Chromium III

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

Chromium occurs in several chemical forms, with chromium III (trivalent chromium, valence 3+) representing the form associated with nutritive effects. Chromium III compounds are important to glucose, fat and protein metabolism, protein biosynthesis, and nucleic acid transformations (Dworzański et al. 2021; Drake 2022). In addition, trivalent chromium can potentiate the action of insulin in target tissues (Nielsen 1994; Stoecker 1999; Drake 2022). The biological effects of chromium strongly depend on its specific chemical form. Nutritive effects

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are exclusively related to chromium III, while all major toxic effects are associated with chromium VI (hexavalent chromium, valence 6+) (Nielsen 1994; Drake 2022).

Chromium III is ubiquitous in the diet and is found in the following foods: meat and meat products, oils and fats, breads and cereals, fish, pulses, spices, green beans, broccoli, nuts, and egg yolk (EFSA 2014a; Drake 2022; Vincent and Lukaski 2018; NIH 2022). The reported adult dietary food intakes of chromium range from 20 to 45 µg per day in the U.S. and 57.3-83.8 µg per day in the EU (IOM 2006; Drake 2022; NIH 2022; EFSA 2014a). Trivalent chromium is also available in dietary supplement products, with typical doses ranging from 100 to 500 µg per day (Drake 2022; NIH 2022). The forms of chromium III found in foods and supplements include chromium chloride and its hexahydrate, chromium sulphate and its hexahydrate, chromium picolinate, chromium nicotinate, and chromium lactate trihydrate (EFSA 2014b; Drake 2022). Chromium nitrate, chromium polynicotinate, chromium histidinate, and chromium–enriched yeast are also used in food supplements (EFSA 2014b; NIH 2022).

This chapter focuses on the derivation of an HOI value for supplemental chromium III (all forms) in adults. Chromium referred to herein reflects chromium III, unless otherwise specified.

Bioavailability

Dietary chromium is poorly absorbed via passive diffusion with an absorption efficiency ranging from 0.1 to 5.2% in humans (EFSA 2014a,b; Vincent and Lukaski 2018; Henriksen and Bügel 2023). The absorption of chromium from food sources varies from 0.4 to 2.5%, depending on dietary source and composition (EFSA 2014b). Available studies have shown that chromium intake is inversely related to dietary intake, as evidenced by a 2% absorption rate for a 10 µg chromium intake and a 0.5% absorption rate for a 40 µg chromium intake in one study (Anderson and Kozlovsky 1985; also reviewed in EFSA 2010b).

Once absorbed, chromium binds to transferrin and is transported to the liver and other tissues such as spleen, soft tissue, and bone for long-term storage (Vincent and Lukaski 2018; Jomova et al. 2025). Around 5% of the absorbed chromium is present in an unbound form (EFSA 2014a; NIH 2022). Most of the chromium is rapidly eliminated from the bloodstream and excreted via urine, with small amounts also excreted in perspiration, bile, and feces (EFSA 2010a, 2014b;

Jomova et al. 2025). Conversely, chromium is released from tissues at a slower rate (Jomova et al. 2025). Unabsorbed chromium is excreted in feces (EFSA 2014b).

