value for selenium.

Korean Nutrition Society (KNS 2020). The KNS published its general approach to evaluating data for setting DRI values. The KNS derived an UL of 400 µg per day for adults (age 19 years and older), including pregnant and lactating individuals. An UL of 300 µg per day was derived for males and females 15-18 years of age.

CRN Recommendations

The goal of this chapter was to determine whether more recent human clinical data are available that might impact the conclusions published in the 3rd edition, which derived an UL value for selenium of 200 µg per day based on RCT data (Clark et al. 1996a, 1996b; Combs and Clark 1997). While not all human clinical trials are specifically designed to evaluate adverse effects, no new trials were identified following CRN's updated methodology that reported any serious adverse effects or symptoms of selenium toxicity associated supplementation. As with any assessment in which not all available data are reviewed, inherent uncertainties with the risk assessment and selection of the UL are recognized.

CRN's safety methodology for deriving supplemental UL values prioritizes data from human clinical studies, when available. The table below summarizes the key human clinical studies considered in deriving the supplemental UL value by CRN according to its principal points of departure for risk assessment (as described in the Methods).[5]

[5] Where numerous relevant studies were identified, those most pertinent to the UL derivation are included in the table as representative studies. Prioritization was given to studies at dose levels informing the UL and studies with higher weighting based on CRN's Methods (e.g., duration, number of participants, randomization, etc.).

Key Studies Considered for the CRN UL for Selenium in Adults: Increased Risk of Symptoms of Selenosis

Reference	Study Design	Participant Description	No. of Subjects	Supplemental Dose(s) (µg/day)	Duration	NOAEL (µg g/day)	LOAEL (µg g/day)
Key studies from 3rd edition and EFSA (2023)							
Yang et al. 1983[a]	Cross-sectional	Chinese population	349 (60 cases)	N/A	N/A	~850 dietary	~910 dietary
Fairris et al. 1989	Randomized, double-blind, placebo-controlled	Psoriasis patients	69	0, 600[b]	3 months	600	N/A
Algotar et al. 2013	Phase 3 randomized, double-blind, placebo-controlled	Men at high risk for prostate cancer	699	0, 200, 400	2.9 years (median)	400	N/A
PRECISE Study[c]	Randomized, double-blind, placebo-controlled	Healthy adults	491	0, 100, 200, 300	5 years	300	N/A
Clark et al. 1996a,b; Combs and Clark 1997	Randomized, double-blind, placebo-controlled	Skin carcinoma patients	1,312	0, 200	4.5 years (mean)	200	N/A
Thompson et al. 2016	Randomized, double-blind, placebo-controlled	Patients with history of colorectal adenoma	1,621	0, 200	2.75 years (median)	200	N/A
SELECT (Lippman et al. 2009)	Randomized, double-blind, placebo-controlled	Healthy men	8,752	0, 200	5.5 years (median)	N/A	200
Key studies identified in update							
Potita et al. 2024	Randomized, double-blind, placebo-controlled	Severe Graves' orbitopathy patients	29	0, 200	6 months	200	N/A
Okunade et al. 2021	Randomized, double-blind, placebo-controlled	HIV-infected pregnant women	180	0, 200	During pregnancy	200	N/A
Salimian et al. 2022	Randomized, double-blind, placebo-controlled	Diabetic hemodialysis patients	60	0, 200	6 months	200	N/A
Walsh et al. 2021	Randomized, double-blind, placebo-controlled	Older women	120	0, 200	6 months	200	N/A
Hu et al. 2021	Open-label, randomized, parallel-controlled	Hashimoto's thyroiditis patients and healthy adults	126	0, 200	6 months	200	N/A

Reference	Study Design	Participant Description	No. of Subjects	Supplemental Dose(s) (µg/day)	Duration	NOAEL (µg g/day)	LOAEL (µg g/day)
Dehghani et al. 2021	Randomized, placebo-controlled	Non-Hodgkin lymphoma patients	32	0, 200	3 months	200	N/A

N/A, not applicable

[a] Also: Yang, Zhou, et al. 1989; Yang, Yin, et al. 1989; Combs 1994; Poirier 199

[b] Also included a group with selenium + vitamin E

[c] Perri et al. 2022; Cold et al. 2015; Rayman et al. 2018; Winther et al. 2015

Previous UL values set by the UK EVM (2003), EC SCF (2002), and IOM (2000) were based on an NOAEL or LOAEL of approximately 850 µg per day or 910 µg per day, respectively, for symptoms of selenium toxicity from a cross-sectional study in a Chinese population (Yang et al. 1983; Yang, Zhou, et al. 1989; Yang, Yin, et al. 1989; Combs 1994; Poirier 1994). More recently, the EFSA (2023) identified an LOAEL of 330 µg per day (130 µg per day from baseline diet plus 200 µg per day intervention) from the SELECT RCT conducted by Lippman et al. (2009).

