The Director General

Maisons-Alfort, 2 July 2012

OPINION
of the French Agency for Food, Environmental and Occupational Health & Safety

on the assessment of the health risks from non-compliance with the parametric value for chromium in water intended for human consumption

ANSES undertakes independent and pluralistic scientific expert assessments.
ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.
It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are made public.

On 12 May 2011, ANSES received a formal request from the French Directorate General for Health (DGS) to conduct the following expert appraisal: health risks from non-compliance with exceeding the parametric value for chromium in water intended for human consumption (drinking water, DW).

1 BACKGROUND TO THE REQUEST

The parametric value of 50 µg/L of chromium in water intended for human consumption (drinking water, DW) was set in Annex I of the Order of 11 January 2007 concerning the parametric values for chemical and indicator parameters for raw water and water intended for human consumption mentioned in Articles R. 1321-2, R. 1321-3, R. 1321-7 and R. 1321-38 of the French Public Health Code.

2 ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 “Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (May 2003)”.

The expert appraisal falls within the sphere of competence of the Expert Committee (CES) on Water, which is leading the response to this Request, and the CES on Chemical and Physical Contaminants and Residues. ANSES entrusted the expert appraisal to the Working Group on Assessment of the health risks from non-compliance with drinking water parametric values.

The approach applied by the Working Group, a health risk assessment (HRA) of non-compliance with DW parametric values, was presented in the AFSSA report (2007).

Both the methodological and scientific aspects of the work were presented to the CESs between 07 February and 10 May 2012. They were adopted by the CES on Water at its meeting on 09 May 2012, and by the CES on Chemical and Physical Contaminants and Residues at its meeting on 10 May 2012.

3 ANALYSIS AND CONCLUSIONS OF THE CESS

3.1 Origin

Chromium (Cr) (Table I) is one of the transition metals. It is the 21st most abundant element in the Earth's crust, with concentrations of about 100 g/tonne (Barnhart, 1997). More than 40 minerals containing chromium have so far been identified. Although chromium can exhibit nine different oxidation states, from -II to +VI, the III state [Cr(III), CAS no. 16065-83-1] and the VI state [Cr(VI), CAS no. 18540-29-9] are the forms most commonly occurring in the environment. Virtually all the chromium found in rocks is of form III, with the most abundant mineral being chromite: $FeCr_2O_4$. Chromium in form III is highly stable.

Chromium(VI), the second most stable state, is rare in nature. Chromates (CrO_4^{2-}) and dichromates ($Cr_2O_7^{2-}$), the forms most commonly occurring in the environment, generally come from industrial or household waste (Barnhart, 1997). Chromium(VI) compounds are powerful antioxidants.

In this report, the word "chromium" refers to total chromium.

Elemental chromium, which is anthropogenic, is a shiny grey metal that is highly resistant to corrosion.

Table I. Physico-chemical properties of chromium

	Empirical formula	CAS No.	Molar mass (g/mol)	Density (g/cm^3)	Melting point (°C)	Boiling point (°C)	Solubility in water (g/L)
Metallic chromium	Cr	7440-47-3	52	7.1	1857	2672	Insoluble

Chromite is the only chromium ore exploited commercially. Chromium's uses are mainly related to its chemistry, its reactivity and its properties (Barnhart, 1997). Chromium compounds are used in industry:

- for the manufacture of metallic chromium and alloys (stainless steel), as well as for protecting various metals;
- as oxidants, catalysts and for the manufacture of other chromium compounds;
- as refractory products, due to the inert nature of chromium(III) oxides;
- as pigments in paint, glass, ceramics and textiles, in photography and for tanning hides;
- in wood preserving as a fixing agent for active substances, although recommendations were made at European level in 2007 to regulate the use of chromium(VI) in these products.

The use and environmental release of chromium(VI) are subject to regulatory restrictions that are described in Annex I.

3.2 Sources of water contamination

In the aquatic environment, chromium can come from soil erosion or atmospheric deposition. The main sources of anthropogenic contamination of water by chromium(III) and chromium(VI) are urban and industrial wastewater, sludge from water treatment plants and leachate from waste treatment facilities.

Chromium can also be found as a constituent or impurity in metallic materials used for products in contact with drinking water (PDW) in permanent facilities for the production, treatment and distribution of DW.

Stainless steels must assay at least 13% chromium (Order of 13 January 1976). The Order of 29 May 1997, as amended, sets maximum levels of chromium in some other metallic PDWs: 3% for carbon steel and 1% for uncoated cast iron. In addition, electroplated chromium coatings of connectors and accessories are permitted, regardless of the nature of the material on which they are applied.

As a result of cooperative work in the field of PDW regulation between four European Member States (France, Germany, Netherlands and United Kingdom, known as the 4MS), an acceptable contribution of 50% from metallic PDWs to the parametric value for chromium in DW (i.e. 25 µg/L) was proposed (4MS, 2011).

The work by the 4MS specifies that the chromium content in stainless steels must be between 16 and 27% (4MS, 2008). It sets maximum levels of chromium as a constituent of other metallic PDWs that are often stricter than the current regulations, such as those for carbon steel (1%). When chromium is not one of the authorised constituents, this work also sets maximum levels for chromium impurities (0.02% in general and 0.01% for tin-plated copper, 4MS, 2011).

Metallic PDWs, even if they comply with regulatory provisions, can leach chromium into water depending on:

- the composition and surface characteristics of the metal;
- the composition of the water;
- the design of the distribution system;
- the age of the distribution system;
- the residence time.

3.2.1 Behaviour in water

Speciation of chromium(VI) or chromium(III) depends primarily on total chromium concentrations, ligands available in the matrix and pH. Of the solid chromium compounds, only chromic oxide [Cr_2O_3, chromium(III)] is stable in an aqueous solution. Chromium hydroxides [$Cr(OH)_2^+$ and $Cr(OH)_3$, chromium(III)] and chromium oxides [CrO_2 and CrO_3, chromium(VI)] are unstable at environmental temperatures and concentrations (Beverskog et Puigdomenech, 1997). Figure 1 shows the stability diagram for soluble chromium compounds depending on the equilibrium potential and pH.

In water, chromium(III) is in the form of a cation which forms highly stable complexes with negatively-charged organic or inorganic ligands, or precipitated hydroxides. Above pH 6, chromium(III) may precipitate as amorphous chromium hydroxide [$Cr(OH)_3(s)$]. Chromium(III) in the aquatic environment has low mobility because of the low solubility of the hydroxides [$Cr(OH)_3$ and $(Cr,Fe)(OH)_3$] and their strong adsorption onto solids. Chromium(III) reaches its minimum solubility in the pH range from 7.5 to 8.5 (Sharma *et al.*, 2008).

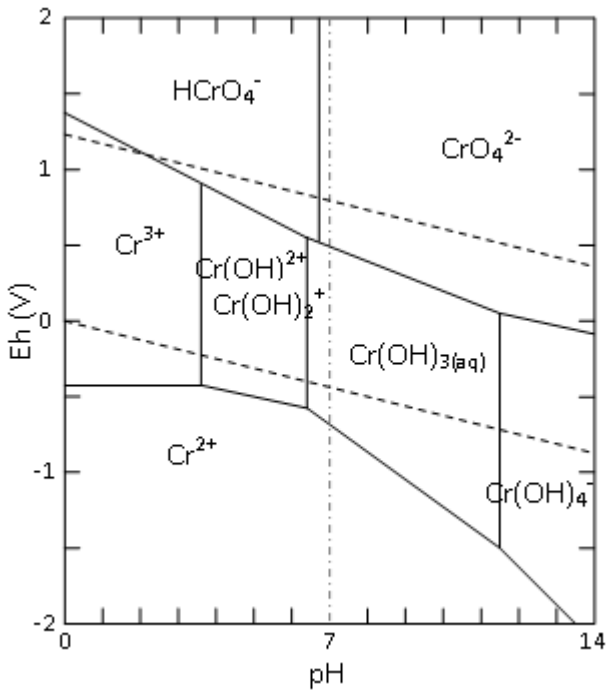

Figure 1. pH-potential diagram of predominance for dissolved chromium species at $[Cr_{(aq)}]_{total} \leq 10^{-6}$ molar and at 25°C according to Beverskog et Puigdomenech (1997).

Chromium(VI) exists in solution as monomer ions [chromic acid (H_2CrO_4), hydrogen chromate ($HCrO_4^-$) and chromate (CrO_4^{2-})] or dimer ions [dichromate ($Cr_2O_7^{2-}$)]. The monomer species colour the water yellow when the chromium(VI) concentration is greater than 1 mg/L. $HCrO_4^-$ ions predominate in acidic water whereas the CrO_4^{2-} form is in the majority when pH is neutral or higher. At low concentrations (< 1 mg/L), the predominant forms of chromium (VI), which are negatively charged, are only adsorbed on positively-charged surfaces, such as oxides and hydroxides of iron, manganese and aluminium. Adsorption is generally limited, and decreases with increasing pH.

In surface waters, the distribution between chromium(III) and chromium(VI) is highly variable. Relatively high concentrations of chromium(VI) can be observed in certain specific contexts (anthropogenic pollution).