Safety Considerations

No serious adverse events have been associated with supplemental chromium in human clinical trials reviewed as part of this assessment. CRN previously developed a supplemental UL for chromium of 1,000 µg elemental per day for adults based on the available clinical trial data reviewed by authoritative agencies at that time (IOM 2001, 2005;[1] EFSA 2010a; EC SCF 2003). The following clinical studies published prior to CRN's previous evaluation (3rd edition) were considered in the assessment to support a supplemental UL of 1,000 µg per day at that time (Anderson et al. 1997a; Kleefstra et al. 2006; Martin et al. 2006; Vrtovec et al. 2005; Campbell et al. 1997; 1999).[2] In a double-blind, placebo-controlled study, patients with type 2 diabetes (n=60 per dose) were administered up to 1,000 µg elemental chromium per day (as chromium picolinate) for four months (Anderson et al. 1997a). The authors concluded that there was no evidence of toxicity in this study. In another double-blind study, patients with type 2 diabetes (n=14 to 17 per dose) consumed 0, 500, or 1,000 µg elemental chromium per day (as chromium picolinate) for six months (Kleefstra et al. 2006). Two patients in the 1,000 µg per day dose group withdrew from the study due to "possible adverse effects." One patient self-reported frequent watery stool, weakness, dizziness, nausea, and headaches, while the other patient self-reported vertigo with nausea and vomiting (Kleefstra et al. 2006). The occurrences of adverse effects were not statistically significant between groups, including when compared to placebo.[3] No adverse events were observed in a double-blinded, randomized, placebo-controlled study that was conducted in type 2 diabetes patients (n=12 to 17 per dose) that administered 1,000 µg

[1] CRN's 3rd edition of this chapter discussed using a large number of clinical trials summarized in Table B-1 from the IOM's 2005 draft monograph as the basis of its supplemental UL derived at that time. However, studies were not discussed in detail in the 3rd edition. The full monograph, including Table B-1, is not currently available for review. Therefore, published studies available at that time, as identified and reviewed by authoritative agencies and review articles, are included in the current chapter. A comprehensive literature search for clinical studies published prior to 2014 was not conducted.

[2] Several of these studies (e.g., Anderson et al. 1997; Kleefstra et al. 2006) allowed the participants to continue their typical standard of care while participating in the study. As such, concomitant medication use occurred in some studies included in this review. In one study (Martin et al. 2006), chromium was administered alongside another medication, as described herein. While this would typically not meet the inclusion criteria for CRN's updated literature search, this older study is included based on its importance to previous authoritative opinions.

[3] Standard statistical analysis was conducted according to the methodology included in CRN's Methodology for 4th Edition Nutrient Chapter Updates.

elemental chromium (as chromium picolinate) per day (with glipizide gastrointestinal therapeutic system) for 24 weeks (Martin et al. 2006). While the study authors stated that the dose used in this study had not previously been associated with any adverse effects, the study did not mention monitoring for such. A double-blind, randomized, placebo-controlled crossover trial in type 2 diabetics (n=30 per dose) administered 0 or 1,000 µg elemental chromium per day (as chromium picolinate) for three months with no reported adverse effects, though the study did not mention monitoring for such (Vrtovec et al. 2005). Campbell et al. (1997, 1999) conducted two separate double-blind studies in older men (aged 56-69 yrs; n=9 per dose) that consumed either a low dose of elemental chromium (< 1 µg per day) or 924 µg elemental chromium per day (as chromium picolinate) for 12 to 13 weeks. While no adverse effects were reported in either study, neither publication specified monitoring for such.

Twenty-one human clinical trials published since the 3rd edition (i.e., 2014) were identified that met the inclusion criteria (see CRN Methodology Chapter).[4,5,6] None of the newly identified studies tested doses as high as 1,000 µg per day, the dose level previously considered in the derivation of CRN's supplemental UL. The 21 studies identified tested elemental chromium doses ranging from 19.5 to 400 µg per day in trials ranging from 7 weeks to 24 weeks, primarily in disease state patient populations. No adverse events were reported by the authors across these studies; however, not all studies monitored for such. Thirteen of the trials investigated elemental chromium doses ranging from 19.5 to 99 µg per day (twelve as chromium picolinate, one each as chromium nicotinate and chromium-enriched yeast, and one unspecified) with durations ranging from 8 weeks to 12 weeks (Amiri Siavashani et al. 2018; Guimarães et al. 2016; Imanparast et al. 2020a, b; Kalbasi et al. 2018; Kooshki et al. 2021 and Moradi et al. 2021;[7] Lee et al. 2016; Paiva et al. 2015; Parastesh et al. 2025; Rocha et al. 2014; Talab et al. 2020; Yanni et al. 2018; Ebrahimzadehkour et al. 2026). Eight studies examined the effects of chromium ranging from 124 to 400 µg elemental per day (as chromium picolinate, chromium dinicocysteinate, chromium-enriched yeast, or unspecified) with durations ranging from 8 weeks