None of the other more than 30 clinical trials were identified by CRN or the EFSA (2023) identified an increased incidence of alopecia or other symptoms of selenosis below ~6,000 µg per day. In addition to Lippman et al. (2009), eight other RCTs identified administered 200 µg per day and specifically assessed the occurrence of these symptoms; however, no increases in such effects were found following selenium intervention (Clark et al. 1996a,b; Combs and Clark 1997; Thompson et al. 2016; Potita et al. 2024; Okunade et al. 2021; Dehghani et al 2021; Salimian et al. 2022; Walsh et al. 2021; Hu et al. 2021). These findings are supported by intervention studies with doses up to 300 µg per day for 3 years (~350 µg per day including diet; PRECISE study), 400 µg per day for 5 years (~510 µg per day including diet; Algotar et al. 2013), and 600 µg per day for 3 months (Fairris et al. 1989), as well as the cross-sectional study by Yang and colleagues that identified a NOAEL of 850 µg per day.

Exact reasons for the discrepancy between effect levels (i.e., NOAEL, LOAEL) observed between the SELECT study and these other studies is not clear; however, variability in dietary levels of selenium was considered as a potential factor. Some populations are reported to have lower dietary intakes of selenium; for example, the mean intake in India was found to be 59 to 76 µg per day for adults (ICMR-NIN 2020). The EFSA (2023) Panel noted that the average dietary intake of approximately 130 µg per day in the Lippman et al. (2009) study was higher than what is "typically observed in European populations," as evidenced the conclusions of its dietary intake assessment which reported intake from foods in the highest consumer adult group (95^{th} percentile) to be up to 113 µg per day. Recent data demonstrate that U.S. adults (age 20 years and older) consume an average of approximately 94 to 132 µg per day from food only (USDA 2022), which is consistent with the dietary intake calculated from the Lippman et al. (2009) study, which was conducted in a U.S. population. However, other U.S. studies with the

same or higher interventional levels of selenium (200, 400, and 600 µg per day) did not result in signs of selenium toxicity, such as alopecia (Thompson et al. 2016; Algotar et al. 2013; Fairris et al. 1989).

Chronic selenium toxicity is selected as the critical effect from which to base the derivation of the CRN supplemental UL. As noted by the EFSA (2023), the alopecia observed in the Lippman et al. (2009) study is an early sign of selenium toxicity and is considered to be a mild effect and is likely reversible. The reversibility of such effects was further demonstrated in study by Vivash et al. (2022; Dilcher et al. 2022), in which alopecia and nail changes were resolved at doses of 6,270 µg selenium or less per day. In addition, the effects observed in the Lippman et al. study were not reported in any other clinical trial reviewed at daily supplemental doses ranging from 100 to 600 µg per day. Therefore, based on the overall dataset, 200 µg per day is maintained as the supplemental NOAEL for selenium for adults following the CRN process (Clark et al. 1996a,b; Combs and Clark 1997; Thompson et al. 2016; Potita et al. 2024; Okunade et al. 2021; Dehghani et al 2021; Salimian et al. 2022; Walsh et al. 2021; Hu et al. 2021). Consistent with CRN's methodology, an UF of 1 is applied to the supplemental NOAEL of 200 µg per day yield an UL of 200 µg per day for supplemental selenium in adults.

Some uncertainty regarding effects in populations with higher dietary intakes is noted. Therefore, individuals with a higher-than-average intake of selenium in the diet, such as from regular consumption of Brazil nuts or fish from areas with elevated selenium levels in soil or water, should consult their healthcare provider before taking selenium-containing supplements.

Quantitative Summary for Selenium

CRN UL (2025), supplemental intake	200 µg/day
IOM UL (2001), total intake	400 µg/day
EFSA (2023), total intake	255 µg/day
EVM (2003), SUL	350 µg/day supplemental intake; 450 µg/day total intake
CNS (2023), total intake	400 µg/day
ICMR-NIN (2020)	Not determined
KNS (2020), total	400 µg/day (19 years and older); 300 µg/day (15-18 years of age)

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