Chromium(VI) is readily reduced by iron (II), dissolved sulfides and some organic compounds with sulfhydryl groups. Chromium(III) is oxidised rapidly by a large excess of manganese dioxide (MnO_2) and slowly by oxygen in natural water. In general, chromium(VI) salts are more soluble than those of chromium(III), making chromium(VI) more mobile (Sharma *et al.*, 2008; WHO, 2003).

Chromium(VI) is a strong oxidising agent that can react with organic matter or other reducing agents to form chromium(III). Chromium(III) may precipitate and settle depending on the water's pH and organic content. Thus, in surface waters rich in organic matter, chromium(VI) will be rapidly converted (US-EPA, 1998b).

3.3 Impact of water treatments on chromium levels

3.3.1 Clarification

Raw water pre-treatments that use oxidants (ozone) can transform chromium(III) into chromium(VI).

Coagulation with aluminium and iron [Fe(III)] salts can eliminate chromium(III), above pH 7.5, through the formation of precipitates of chromium hydroxide $Cr(OH)_3$ or chromium carbonate $(Cr_2(CO_3)_3$ co-precipitating with $Al(OH)_3$ or $Fe(OH)_3$. However, these two coagulants are not effective for the removal of chromium(VI) (Fatoki et Ogunfowokan, 2002; Sharma *et al.*, 2008).

Eliminating chromium(VI) by precipitation requires a preliminary step of reduction that can be done using iron(II) (Barrera-Díaz *et al.*, 2003; Lee et Hering, 2003; Philipot *et al.*, 1985; Zotter et Licsko, 1992). The advantage of iron(II) is its oxidation to iron(III) during the reduction of chromium(VI), with the iron(III) then serving as a coagulant (Zotter et Licsko, 1992). The iron(II) can be added as sulphates (Beukes *et al.*, 1999; Lee et Hering, 2003; Philipot *et al.*, 1985).

Eliminating chromium by coagulation-precipitation depends on the pH, and the process is ineffective if the metal is present as complexes or anions (e.g. CrO_4^{2-}) (Sharma *et al.*, 2008).

3.3.2 Adsorption

Various adsorbents have been studied for the removal of chromium(VI). Most of these studies were conducted at the laboratory scale and usually on highly contaminated water (Mohan et Pittman Jr, 2006). They mainly involved modified activated carbon (Selomulya *et al.*, 1999), sand coated with iron oxides (Bailey *et al.*, 1992) and granular ferric hydroxide (Asgari *et al.*, 2008).

There is no evidence that activated carbon is effective for reducing chromium levels for the purpose of DW production.

3.3.3 Ion exchange

Considering the positive charge of the ionic compounds of chromium(III) and the negative charge of those of chromium(VI), two ion exchange steps are necessary: a cation exchange resin for chromium(III) and an anion exchange resin for chromium(VI). In practice, there are no anion exchange resins specific to chromium(VI) because it competes with the majority anions in water.

3.3.4 Membrane retention

For chromium(VI), ultrafiltration has low efficiency (less than 10%) (Yoon *et al.*, 2009). The yield of nanofiltration ranges from 35 to 55% (Hafiane *et al.*, 2000; Yoon *et al.*, 2009) and that of reverse osmosis is greater than 95% (Mousavi Rad *et al.*, 2009; Yoon *et al.*, 2009).

3.3.5 Chlorination and oxidation

In water, free chromium(III) can be oxidised to chromium(VI) by free chlorine (Jiang *et al.*, 2006; Lai et McNeill, 2006; Saputro *et al.*, 2011) with transformation half-lives of 3 hours at pH 5 and 7, and 14 hours at pH 8 (Saputro *et al.*, 2011). Given the prolonged contact time in the drinking water distribution system, a free chlorine residual would enable the oxidation of chromium(III) to chromium(VI) (Lai et McNeill, 2006).

3.4 Analytical methods

3.4.1 Storage and pre-treatment of samples

3.4.1.1 Total chromium

Samples are collected in plastic or brown glass bottles and acidified with HNO_3 to a pH below 2. When conducting tests for the regulatory monitoring of water quality, the mineralisation step is not required (Circular DGS-SD7A no. 2003-445). Samples remain stable for 1 month.

3.4.1.2 Chromium(VI)

Sample storage conditions for assaying of chromium(VI) are more stringent: samples must be stored at around 4°C and analysed preferably within 24 hours of collection.

3.4.2 Analytical techniques

3.4.2.1 Total chromium

There are three standard methods for determining total chromium in water:

- NF EN ISO 11885: determination of selected elements by inductively coupled plasma optical emission spectrometry (ICP-OES);
- NF EN ISO 17294-2: application of inductively coupled plasma mass spectrometry (ICP-MS);
- NF EN 1233: determination of chromium – atomic absorption spectrometric method. This atomic absorption method is also described in the multi-element standard NF EN ISO 15586: Determination of trace elements using atomic absorption spectrometry with graphite furnace.

In France, 70 laboratories are authorised by the French Ministry of Health (and therefore accredited) for the determination of total chromium in DW, 73% of them for the ICP-OES method, 31% for ICP-MS and 21% for atomic absorption.

3.4.2.2 Chromium(VI)

The standard methods for determination of chromium(VI) are based on colorimetric reactions with 1,5-diphenylcarbazide. These methods may be manual or may rely on automated continuous flow:

- ISO 11083 and NF T 90-043: determination of chromium(VI) – molecular absorption spectrometry method (UV-visible);
- NF EN ISO 23913: determination of chromium(VI) – method using flow analysis (FIA and CFA) and spectrometric detection;
- NF EN ISO 18412: determination of chromium(VI) – photometric method for weakly contaminated water.

Only seven laboratories in France are approved for the determination of chromium(VI) in DW. There are about 30 accredited laboratories, mainly for molecular absorption spectrometry (88%).

3.4.3 Performance

The Order of 17 September 2003 states that for chromium, the precision, fidelity and limit of detection must not exceed 10% of the parametric value (i.e. 5 µg/L) and that the limit of quantification (LoQ) must not be greater than 10 µg/L.

3.4.3.1 Total chromium

The limits of quantification for total chromium depend on the methods used. They are usually around 1 µg/L with ICP-MS and from 5 to 10 µg/L with ICP-OES or atomic absorption. Figure 2 shows the LoQ distribution achieved by the laboratories approved for

the regulatory monitoring of water quality. The median LoQ is 5 µg/L and the average is 4 µg/L. All the approved laboratories have an LoQ that meets the requirements of the "method" Order of 17 September 2003.

The expanded intralaboratory uncertainties (k=2) are of the order of 10 to 20% whereas the interlaboratory uncertainties range from 30 to 40% depending on the level of concentration measured.

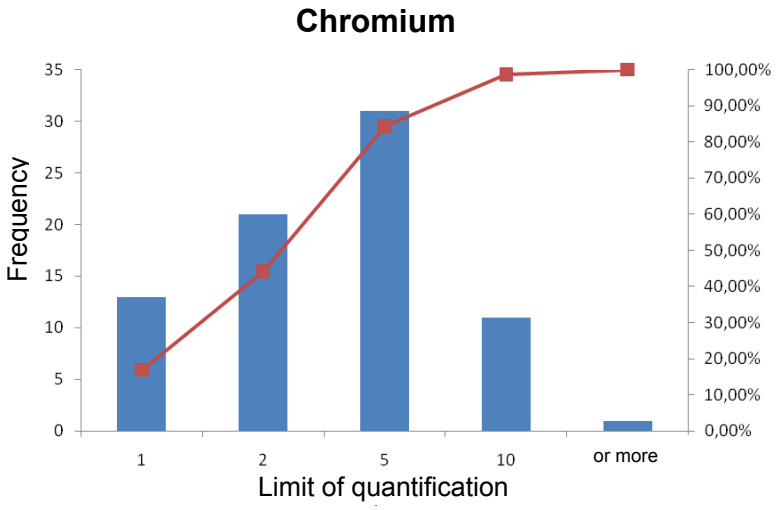

Figure 2. LoQ distribution for total chromium (µg/L) among laboratories approved for the regulatory monitoring of water quality.

3.4.3.2 Chromium(VI)

For chromium(VI), the median LoQ is 10 µg/L and the average is 12 µg/L. The intralaboratory uncertainties (k=2) are of the order of 10 to 15% while the interlaboratory uncertainties are around 20 to 30% depending on the level of concentration measured.

3.4.4 Interference

The interference encountered depends on the method used. It is mainly related to:

- spectral and non-spectral interference for instrumental methods. The laboratory's in-house quality control can usually deal with this interference in DW (internal standards, background correction, spectra studies, etc.);
- for the determination of chromium(VI), reducing agents, which may lead to results being underestimated; this interference is however very limited in the field of DW.

3.5 Exposure assessment

3.5.1 Dietary exposure

In France, two studies have been conducted to assess dietary exposure of the general population to numerous contaminants: the Total Diet Studies (TDS) 1 (Leblanc J.C., 2004) and 2 (Anses, 2011a; b; Noël *et al.*, 2012). In both cases, total chromium was assayed in food.