[4] Additional studies were identified in which participants received chromium as part of a combination test material. These studies did not meet the inclusion criteria based on CRN's Methodology and were therefore not included in this review.
[5] Literature search conducted July 2026
[6] One additional publication (Silpa et al. 2024) met the criteria for inclusion but did not provide dosing information and therefore is not included in the 21 reported here.
[7] These two publications appear to be reporting on the same study/cohort.

to 12 weeks (Ashoush et al. 2016; Dou et al. 2016; Farrokhian et al. 2020; Nussbaumerova et al. 2018; Saiyed and Lugo 2016; Sala et al. 2017; Zhao et al. 2024; Mahmoud et al. 2026).

In addition, the study published by Kooshki et al. (2021) and Moradi et al. (2021) demonstrated that there was no effect on liver enzymes nor any effect on liver steatosis severity in patients with non-alcoholic fatty liver disease after consumption of 400 µg elemental chromium per day for 3 months. This finding is of particular interest given that impaired liver function after the consumption of elemental chromium at doses ranging from 1,200 to 2,400 µg per day was previously raised as a concern, though supporting data are lacking (Drake 2022).

Other anecdotal reports have attributed adverse effects to supplements of chromium in general (IOM 2001; EVM 2003) and to chromium picolinate in particular (Wasser et al. 1997). One report, concerning a single case of renal failure in a person who was taking chromium picolinate, attributed the disease to the chromium supplement (Wasser et al. 1997). The authors acknowledged that the patient also received "antihypertensive agents," but nonetheless attributed the effect solely to chromium picolinate; the renal toxicity of antihypertensive agents and pathological effects of poorly controlled hypertension apparently were not considered. Critical letters were published in response to the report (Michenfelder et al. 1997; Hathcock 1997), pointing out the flaws in the conclusion. Despite these methodological issues and the critical response, the case is often cited without caveat (Hepburn et al. 2003; IOM 2006).

Overall, available studies had no reports of adverse effects in humans due to chromium supplementation. Furthermore, animal data previously reviewed by authoritative agencies and CRN's 3rd edition also suggest that orally administered chromium is extremely innocuous (Dourson 1994; Nielsen 1994; Hathcock 1996; IOM 2001; EVM 2003; EFSA 2010b). For example, ingestion of various chromium compounds did not produce carcinogenicity in mice and rats in long-term studies (Schroeder et al. 1964, 1965; Ivankovic and Preussman 1975). In addition, the National Toxicology Program (NTP) of the U.S. Department of Health and Human Services (HHS) performed carcinogenicity studies on chromium picolinate monohydrate and concluded that there was *no evidence of carcinogenic activity* due to the tested substance in female rats or in male or female mice (NTP 2010; Stout et al. 2009). The NTP stated that there was *equivocal evidence of carcinogenic activity* in male rats based on an increase in the

incidence of preputial gland adenomas in the middle dose group only that was "possibly associated with exposure to chromium picolinate."

Official Reviews

World Health Organization (WHO 1996). The WHO reviewed the available data regarding the "nutritional significance" and metabolism of chromium. The WHO stated that the "relatively non-toxic nature of chromium as found in food indicates that the tolerable limit for chromium is quite high." Typical dietary intake and supplementation of 125 to 200 µg chromium per day was shown to be beneficial in reversing hypoglycemia and impaired glucose tolerance as well as for improving circulating insulin levels and lipid profile (e.g., Jeejeebhoy et al. 1977; Freund et al. 1979; Brown et al. 1986). The WHO concluded that the available data "suggest that the upper limit of the safe range of population mean intakes could be above 250 µg per day, but until more is known about chromium, supplementation of this element should not exceed this amount."