The data in the literature cannot be used to quantify the share of chromium(III) and chromium(VI) in food. A further study of chromium speciation in these foods has been initiated by ANSES.

3.5.1.1 Analytical methods used

According to the TDS 2 report, inorganic contaminants and minerals were screened for in all the food samples by an ICP-MS detection method after closed-vessel microwave

digestion, which has been validated and accredited by COFRAC. When concentrations were above the LoQ of 0.020 mg/kg, the average of the replicates tested (n=2) was used, combined with a measurement uncertainty (Anses, 2011a; Noël *et al.*, 2012).

3.5.1.2 Contamination of food with total chromium

Among the samples analysed in the TDS 2, only 5% had a chromium level lower than the limit of detection or the LoQ. The highest mean concentrations were found in oils (1.0 mg/kg), chocolate (0.87 mg/kg), butter (0.64 mg/kg) and margarine (0.59 mg/kg). The other groups all had mean concentrations of less than 0.5 mg/kg. For all food groups, the mean concentrations were higher than those found in the first TDS (by a factor of 5 on average). The TDS 2 report speculates that this increase could be related to the use of stainless steel equipment for milling samples (Anses, 2011a; Noël *et al.*, 2012).The estimate of the average levels of total chromium in foods, in mg/kg of fresh weight, is given in Annex II.

3.5.1.3 National dietary exposure

According to the TDS 2 report, the average intake of chromium in the French population is estimated to be 277 µg/day in adults and 223 µg/day in children (3 to 17 years old). These mean exposures are higher than those estimated by the TDS 1 (by a factor of 3-4) and for the European population (EFSA 2009b).

In adults, the main contributors to chromium intake are bread and dried bread products (8%), and alcoholic beverages (5% for both groups). In children, the main contributors to chromium intake are milk (9%) and pasta (6%).

The details of dietary intake (excluding water) of total chromium for the French child and adult population are given in Annex II.

3.5.2 Water contamination – SISE-Eaux database extraction

Data were extracted from the SISE-EAUX (Health & Environment Information System on Water) database for the period 1 January 2001 to 31 March 2011 according to the concept of logical distribution unit (DU) (at the consumer's tap or failing that, on leaving the plant). The results excluded from the raw data those below a LoQ strictly greater than 50 µg/L (3 results), non-quantified results relating to a LoQ strictly less than 0.5 µg/L (80 results) and 2579 outliers (input errors). This extraction identified 138,799 usable results with 138,445 relating to total chromium and 354 relating to chromium(VI). The results are expressed in micrograms of chromium per litre.

The results from the SISE-EAUX database, which overwhelmingly focus on the total chromium parameter, and the data from the literature, cannot be used to estimate the relative contributions of chromium(III) and chromium(VI).

Between 1 January 2001 and 31 March 2011, 14 cases of non-compliance in total chromium were reported out of the 138,445 results available. Concentrations measured in these non-compliant water samples ranged from 51 to 199 µg/L, with a median of 63 µg/L. The French Regional Health Agencies (ARS) concerned responded that these results did not seem robust.

Of the 138,445 results available for total chromium, 133,191 (96.2%) are below an LoQ. The histogram showing the number of results below a corresponding LoQ is given in Figure 3.

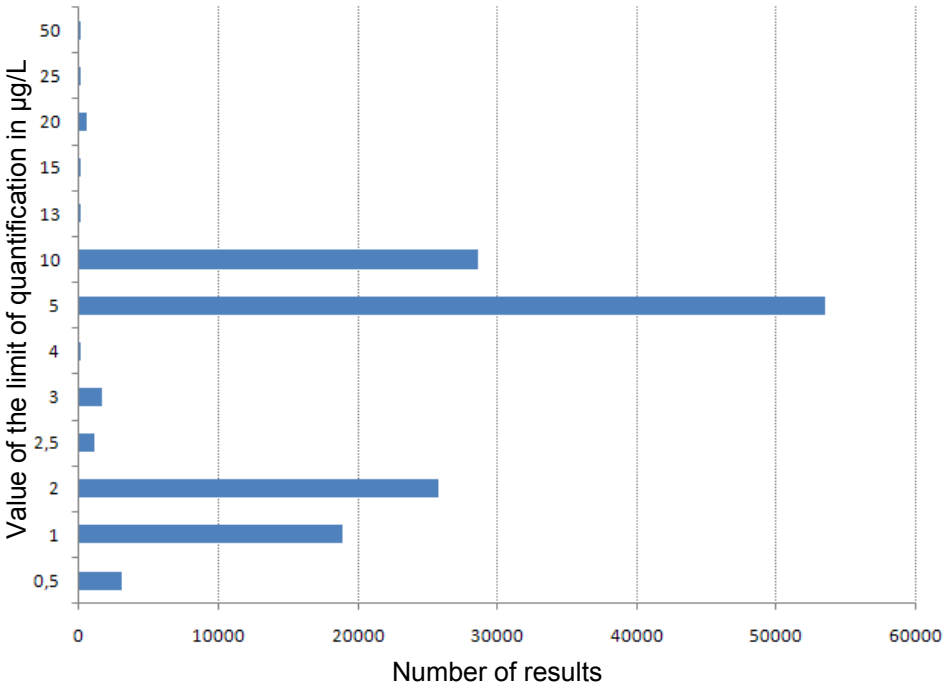

Figure 3. Histogram of the limits of quantification found in the SISE-Eaux database between January 2001 and March 2011 for the total chromium parameter

The data were processed according to three scenarios to take into account results below an LoQ:

- **Scenario S1:** values below an LoQ were considered equal to 0;
- **Scenario S2:** values below an LoQ were considered equal to half this limit;
- **Scenario S3:** values below an LoQ were considered equal to this limit.

Table II summarises the distribution of total chromium contamination in DW at the consumer's tap according to these three scenarios.

Table II. Distribution of the concentration of total chromium in water at the consumer's tap (µg/L)

	P5	P25	median	average	P75	P95
S1	0	0	0	0.2	0	0*
S2	0.5	1.0	2.5	2.5	2.5	5.0
S3	1.0	2.0	5.0	4.9	5.0	10.0

* 96% of results are below a limit of quantification

3.5.3 Contribution of water to dietary exposure to total chromium in France

Table IIIshows estimated daily intake (µg/day) and exposure (µg/kg bw/d) to total chromium in adults and children from consumption of water from the public distribution service, and water's contribution to average intake and average exposure.

These estimates were obtained by considering the results for tap water contamination relative to scenarios S1 and S3 when these are not quantified (these scenarios are described in Section 3.5.2). The average from the distribution of tap water contamination was used in these calculations of intake, exposure and contribution to total chromium.

Table III. Average, 5th and 95th percentiles of the distribution of total chromium intakes (µg/day) and exposure (µg/kg bw/d) from consumption of tap water, and average contribution (%) of tap water to daily intake and total exposure, in adults and children

Population	Adults		Children	
Scenario	S1	S3	S1	S3
Average daily intake	0.07	1.72	0.05	1.26
Average daily exposure	0.001	0.03	0.001	0.04
P5 Average intake	0.005	0.14	0.004	0.10
P5 Average exposure	0.000	0.002	0.000	0.003
P95 Average intake	0.29	7.42	0.17	4.42
P95 Average exposure	0.004	0.11	0.005	0.14
Contribution to average intake (%)	0.03	0.63	0.02	0.57
Contribution to average exposure (%)	0.03	0.63	0.02	0.54

The contribution of tap water to the average dietary exposure to total chromium is less than 1%.

3.6 Health effects via the oral route

Based on the work of the OEHHA (2011), the Working Group considers that the primary route of exposure to chromium via DW is ingestion.

3.6.1 Absorption – Distribution – Metabolism – Elimination

3.6.1.1 Absorption

Absorption of chromium by the oral route is low. Most studies report gastrointestinal absorption below 10% (Anderson *et al.*, 1983). Absorption varies according to:

- the oxidation state of the chromium: chromium(III) compounds are absorbed less than those of chromium(VI) (Anderson *et al.*, 1983; Collins *et al.*, 2010; Donaldson et Barreras, 1966; Fébel *et al.*, 2001; Kerger *et al.*, 1996);
- the chromium compound: soluble forms are absorbed more than insoluble forms (DiSilvestro et Dy, 2007; Finley *et al.*, 1996);
- the dose and frequency of administration (Anderson *et al.*, 1983; Kerger *et al.*, 1997).

Ingestion of chromium in a single dose causes a peak plasma concentration 90 minutes after ingestion (Kerger *et al.*, 1996).

Saliva and gastric juice are able to reduce chromium(VI) to chromium(III) by as much as several milligrams of chromium(VI) per day. Donaldson et Barreras (1966) have shown that, in humans, chromium reduction in the stomach decreased the proportion of chromium absorbed in the small intestine (urinary excretion after direct injection of chromium(VI) in the duodenum was about 10% compared with 2% for ingestion). *In vitro,* the reaction is complete in 10 to 20 minutes, with a half-reaction time of one minute (De Flora, 2000; De Flora *et al.*, 1997). Chromium(VI) reduction by gastric juice is increased during digestion (De Flora *et al.*, 1987; Kerger *et al.*, 1997; Proctor *et al.*, 2011). These authors therefore hypothesise that chromium(VI) is only absorbed when the reduction capacity of the gastrointestinal tract is exceeded.

This assumption is challenged by other authors (e.g. by Collins *et al.*, 2010; OEHHA, 2011; Stout *et al.*, 2009; Zhitkovich, 2011) who consider that a fraction of the chromium(VI) is absorbed unchanged, regardless of the initial concentration. They justify their position by

the differences in absorption, distribution, metabolism and elimination observed after exposure to chromium(VI) and after exposure to chromium(III).

3.6.1.2 Distribution

In humans, post-mortem analyses have shown that chromium is present in all organs with higher concentrations in the kidneys, liver, lungs, heart, pancreas and spleen (Schroeder *et al.*, 1962). Distribution studies in animals have confirmed this fairly ubiquitous chromium distribution in the body (ATSDR, 2008).

Ingestion of chromium(VI) causes an increase in chromium concentrations in the liver, spleen and kidneys, and in red blood cells (NTP, 2008b; Thomann *et al.*, 1994; Witmer *et al.*, 1991). After administration of chromium(III), increased plasma levels of chromium are observed (Kerger *et al.*, 1996).

Chromium(VI) in the form of chromate (CrO_4^{2-}) structurally resembles sulfate and phosphate. It is absorbed by cells through sulfate transporters (Collins *et al.*, 2010; Costa, 1997), while chromium(III), which is not a substrate for this transporter (Proctor *et al.*, 2002), can only enter cells by diffusion or endocytosis. Exposure to equivalent doses of chromium(VI) and chromium(III) leads to higher chromium concentrations in tissues with chromium(VI), which agrees with these transport mechanisms (Collins *et al.*, 2010; Costa et Klein, 2006).

Moreover, soluble chromium(VI) compounds are better at penetrating physiological barriers, particularly the mucosal surfaces, thus promoting systemic distribution compared with the less soluble or insoluble compounds whose action is more local (ATSDR, 2008; Costa et Klein, 2006).

3.6.1.3 Metabolism

Chromium(VI) is reduced to chromium(III) both inside and outside cells mainly under the action of ascorbate, glutathione and/or cysteine (Myers et Myers, 1998; Paustenbach *et al.*, 2003; Pratt et Myers, 1993; Zhitkovich, 2011). During this reduction, the chromium element goes through different transition states (chromium V and IV) to produce chromium(III) (Liu *et al.*, 1994; Liu *et al.*, 1997), which has a strong ability to form stable complexes with macromolecules (Norseth *et al.*, 1982; Warren *et al.*, 1981; Wiegand *et al.*, 1986; Yamamoto *et al.*, 1981).

Due to the low bioavailability of chromium(III) by the oral route, it has been suggested that extracellular reduction, mainly in the stomach, could have a protective effect with respect to the toxic and carcinogenic effects of chromium(VI) following oral exposure (De Flora, 2000; De Flora *et al.*, 1997; De Flora *et al.*, 1989; Paustenbach *et al.*, 2003; Proctor *et al.*, 2002).

Biological systems are unable to oxidise chromium(III) to chromium(VI), with the exception of bacteria producing hyperoxidised forms of manganese (Murray et Tebo, 2006).

3.6.1.4 Elimination

Chromium that has been ingested is primarily eliminated through the faeces. When chromium is absorbed, elimination is via urine (Bryson et Goodall, 1983; OEHHA, 2011; Yamamoto *et al.*, 1981). The urinary elimination half-life depends on the forms of chromium ingested (Kerger *et al.*, 1997; Kerger *et al.*, 1996).

3.6.2 Oral toxicity of chromium(VI)

The toxicity of chromium(VI) by ingestion mainly affects the stomach, liver, kidneys and blood cells. The clinical pictures in humans and animals are similar regardless of the chromium(VI) compound ingested (see below).

3.6.2.1 Chronic toxicity of chromium(VI)

No effects were reported in rats exposed to potassium chromate for one year by drinking water at doses of up to 3.6 mg Cr(VI)/kg bw/d (Mackenzie *et al.*, 1958).

In rodents exposed to chromium(VI) in drinking water, the chronic toxicity studies conducted by the NTP (2008b) found a lowest observed adverse effect level (LOAEL) equal to the lowest doses tested (0.24 mg Cr(VI)/kg bw/d for female rats and 0.38 mg Cr(VI)/kg bw/day for male and female mice); the effects observed concerned the liver (chronic inflammation of the liver in female rats, histiocytic cell infiltration in the liver of female mice) and gastrointestinal tract (diffuse epithelial hyperplasia in the duodenum of male and female mice, histiocytic cell infiltration in the mesenteric lymph nodes of male and female mice, cytoplasmic alteration of acinar epithelial cells in the pancreas of female mice). Similar effects were observed in other studies with LOAELs at or above those reported by the NTP (ATSDR, 2008; OEHHA, 2011; US-EPA, 2010).

In humans, chronic exposure to chromium(VI) via drinking water has been reported in China by Zhang et Li (1987). The effects related to this chronic ingestion, at estimated doses of around 0.57 mg Cr(VI)/kg bw/d, are gastrointestinal (mouth ulcers, diarrhoea, abdominal pain, dyspepsia and vomiting) and haematological effects (leukocytosis and immature neutrophils).

3.6.2.2 Mutagenicity and carcinogenicity of chromium(VI)

The carcinogenicity of chromium(VI) by inhalation in the workplace is proven (respiratory cancer) and has led to its classification as a human carcinogen by the IARC, US EPA and the European Union (Table IV).

Chromium(VI) induces genotoxicity both *in vitro* and *in vivo.* However, the mechanisms of carcinogenicity are not fully understood.

In the cell, chromium(VI) is reduced to chromium(III) through different transition states (chromium V and chromium IV). These intermediate forms result in the formation of reactive oxygen species that lead to various types of DNA lesions (IARC, 2012).

Table IV. Classification of chromium(VI) compounds for carcinogenicity

	European Union (2011)	IARC (2012)	US EPA (2010)
Chromium(VI) compounds	Depending on the compounds*, categories 1A substance known to have carcinogenic potential for humans 1B substance presumed to have carcinogenic potential for humans or 2 suspected as a human carcinogen	Group 1 Carcinogenic to humans	Class A Known human carcinogen

* With the exception of barium chromate

The chromium(III) formed also reacts with DNA inducing adducts, most of which are ternary adducts with ascorbate, cysteine or glutathione; the complex formed binds to DNA by phosphate (Guttmann *et al.*, 2008; IARC, 2012).

Studies of oral carcinogenicity in animals

Regarding oral carcinogenicity, an increased incidence of rare tumours of the epithelium of the oral cavity (buccal mucosa and tongue) was observed in male and female rats exposed to chromium(VI) in the form of sodium dichromate in drinking water for two years, at a concentration of 180 mg Cr(VI)/L (corresponding to 6-7 mg Cr(VI)/kg bw/d) (NTP, 2008b; Stout *et al.*, 2009). During this same NTP study, a significant increase in the

incidence of adenomas and carcinomas of the epithelium of the duodenum, jejunum and ileum (combined) was observed in male mice from 30 mg Cr(VI)/L (i.e. 2.4 mg Cr(VI)/kg bw/d) and in females from 60 mg Cr(VI)/L (i.e. 3.1 mg Cr(VI)/kg bw/d) ($p < 0.05$) (NTP, 2008b; Stout *et al.*, 2009).

The extrapolation to humans of effects observed in the NTP study (2008b) has been criticised by some authors (De Flora *et al.*, 2008; Proctor *et al.*, 2011) who argue that humans, through drinking water, are exposed to much lower doses than those used in studies with laboratory animals (by a factor of about 5000) and that at these doses all the chromium(VI) would therefore be reduced to chromium(III) before absorption.

Thompson *et al.* (2011) conducted a mechanistic study on mice exposed to sodium dichromate in drinking water for 90 days at concentrations of between 0.1 and 181 mg Cr(VI)/L. For these authors, the carcinogenicity of chromium(VI) by ingestion is unrelated to its genotoxic potential and is due to oxidative stress, villous cytotoxicity and a crypt hyperplasia observed in the mouse intestine (Thompson *et al.*, 2011).

For McCarroll *et al.* (2010), the available evidence on the genotoxicity of chromium(VI) supports the plausibility of a mutagenic mode of action.

Studies in humans

Very few studies have investigated the carcinogenic effects following chronic ingestion of chromium(VI) from consumption of drinking water. None have been able to show a causal relationship. Only association relationships have been found in studies conducted in China and Greece.

In China, through a retrospective analysis of causes of death, for the period 1970-1978, Zhang et Li (1987) reported increased mortality rates from cancer ("all causes", "stomach cancer" and "lung cancer") in the area of Jinzhou, where drinking water was contaminated by industrial discharges. These results were confirmed by Beaumont *et al.* (2008) after reconstruction of the history of the chromium(VI) water pollution episode and reanalysis of the data presented previously by Zhang et Li (1987) (relative risks for stomach cancer and lung cancer were respectively equal to 1.69 [1.12-2.44] and 1.78 [1.03-2.87]). However, methodological weaknesses mean that the published results should be considered with caution.