IOM (2001, 2005). The IOM (2001) considered the evidence related to chronic renal failure, genotoxicity, carcinogenicity, hepatotoxicity, reproductive toxicity, and other possible effects and could not identify a hazard or dose-response relationship for soluble salts of dietary chromium based on the available dataset. Thus, the IOM did not set an UL but noted the lack of adverse effects associated with excessive intake of chromium from food or supplements.

In 2005, the organization released a draft monograph on the safety of chromium picolinate, which reviewed the available human and animal data for various forms of chromium, including chromium picolinate (IOM 2005). The human clinical data on chromium picolinate included: 17 randomized, double-blind, placebo-controlled human clinical trials of oral chromium picolinate; 2 similar trials ("confounded by the choice of subjects with gestational diabetes or publication in German"); 3 crossover-design trials; 1 uncontrolled study in subjects with diabetes; 1 phase II study; 2 pilot studies; 1 questionnaire; 11 clinical case reports; 1 case series report; and 21 spontaneous adverse event reports to Special Nutrition / Adverse Event Monitoring System. The IOM (2005) concluded that "there was no consistent evidence of reasonable expectation of harm" from consumption of chromium picolinate up to 1,600 µg per day (200 µg elemental chromium per day) based on clinical studies. The IOM did not assess an UL determination as part of this draft

monograph for chromium picolinate.

EVM (2003). The UK's EVM found no credible evidence of adverse effects for chromium but identified a guidance level of 10,000 µg (10 mg) per day, based on extrapolation from animal data on chromium chloride and chromium picolinate. In making this decision, the EVM derived its guidance level directly from the experiments of Anderson et al. (1997b), who performed histopathological examinations of rats and found no adverse effects resulting from chromium chloride or chromium picolinate (the rats were fed 15 mg of elemental chromium per kg of body weight per day) (Anderson et al. 1997b). A composite UF of 100 was applied by the EVM to the highest level of chromium chloride used, which was identified as the NOAEL. In the Anderson et al. study relied upon by the EVM, chromium chloride and chromium picolinate were used with the same levels of elemental chromium, and each produced no evidence of toxicity. The EVM elected not to apply the guidance level derived from the Anderson et al. data to the picolinate form based on findings of DNA damage caused by chromium picolinate to mammalian cells *in vitro*. Subsequently, the Committee on Mutagenicity reviewed further data and concluded that the balance of the evidence suggested that chromium picolinate was not genotoxic. Accordingly, the UK Food Standards Agency (FSA) stated in 2004 that there is no need to avoid chromium picolinate (FSA 2004).

EFSA (2009a,b, 2010a,b, 2014b). In 2003, the European Commission Scientific Committee on Food (EC SCF 2003) reviewed chromium toxicity and reached conclusions aligned with those of the IOM (2001). The animal data of Anderson et al. (1997b) were considered, but, given the absence of adverse effects, the EC SCF decided not to set an UL for chromium.

In 2009, the EFSA evaluated the safety of chromium nitrate and chromium picolinate as a source of chromium added for nutritional purposes in food supplements (EFSA 2009a,b). In both evaluations, the EFSA Panel concluded that chromium supplementation should not exceed the WHO recommendation of 250 µg chromium per day based on the available data. In 2010, the EFSA evaluated the safety of chromium as a nutrient added to food for particular nutritional uses and foods intended for the general population (including supplements), with a focus on the potential genotoxicity of chromium (EFSA 2010b). The EFSA also evaluated the safety of chromium picolinate in the same year (EFSA 2010a). The EFSA concluded that the safety of