In Greece, the ecological study conducted by Linos *et al.* (2011) showed a significant increase in mortality from primary liver cancer in men and women (SMR = 1104 – CI95% = [405; 2403]), from genital cancer in women (SMR = 368 – CI95% = [119; 858]), and from lung cancer (SMR = 145 – CI95% = [101; 203]). These results were observed in a population living in an industrial area (municipality of Oinofita) and probably exposed for over 20 years; chromium(VI) concentrations measured in 2007 and 2008 ranged between 41 and 156 µg/L.

Overall, although the mechanisms of the oral carcinogenicity of chromium(VI) are not fully understood, oxidative stress does not appear to be the only mechanism involved. **Therefore, in the current state of knowledge, a non-threshold mechanism of action cannot be ruled out.**

3.6.2.3 Effects of chromium(VI) on reproduction and development

In rodents, some studies show effects on the male reproductive tract but two studies conducted by the NTP showed no treatment-related effects in similar conditions (NTP, 1996a; b). Conflicting data have also been reported in females.

The data obtained in rodents have shown that chromium(VI) has an impact on *in utero* development (Junaid *et al.*, 1996a; Junaid *et al.*, 1996b; NTP, 1996a; b; 1997).

In humans, no study has specifically investigated the effects on reproduction or development following oral exposure to chromium(VI) (ATSDR, 2008).

Some chromium(VI) compounds have been classified by the European Union for their toxicity to reproduction and development (EC Regulation 1272/2008 as amended).

3.6.3 Oral toxicity of chromium(III)

3.6.3.1 Sub-chronic and chronic toxicity of chromium(III)

In animals, conflicting results have been reported on changes in body weight in rats and mice subjected to sub-chronic and chronic oral exposure to chromium(III) compounds (ATSDR, 2008).

Changes in body weight were observed in rodents with LOAELs of 0.2 mg Cr(III)/kg bw/d in the form of chromium nicotinate, for exposure over 52 weeks (Shara *et al.*, 2007) and 40 mg Cr(III)/kg bw/d as chromium trichloride for exposure over 12 weeks (Bataineh *et al.*, 1997).

No adverse effects were demonstrated in male and female rats exposed to chromium oxide in the diet for 600 days up to the maximum dose tested of 1468 mg Cr(III)/kg bw/d (Ivankovic et Preussmann, 1975), nor in rats exposed to chromium chloride in drinking water for one year up to the maximum dose of 3.6 mg Cr(III)/kg bw/d (Mackenzie *et al.*, 1958). The NTP's chronic toxicity study in rats and mice exposed to chromium picolinate in the diet did not find any significant decrease in body weight in rats and mice (NTP, 2008a).

3.6.3.2 Mutagenicity and carcinogenicity of chromium(III)

In the cell, chromium(III) can react with DNA to produce different types of lesions. However, as stated by the IARC (2012), the cell wall is almost impermeable to chromium(III), and this could explain the conflicting results observed in the various tests conducted *in vitro* and *in vivo*. Efsa (2010) concluded that chromium(III) was not genotoxic *in vivo,* nor carcinogenic.

A toxicity study by the NTP (2008a) showed an increased incidence of preputial gland neoplasms in male rats. No increase in tumours was observed in female rats or male or female mice. The NTP (2008a) therefore considers that chromium(III) cannot be classified as a carcinogen. In the study by Ivankovic et Preussmann (1975), no carcinogenic effect was demonstrated in male and female rats exposed to chromium(III) in the diet for 600 days.

No epidemiological study on the carcinogenicity of chromium(III) in humans is available.

Chromium(III) has not been classified for its carcinogenicity by the US EPA or the European Union. According to the IARC, it is not classifiable as to its carcinogenicity to humans (Group 3).

3.6.3.3 Effects of chromium(III) on reproduction and development

In animals, conflicting results have been reported for the effects of chromium(III) on reproduction or development. It is therefore impossible to conclude with any certainty (Bataineh *et al.*, 1997; Elbetieha et Al-Hamood, 1997; NTP, 2008a; Shara *et al.*, 2005).

For humans, there is no evidence that chromium(III) has an effect on development or reproduction (ATSDR, 2008).

3.6.4 Chromium(III) as an essential element

It has been suggested that chromium is an essential element for rats (Schwarz et Mertz, 1959), and for humans (Jeejebhoy, 1977). However, this point remains controversial (ATSDR, 2008). In 2010, EFSA concluded that the use of chromium(III) as a food complement and/or supplement was not of concern provided that this intake did not exceed 250 µg/day, the maximum value for taking chromium complements and/or supplements proposed by the WHO (1996). For humans, the recommended daily population reference intakes (PRI) for chromium are between 40 µg/day (Directive 2008/100/EC) and 120 µg/day (FDA, 2009) for adult subjects.

3.7 Clinical deficiencies or insufficient intakes of chromium are rare in the general population. Some cases have been observed in patients fed artificially for a long period. The TDS 2 report adds that: "*The symptoms are an alteration in the use of glucose and impaired tolerance of it (alteration in the number of insulin receptors and their capacity for binding), an alteration in lipid metabolism, an alteration in nitrogen metabolism, and weight loss. In cases of severe deficiency, neurological effects may be observed. In children, no deficiency in chromium has been described except in cases of severe protein-energy malnutrition. The population reference intake is 50-70 µg CrIII/day for adults (Roussel, 2001). It is difficult to suggest a population reference intake for children in view of the uncertainty concerning both their needs and the risks of deficiency.*" In humans, dietary supplementation with chromium(III) is sometimes recommended to help weight loss, although the role of chromium is controversial (Anderson, 1998; Trent et Thieding-Cancel, 1995). Oral human toxicity values

3.7.1 Oral human toxicity values for chromium(VI)

US EPA

In 1998, the US EPA established an oral reference dose (RfD) of 3 µg/kg bw/d for the non-carcinogenic effects of chromium(VI), based on the study by Mackenzie *et al.* (1958) in rats exposed via drinking water for 1 year. An uncertainty factor of 900 (10 for interspecies variability, 10 for intraspecies variability, 3 for an insufficient study duration, and 3 in view of the results in humans from the study by Zhang et Li (1987)) was applied to the adjusted no observed adverse effect level (NOAEL) of 2.5 mg/kg bw/day. This value is considered to have a low degree of confidence.

In 2010, the US EPA adopted an oral RfD of 0.9 µg/kg bw/d for the non-carcinogenic effects of chromium(VI) based on the benchmark dose (BMD) modeling of data from the study by the NTP (2008b). A $BMDL_{10}$ of 0.09 mg/kg bw/d was calculated based on the incidence of diffuse epithelial hyperplasia in the duodenum of female mice. An uncertainty factor of 100 was applied to this value (10 for interspecies variability and 10 for intraspecies variability).

In the same report, the US EPA also established an oral cancer slope factor of 0.5 $(mg/kg\ bw/d)^{-1}$ from the study by the NTP (2008b). The slope factor was derived from the BMD for incidences of small intestinal neoplasms in male mice, and then extrapolated to humans by allometric adjustment.

RIVM

In 2001, the RIVM established a provisional tolerable daily intake (TDI) of 5 µg/kg bw/d for chromium(VI), based on the toxicity study in rats by Mackenzie *et al.* (1958). An uncertainty factor of 500 (10 for interspecies variability, 10 for intraspecies variability, 5 for an insufficient study duration) was applied to the adjusted NOAEL of 2.4 mg/kg bw/d.

ATSDR

A minimal risk level (MRL) for chromium(VI) was set at 1 µg/kg bw/d by the ATSDR (2008) for the non-carcinogenic oral effects. The study used was that of the NTP (2008b). This study enabled a BMD modeling for ingestion ($BDML_{10}$ of 0.09 mg/kg bw/d) for diffuse epithelial hyperplasia in the duodenum of female mice. An uncertainty factor of 100 (10 for interspecies variability and 10 for intraspecies variability) was applied to obtain the reference value.

OEHHA

In 2011, the OEHHA established an oral RfD of 0.2 µg/kg bw/d for the non-carcinogenic effects of chromium(VI) on the basis of the toxicity study by the NTP (2008b). An uncertainty factor of 1000 (10 for using a LOAEL, 10 for interspecies variability and 10 for intraspecies variability) was applied to the LOAEL of 0.2 mg/kg bw/d for chronic inflammation and fatty liver in female rats.

The OEHHA also established a cancer slope factor of 0.5 $(mg/kg\ bw/d)^{-1}$ for chromium(VI), based on the study by the NTP (2008b). A $BMDL_{10}$ of 1.2 mg/kg bw/d was calculated from the experimental data for the combined incidences of carcinomas and adenomas of the small intestine in male mice. This value was then extrapolated to humans by dosimetric adjustment to obtain the slope factor.

WHO

In a draft report, the WHO established a tolerable daily intake of 1 µg/kg bw/d of chromium(VI) for the non-carcinogenic oral effects. The study used was that of the NTP (2008b). This study enabled a BMD modeling for ingestion ($BDML_{10}$ of 0.094 mg/kg bw/d) from diffuse epithelial hyperplasia in the duodenum observed in female mice. An uncertainty factor of 100 (10 for interspecies variability and 10 for intraspecies variability) was applied to obtain the reference value.

In the same interim report, the WHO established a cancer slope factor of 0.5 $(mg/kg\ bw/d)^{-1}$ for the carcinogenic effects of chromium(VI) by adopting the combined incidences of carcinomas and adenomas of the small intestine of male mice obtained in the study by the NTP (2008b). The $BMDL_{10}$ calculated by the US-EPA (2010) were extrapolated to humans by dosimetric adjustment.

Table V summarises the oral human toxicity values established for the non-carcinogenic effects of chromium(VI).

Table V. Oral human toxicity values for the non-carcinogenic effects of chromium(VI)

Source	Value	Study	Method	Population	Critical effects
ATSDR (2008)	1 µg/kg bw/d	NTP, 2008b	Benchmark dose + Uncertainty factor	Female mice	Diffuse epithelial hyperplasia in the duodenum
OEHHA (2011)	0.2 µg/kg bw/d	NTP, 2008b	LOAEL + Uncertainty factor	Female rats	Chronic inflammation, fatty liver
WHO (2011a)	1 µg/kg bw/d	NTP, 2008b	Benchmark dose + Uncertainty factor	Female mice	Diffuse epithelial hyperplasia in the duodenum
RIVM (2001)	5 µg/kg bw/d	Mackenzie *et al.*, 1958	NOAEL+ Uncertainty factor	Rats	No observed effect
US-EPA (1998a)	3 µg/kg bw/d	Mackenzie *et al.*, 1958	NOAEL+ Uncertainty factor	Rats	No observed effect
US-EPA (2010)	0.9 µg/kg bw/d	NTP, 2008b	Benchmark Dose + Uncertainty factor	Female mice	Diffuse epithelial hyperplasia in the duodenum

Table VI summarises the oral human toxicity values established for the carcinogenic effects of chromium(VI).

Table VI. Oral human toxicity values for the carcinogenic effects of chromium(VI)

Source	Slope factor	Study	Method	Population	Critical effects
OEHHA (2011)	0.5 $(mg/kg\ bw/d)^{-1}$	NTP, 2008b	Benchmark dose	Male mice	Adenomas and carcinomas of the small intestine
US-EPA (2010)	0.5 $(mg/kg\ bw/d)^{-1}$	NTP, 2008b	Benchmark dose	Male mice	Adenomas and carcinomas of the small intestine
WHO (2011a)	0.5 $(mg/kg\ bw/d)^{-1}$	NTP, 2008b	Benchmark dose	Male mice	Adenomas and carcinomas of the small intestine

3.7.2 Oral human toxicity values for chromium(III)

US EPA

In 1998, the US EPA established an oral RfD for chromium(III) of 1500 µg/kg bw/d based on the study by Ivankovic and Preussmann (1975). An uncertainty factor of 1000 (10 for interspecies variability, 10 for intraspecies variability and 10 for the weakness of the data) was applied to the NOAEL of 1468 mg/kg bw/d.

RIVM

In 2001, the RIVM established a TDI of 5 µg/kg bw/d for the non-carcinogenic effects of soluble chromium(III) compounds by ingestion. This value is derived from an NOAEL of 2.5 mg/kg bw/d for rats exposed to chromium(III) (as $CrCl_3$) in drinking water for one year (Mackenzie *et al.*, 1958). An uncertainty factor of 500 was applied (10 for interspecies variability, 10 for intraspecies variability and 5 for insufficient study duration). Given that the oral toxicity of insoluble chromium(III) compounds is approximately 1000 times lower than that of soluble chromium(III) compounds, a TDI of 5000 µg/kg bw/d was chosen for the insoluble chromium(III) compounds.

Table VII summarises the oral human toxicity values established for the non-carcinogenic effects of chromium(III).

Table VII. Oral human toxicity values for the non-carcinogenic effects of chromium(III)

Source	Value	Study	Method	Population	Critical effects
RIVM (2001) Soluble compounds	5 µg/kg bw/d	Mackenzie *et al.*, 1958	NOAEL + Uncertainty factor	Rats	No observed effect
RIVM (2001) Insoluble compounds	5000 µg/kg bw/d	Mackenzie *et al.*, 1958	NOAEL + Uncertainty factor	Rats	No observed effect
US-EPA (1998b)	1500 µg/kg bw/d	Ivankovic et Preussmann, 1975	NOAEL + Uncertainty factor	Rats	No observed effect

3.8 Reference values in water intended for human consumption

In France, the parametric value for total chromium in the water supply has been set at 50 µg/L by the Public Health Code.

Several recommendations and parameter values are found in the literature. These values are shown in Table VIII

Table VIII. Reference values for chromium in DW proposed by different agencies

Directive 98/83/EC Annex I.B.	WHO (2011b)	US EPA	Health Canada	OEHHA (2011)	
Total chromium	Total chromium	Total chromium	Total chromium	Chromium(VI) Carcinogenic effects	Chromium(VI) Non-carcinogenic effects
50 µg/L	GV (P): 50 µg/L	MCL: 100 µg/L	MAC: 50 µg/L	PHG: 0.02 µg/L	Concentration offering protection for health* 4.1 µg/L (adults) 2.4 µg/L (children)

GV (P): Provisional guideline value
MCL: Maximum Contaminant Level
MAC: Maximum Acceptable Concentration
PHG: Public Health Goal
* Based on water consumption of 0.039 L/kg bw/d for adults and 0.067 L/kg bw/d for children (Kahn et Stralka, 2009; US-EPA, 2008)

WHO

When the guideline value was established in 1958, no adequate toxicity study was available to provide a NOAEL. The value originally proposed of 50 µg/L for chromium(VI) for health concerns was extended to total chromium because of difficulties in analysing chromium(VI). In the fourth edition of the guidelines for quality of DW, the WHO (2011b) indicates that this value is provisional because of uncertainties in the toxicological database.

US EPA

In 1987, the US EPA set the standard for total chromium in DW at 100 µg/L. Following the work of the NTP (2008b), a new assessment of the health risks associated with ingestion of chromium(VI) is underway (US-EPA, 2010); the US EPA announced the possibility of revising the standard for chromium in DW following this work.

Health Canada

In Canada, the standard of 50 µg/L for total chromium in DW was established in 1979 and updated in 1986 (Health Canada, 1986; 2010). This value is proposed for total chromium, despite the harmful effects of chromium being attributed to chromium(VI), taking into account that chromium(III) may be oxidized to chromium(VI) during drinking water treatment or in the water distribution system (Health Canada, 1986). In its 2010 guidelines for drinking water quality, Health Canada announced an upcoming review of the chromium value (Health Canada, 2010).

OEHHA

In July 2011, the OEHHA proposed a guideline value of 0.02 µg/L for chromium(VI) in DW. This concentration was established on the basis of non-threshold carcinogenic effects by ingestion and inhalation, taking into account the greater susceptibility of young children. This value is a public health objective.

In the same report, after calculating a TDI of 0.2 mg/kg bw/d for non-carcinogenic effects (see Section 3.7.1), the OEHHA (2011) estimated the concentrations of chromium(VI) in DW considered to be health-protective. For adults, this concentration is 4.1 µg/L using the 95th percentile of water consumption, or 0.039 L/kg bw/d (Kahn et Stralka, 2009; US-EPA, 2008). For children this concentration is 2.4 µg/L with water consumption of 0.067 L/kg bw/d.

The standard in force in California (Maximum Contaminant Level) is 50 µg/L of total chromium. The establishment of a limit for chromium(VI) is under consideration.

3.9 Assessment of the health risks from non-compliance with the parametric value for chromium in DW

As the oral toxicity of chromium(VI) is of greater concern than that of chromium(III), the WG decided to conduct the health risk assessment based on the toxicity of chromium(VI).

3.9.1 Choice of the human toxicity value

The WG considered both types of chromium(VI) effects by the oral route: non-carcinogenic (threshold) and carcinogenic (no threshold). Two values were therefore selected:

- for non-carcinogenic effects, the TDI selected is **1 µg/kg bw/d,** as proposed, provisionally, after a benchmark dose approach, by the ATSDR (2008), US EPA (2010) and WHO (2011a);
- for carcinogenic effects, the slope factor applied is **0.5 (mg/kg bw/d)$^{-1}$**, as proposed by the OEHHA (2011) and provisionally by the US EPA (2010) and WHO (2011a).

3.9.2 Characterisation of the health risk associated with ingestion of drinking water

The health risks associated with chromium(VI) in drinking water were characterised on the basis of daily water consumption of 2 L, a body weight of 60 kg and a lifetime exposure of 70 years, following the methodology established by the Agency (Afssa, 2007). As exposure to chromium(VI) through water and food has not been characterised at the national level, for non-carcinogenic effects, the share of the TDI allocated to exposure from water was set by default to 20% of the TDI, following the recommendations of the OMS (2011).

Thus, based on the TDI for chromium(VI), the maximum concentration of chromium(VI) without non-carcinogenic effects would be **6 µg/L**.

The level of individual excess risk for the carcinogenic effects of chromium(VI) associated with this concentration would be **1.10^{-4}**.