chromium, and particularly chromium picolinate, as a nutrient added to food is not of concern, provided that the ingestion of chromium from the food is not greater than 250 µg per day. The EFSA's conclusion was based on the following: (1) the maximum intake levels for supplemental intake established by the WHO would be in the same order of magnitude as normal dietary intake of chromium in the European Union; (2) chromium picolinate (and other sources of chromium) might cause DNA damage at high concentrations *in vitro*; (3) the DNA damage that may occur *in vitro* has not been reported in *in vivo* genotoxicity assays; (4) chromium is not carcinogenic; and (5) there is a large margin of safety between an intake of 250 µg per day (4.1 µg per kg per day in a 60-kg adult) and the NOAEL of 6,100 mg chromium picolinate monohydrate per kg per day (727 mg chromium per kg per day) for mice and of 2,400 mg chromium picolinate monohydrate per kg per day (300 mg chromium per kg per day) for rats in the long-term studies conducted by the NTP (2010).

In 2014, the EFSA Panel on Contaminants in the Food Chain (CONTAM) provided a Scientific Opinion regarding the risks to public health related to the presence of chromium in food and drinking water (EFSA 2014b). The CONTAM Panel derived a tolerable daily intake (TDI)[8] of 300 µg elemental chromium per kg body weight per day using a chronic, oral toxicity study in rats. This is equivalent to 18 mg chromium per day or 18,000 µg per day, based on a 60 kg-adult. While the EFSA (2014b) did not specifically address whether the new TDI supersedes the previous conclusion that chromium supplementation should not exceed the WHO recommendation of 250 µg chromium per day (EFSA 2009a,b), the Panel acknowledged that the TDI is well above the estimated combined exposure even when including the "significant exposure" from supplemental intake in adults (i.e., from fortified foods, foods or feed for particular nutritional uses [PARNUTS], and food supplements). The EFSA estimated supplemental intake to range from 910 µg per day for a typical intake up to 1,540 µg per day for an upper intake level. The 2014 Opinion also stated that there were "no human data that could be identified to perform a dose-response assessment of chromium or any chromium species for oral exposure."

Chinese Nutrition Society (CNS 2023). The CNS has not derived an UL for chromium.

[8] EFSA's definition of tolerable daily intake (TDI), in terms of food safety, is "the maximum amount of a chemical or contaminant that a person can consume every day over a lifetime without appreciable health risk." https://www.efsa.europa.eu/en/glossary/tolerable-daily-intake

Indian Council of Medical Research - National Institute of Nutrition (ICMR-NIN 2020). The ICMR-NIN has not derived an UL for chromium but noted that, "there has not been any evidence or adverse effects reported on chromium overload."

Korean Nutrition Society (KNS 2020). The KNS published its general approach to evaluating data for setting DRI values. The KNS has not derived an UL value for chromium.

CRN Recommendations

CRN previously derived an UL value for elemental chromium of 1,000 µg per day. The goal of the current chapter was to determine whether more recent human clinical data are available that might impact the conclusions published in the 3rd edition. While not all human clinical trials are specifically designed to evaluate adverse effects, no new trials were identified that reported any serious adverse effects with supplemental elemental chromium. Following CRN's methodology (see Methodology Chapter), and due to the lack of any known adverse effects for chromium, an HOI was established by CRN in this update. As with any assessment in which not all available data are reviewed, inherent uncertainties with the risk assessment and selection of the HOI are recognized.

CRN's safety methodology for deriving supplemental HOI values prioritizes data from human clinical studies when available. The table below summarizes the key human clinical studies considered in deriving the supplemental HOI value by CRN according to its principal points of departure for risk assessment (as described in the Methodology Chapter).[9]

[9] 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 methodology (e.g., duration, number of participants, randomization, etc.).