The proportion of chromium(VI) relative to the total chromium concentration has not been measured in DW in France. To provide an estimate of the health risks associated with ingestion of chromium in DW at the parametric value and at the measured concentrations, expressed as total chromium, several assumptions about the proportion of chromium(VI) were developed. The resulting risk characterisations are listed in Annex III.

3.10 Conclusion and recommendations

The CES on Water and the CES on Chemical and Physical Contaminants and Residues:

- find that exceeding the parametric value of 50 µg/L set for the "total chromium" parameter in DW is not acceptable;
- believe that the parametric value for chromium should be revised, mainly because of the effects potentially induced by chromium(VI);
- recommend, as soon as possible:
  - that the laboratories authorised for state water- quality control of DW significantly lower the limit of quantification for total chromium and chromium(VI) to values of around a tenth of a µg/L;
  - a campaign to measure total chromium and chromium(VI) in DW with these new limits of quantification, to characterise population exposure to chromium(VI). Samples should be taken at the consumer's tap before and after allowing water to flow, and the sampling plan should include the sites most

susceptible to corrosion and low-mineralised water, especially in the DROM-COMs[1];

- a study of chromium speciation in foods, in order to characterise the exposure of the French population through food and to calculate the share of exposure attributable to drinking water.

The CES on Water and the CES on Chemical and Physical Contaminants and Residues consider that a maximum concentration of 6 µg/L for chromium(VI) would be a provisional realistic objective. However, given the current analytical difficulties associated with measuring such a low concentration of chromium(VI), total chromium could be measured first. If this threshold of 6 µg/L of total chromium were exceeded, additional analysis would then be necessary to measure the proportion of chromium(VI).

4 AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety adopts the conclusions and recommendations of the CES on Water and the CES on Chemical and Physical Contaminants and Residues.

The Director General

Marc Mortureux

KEYWORDS

Chromium – Chromium(VI) – Water intended for human consumption

BIBLIOGRAPHY

Publications

4MS (2008) Procedure for the acceptance of metallic materials used for products in contact with drinking water.

4MS (2011) Acceptance of metallic materials used for products in contact with drinking water.

Afssa (2007) Evaluation des risques sanitaires liés aux situations de dépassement des limites et références de qualité des eaux destinées à la consommation humaine. Tome I. Agence française de sécurité sanitaire des aliments. Maisons-Alfort.

Anderson RA (1998) Effects of chromium on body composition and weight loss. *Nutrition Reviews* 56, 266-270.

Anderson RA, Polansky MM, Bryden NA, Patterson KY, Veillon C et Glinsmann WH (1983) Effects of chromium supplementation on urinary Cr excretion of human subjects and correlation of Cr excretion with selected clinical parameters. *Journal Nutr* 113, 276-281.

Anses (2011a) Étude de l'alimentation totale française 2 - Tome 1. Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. http://www.anses.fr/Documents/PASER2006sa0361Ra1.pdf. Maisons-Alfort.

Anses (2011b) Étude de l'alimentation totale française 2 - Tome 2. Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. http://www.anses.fr/Documents/PASER2006sa0361Ra2.pdf. Maisons-Alfort.

[1] France's overseas territories (*Département et région d'outre mer – collectivité d'outre mer*).

Asgari AR, Vaezi F, Nasseri S, Dördelmann O, Mahvi AH et Fard ED (2008) Removal of hexavalent chromium from drinking water by granular ferric hydroxide. *Iranian Journal of Environmental Health Science and Engineering* 5, 277-282.

ATSDR (2008) Draft - Toxicological profile for chromium. Draft. Agency for toxic substances and disease registry. Atlanta.

Bailey RP, Bennett T et Benjamin MM (1992) Sorption onto and recovery of Cr(VI) using iron-oxide-coated sand. *Water Science and Technology* 26, 1239-1244.

Barnhart J (1997) Occurrences, uses and properties of chromium. *Regulatory Toxicology and Pharmacology* 26, S3-S7.

Barrera-Díaz C, Palomar-Pardavé M, Romero-Romo M et Martínez S (2003) Chemical and electrochemical considerations on the removal process of hexavalent chromium from aqueous media. *Journal of Applied Electrochemistry* 33, 61-71.

Bataineh H, al-Hamood MH, Elbetieha A et Bani Hani I (1997) Effect of long-term ingestion of chromium compounds on aggression, sex behavior and fertility in adult male rat. *Drug Chem Toxicol* 20, 133-149.

Beaumont JJ, Sedman RM, Reynolds SD, Sherman CD, Li LH, Howd RA, Sandy MS, Zeise L et Alexeeff GV (2008) Cancer mortality in a Chinese population exposed to hexavalent chromium in drinking water. *Epidemiology* 19, 12-23.

Beukes JP, Pienaar JJ, Lachmann G et Giesekke EW (1999) The reduction of hexavalent chromium by sulphite in wastewater. *Water SA* 25, 363-370.

Beverskog B et Puigdomenech I (1997) Revised pourbaix diagrams for chromium at 25-300 °C. *Corrosion Science* 39, 43-57.

Bryson WG et Goodall CM (1983) Differential toxicity and clearance kinetics of chromium(III) or (VI) in mice. *Carcinogenesis* 4, 1535-1539.

Collins BJ, Stout MD, Levine KE, Kissling GE, Melnick RL, Fennell TR, Walden R, Abdo K, Pritchard JB, Fernando RA, Burka LT et Hooth MJ (2010) Exposure to hexavalent chromium resulted in significantly higher tissue chromium burden compared with trivalent chromium following similar oral doses to male F344/N rats and female B6C3F1 mice. *Toxicological Sciences* 118, 368-379.

Costa M (1997) Toxicity and carcinogenicity of Cr(VI) in animal models and humans. *Critical Reviews in Toxicology* 27, 431-442.

Costa M et Klein CB (2006) Toxicity and carcinogenicity of chromium compounds in humans. *Critical Reviews in Toxicology* 36, 155-163.

De Flora S (2000) Threshold mechanisms and site specificity in chromium(VI) carcinogenesis. *Carcinogenesis* 21, 533-541.

De Flora S, Badolati GS, Serra D, Picciotto A, Magnolia MR et Savarino V (1987) Circadian reduction of chromium in the gastric environment. *Mutation Research Letters* 192, 169-174.

De Flora S, Camoirano A, Bagnasco M, Bennicelli C, Corbett GE et Kerger BD (1997) Estimates of the chromium(VI) reducing capacity in human body compartments as a mechanism for attenuating its potential toxicity and carcinogenicity. *Carcinogenesis* 18, 531-537.

De Flora S, D'Agostini F, Balansky R, Micale R, Baluce B et Izzotti A (2008) Lack of genotoxic effects in hematopoietic and gastrointestinal cells of mice receiving chromium(VI) with the drinking water. *Mutation Research/Reviews in Mutation Research* 659, 60-67.

De Flora S, Serra D, Camoirano A et Zanacchi P (1989) Metabolic reduction of chromium, as related to its carcinogenic properties. *Biological Trace Element Research* 21, 179-187.

DiSilvestro RA et Dy E (2007) Comparison of acute absorption of commercially available chromium supplements. *Journal of Trace Elements in Medicine and Biology* 21, 120-124.

Donaldson RM, Jr. et Barreras RF (1966) Intestinal absorption of trace quantities of chromium. *Journal of Laboratory and Clinical Medicine* 68, 484-493.

Efsa (2010) Scientific opinion on the safety of trivalent chromium as a nutrient added for nutrional purposes to foodstuffs for particular nutritional uses and foods intended for the general population (including food supplements). European food safety authority. Parma.

Elbetieha A et Al-Hamood MH (1997) Long-term exposure of male and female mice to trivalent and hexavalent chromium compounds: effect on fertility. *Toxicology* 116, 39-47.

Fatoki OS et Ogunfowokan AO (2002) Effect of coagulant treatment on the metal composition of raw water. *Water SA* 28, 293-298.

FDA (2009) Guidance for industry: a food labeling guide. Food and drug administration. College Park.

Fébel H, Szegedi B et Huszár S (2001) Absorption of inorganic, trivalent and hexavalent chromium following oral and intrajejunal doses in rats. *Acta Veterinaria Hungarica* 49, 203-209.

Finley BL, Scott PK, Norton RL, Gargas ML et Paustenbach DJ (1996) Urinary chromium concentrations in humans following ingestion of safe doses of hexavalent and trivalent chromium: implications for biomonitoring. *Journal of Toxicology and Environmental Health* 48, 479-499.

Guttmann D, Poage G, Johnston T et Zhitkovich A (2008) Reduction with glutathione is a weakly mutagenic pathway in chromium(VI) metabolism. *Chemical Research in Toxicology* 21, 2188-2194.

Hafiane A, Lemordant D et Dhahbi M (2000) Removal of hexavalent chromium by nanofiltration. *Desalination* 130, 305-312.

Health Canada (1986) Le chrome. Health Canada.

Health Canada (2010) Guidelines for Canadian drinking water quality. Health Canada.

IARC (2012) Chromium (VI) compounds. IARC Monographs. International Agency for Research Research on Cancer. 100 C.