Studies Considered for the CRN UL for Chromium III in Adults

Reference	Study Design	Participant Description	No. of Subjects	Supplemental Dose(s) (µg/day)[a]	Duration[b]	NOAEL (µg/day)
Key studies from 3rd Edition						
Vrtovec et al. 2005	Double-blind, randomized, placebo-controlled crossover	Patients with type 2 diabetes	60	0, 1,000	6 months	1,000
Kleefstra et al. 2006	Double-blind, randomized, placebo-controlled	Patients with type 2 diabetes	46	0, 500, 1,000	6 months	1,000
Martin et al. 2006	Double-blind, randomized, placebo-controlled	Patients with type 2 diabetes	37	0, 1,000	6 months	1,000
Anderson et al. 1997a	Double-blind, placebo-controlled	Patients with type 2 diabetes	180	0, 200, 1,000	4 months	1,000
Campbell et al. 1997	Double-blind	Older men	18	< 1, 924	3 months	924
Campbell et al. 1999	Double-blind	Older men	18	< 1, 924	3 months	924

[a] Presented as µg elemental chromium. When applicable, doses were converted from µg test material (e.g., "chromium picolinate") to µg elemental chromium.
[b] Studies reporting duration in weeks were converted to months in this table based on 4 weeks per month.

ULs for chromium have not been established by authoritative agencies, such as IOM (2001) or EC SCF (2003), due to insufficient data from which to conduct a risk assessment (see *Official Reviews*). However, the EVM (2003) set a guidance level of 10,000 µg per day for total intake and the EFSA (2014b) derived a TDI value of 0.3 mg chromium per kg body weight per day. While the EFSA (2014b) did not discuss whether the TDI supersedes the previous maximum value added to foods (including supplements) of 250 µg per day established by the EFSA (2009a,b), the CONTAM

Panel acknowledged the significant contribution of chromium from supplements and confirmed that the total exposure remains below the TDI.

No serious adverse events have been associated with supplemental chromium in human clinical trials reviewed. In addition, supplemental chromium is poorly absorbed following ingestion. In its 3rd edition, CRN derived a supplemental UL of 1,000 µg elemental chromium per day based on clinical studies reviewed in the IOM (2005) draft monograph and discussed in other authoritative reviews. Available studies administering ~1,000 µg elemental chromium per day for a duration of 12 to 24 weeks did not report any adverse effects, though not all studies specified monitoring for such events (Anderson et al. 1997a; Vrtovec et al. 2005; Campbell et al. 1997, 1999; Kleefstra et al. 2006; Martin et al. 2006). In addition, the EVM guidance level for chromium has been established since 2003. Since that time, no new data have become available that identify any serious adverse effects in clinical trials with chromium. Therefore, the long-standing supplemental CRN UL is maintained and carried forward as an HOI. Based on the human studies available, 1,000 µg elemental chromium per day is selected as the supplemental NOAEL for adults following the CRN process. As described in CRN's Methods, if the supplemental intake dose-response relationship is identified from the strongest data and assessed conservatively, no additional uncertainty factor is needed (that is, the implicit UF is 1.0). Consistent with CRN's methodology, an UF of 1 is applied to yield an HOI of 1,000 µg per day for adults for supplemental elemental chromium III (any form).

This selection is further supported by the evaluation conducted by the EFSA (2014b) and its TDI of 0.3 mg chromium per kg body weight per day, which equates to 18 mg (18,000 µg) per day in a 60-kg adult. The lower CRN UL is due to differences in methodologies used by the EFSA (2014b), and the EVM (2003) for its guidance level, which relied on animal studies. CRN's current methodology prioritizes human data over animal toxicological data, when available.

Quantitative Summary for Chromium III in Adults

CRN (2026) UL, supplemental intake	1,000 µg/day
IOM (2001) UL, total intake	Not determined
EC SCF (2003) UL, total intake	Not determined
EFSA (2014b) TDI	300 µg/kg bw/day (i.e., 18,000 µg/day for a 60-kg adult)
EFSA (2009a,b), maximum added to foods (including food supplements)	250 µg/day
EVM (2003), guidance level, total intake	10,000 µg/day
CNS (2023)	Not determined
ICMR-NIN (2020)	Not determined
KNS (2020)	Not determined

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