INERIS (2011) Chrome et ses composés. Institut national de l'environnement industriel et des risques. France.

Ivankovic S et Preussmann R (1975) Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long-term feeding experiments in rats. *Food and Cosmetics Toxicology* 13, 347-351.

Jeejebhoy (1977) Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition. *The American Journal of Clinical Nutrition* 30, 531-538.

Jiang H, Rao L, Zhang Z et Rai D (2006) Characterization and oxidation of chromium(III) by sodium hypochlorite in alkaline solutions. *Inorganica Chimica Acta* 359, 3237-3242.

Junaid M, Murthy RC et Saxena DK (1996a) Embryo- and fetotoxicity of chromium in pregestationally exposed mice. *Bulletin of Environmental Contamination and Toxicology* 57, 327-334.

Junaid M, Murthy RC et Saxena DK (1996b) Embryotoxicity of orally administered chromium in mice: Exposure during the period of organogenesis. *Toxicology Letters* 84, 143-148.

Kahn HD et Stralka K (2009) Estimated daily average per capita water ingestion by child and adult age categories based on USDA's 1994-1996 and 1998 continuing survey of food intakes by individuals. *Journal of Exposure Science and Environmental Epidemiology* 19, 396-404.

Kerger BD, Finley BL, Corbett GE, Dodge DG et Paustenbach DJ (1997) Ingestion of chromium(VI) in drinking water by human volunteers: absorption, distribution, and excretion of single and repeated doses. *Journal of Toxicology and Environmental Health* 50, 67-95.

Kerger BD, Paustenbach DJ, Corbett GE et Finley BL (1996) Absorption and elimination of trivalent and hexavalent chromium in humans following ingestion of a bolus dose in drinking water. *Toxicology and Applied Pharmacology* 141, 145-158.

Lai H et McNeill LS (2006) Chromium redox chemistry in drinking water systems. *Journal of Environmental Engineering* 132, 842-851.

Leblanc J.C. VP, Guérin T., Volatier J.L. (2004) Etude de l'alimentation totale française. Mycotoxines, minéraux et éléments traces. http://www.anses.fr/Documents/PASER2006sa0361Ra2.pdf.

Lee G et Hering JG (2003) Removal of chromium(VI) from drinking water by redox-assisted coagulation with iron(II). *Journal of Water Supply: Research and Technology - AQUA* 52, 319-332.

Linos A, Petralias A, Christophi CA, Christoforidou E, Kouroutou P, Stoltidis M, Veloudaki A, Tzala E, Makris KC et Karagas MR (2011) Oral ingestion of hexavalent chromium through drinking water and cancer mortality in an industrial area of Greece - An ecological study. *Environmental Health* 10, 50.

Liu KJ, Jiang J, Swartz HM et Shi X (1994) Low-frequency EPR detection of chromium(V) formation by chromium(VI) reduction in whole live mice. *Archives of Biochemistry and Biophysics* 313, 248-252.

Liu KJ, Mader K, Shi X et Swartz HM (1997) Reduction of carcinogenic chromium(VI) on the skin of living rats. *Magnetic Resonance in Medicine* 38, 524-526.

Mackenzie RD, Byerrum RU, Decker CF, Hoppert CA et Langham RF (1958) Chronic toxicity studies. II. Hexavalent and trivalent chromium administered in drinking water to rats. *AMA Arch Ind Health* 18, 232-234.

McCarroll N, Keshava N, Chen J, Akerman G, Kligerman A et Rinde E (2010) An evaluation of the mode of action framework for mutagenic carcinogens case study II: Chromium (VI). *Environmental and Molecular Mutagenesis* 51, 89-111.

Mohan D et Pittman Jr CU (2006) Activated carbons and low cost adsorbents for remediation of tri- and hexavalent chromium from water. *Journal of Hazardous Materials* 137, 762-811.

Mousavi Rad SA, Mirbagheri SA et Mohammadi T (2009) Using reverse osmosis membrane for chromium removal from aqueous solution. *Proceedings of World Academy of Science, Engineering and Technology* 57, 348-352.

Murray KJ et Tebo BM (2006) Cr(III) is indirectly oxidized by the Mn(II)-oxidizing bacterium *Bacillus sp.* strain SG-1. *Environmental Science & Technology* 41, 528-533.

Myers CR et Myers JM (1998) Iron stimulates the rate of reduction of hexavalent chromium by human microsomes. *Carcinogenesis* 19, 1029-1038.

Noël L, Chekri R, Millour S, Vastel C, Kadar A, Sirot V, Leblanc J-C et Guérin T (2012) Li, Cr, Mn, Co, Ni, Cu, Zn, Se and Mo levels in foodstuffs from the Second French TDS. *Food Chemistry* 132, 1502-1513.

Norseth T, Alexander J et Langard S (1982) Biliary excretion of chromium in the rat: A role of glutathione. *Acta Pharmacologica et Toxicologica* 51, 450-455.

NTP (1996a) Reproductive toxicity (testicular) of potassium dichromate (hexavalent) (CAS 7778-50-9) administered in diet to BALB/c mice National Toxicology Program.

NTP (1996b) Reproductive toxicity of potassium dichromate (hexavalent) (CAS 7778-50-9) administered in diet to SD rats. National Toxicology Program.

NTP (1997) Reproductive toxicity of potassium dichromate (hexavalent) (CAS 7778-50-9) administered in diet to BALB/c mice National Toxicology Program.

NTP (2008a) NTP toxicology and carcinogenesis studies of chromium picolinate monohydrate (CAS No. 27882-76-4) in F344/N rats and B6C3F1 mice (feed studies). http://ntp.niehs.nih.gov/files/TR556board_webRev.pdf.

NTP (2008b) NTP toxicology and carcinogenesis studies of sodium dichromate dihydrate (CAS No. 7789-12-0) in F344/N rats and B6C3F1 mice (drinking water studies). National Toxicology Program. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=18716633.

OEHHA (2011) Public health goal for hexavalent chromium (Cr VI) in drinking water. Office of environmental health hazard assessment.

OMS (2011) Guidelines for drinking-water quality, 4rd edition. Organisation mondiale de la santé. Genève.

Paustenbach DJ, Finley BL, Mowat FS et Kerger BD (2003) Human health risk and exposure assessment of chromium (VI) in tap water. *Journal of Toxicology and Environmental Health - Part A* 66, 1295-1339.

Philipot JM, Chaffange F et Sibony J (1985) Hexavalent chromium removal from drinking water. *Water Science and Technology* 17, 1121-1132.

Pratt PF et Myers CR (1993) Enzymatic reduction of chromium(VI) by human hepatic microsomes. *Carcinogenesis* 14, 2051-2057.

Proctor DM, Otani JM, Finley BL, Paustenbach DJ, Bland JA, Speizer N et Sargent EV (2002) Is hexavalent chromium carcinogenic via ingestion? A weight-of-evidence review. *Journal of Toxicology and Environmental Health - Part A* 65, 701-746.

Proctor DM, Thompson CM, Suh M et Harris MA (2011) A response to "A quantitative assessment of the carcinogenicity of hexavalent chromium by the oral route and its relevance to human exposure". *Environmental Research* 111, 468-470; discussion 471-462.

RIVM (2001) Re-evaluation of human-toxicological maximum permissible risk levels. National institute of public health an the environment. 711701025. Bilthoven.

Roussel AM (2001) Chrome. In 'Apports nutritionnels conseillés pour la population française, 3e édition'. (Ed. Tec&Doc) pp. 168-170. (Lavoisier: Paris).

Saputro S, Yoshimura K, Takehara K, Matsuoka S et Narsito (2011) Oxidation of chromium(III) by free chlorine in tap water during the chlorination process studied by an improved solid-phase spectrometry. *Analytical Sciences* 27, 649-652.

Schroeder HA, Balassa JJ et Tipton IH (1962) Abnormal trace metals in man--Chromium. *Journal of Chronic Diseases* 15, 941-964.

Schwarz K et Mertz W (1959) Chromium(III) and the glucose tolerance factor. *Archives of Biochemistry and Biophysics* 85, 292-295.

Selomulya C, Meeyoo V et Amal R (1999) Mechanisms of Cr(VI) removal from water by various types of activated carbons. *Journal of Chemical Technology & Biotechnology* 74, 111-122.

Shara M, Kincaid AE, Limpach AL, Sandstrom R, Barrett L, Norton N, Bramble JD, Yasmin T, Tran J, Chatterjee A, Bagchi M et Bagchi D (2007) Long-term safety evaluation of a novel oxygen-coordinated niacin-bound chromium (III) complex. *Journal of Inorganic Biochemistry* 101, 1059-1069.

Shara M, Yasmin T, Kincaid AE, Limpach AL, Bartz J, Brenneman KA, Chatterjee A, Bagchi M, Stohs SJ et Bagchi D (2005) Safety and toxicological evaluation of a novel niacin-bound chromium (III) complex. *Journal of Inorganic Biochemistry* 99, 2161-2183.

Sharma SK, Petrusevski B et Amy G (2008) Chromium removal from water: A review. *Journal of Water Supply: Research and Technology - AQUA* 57, 541-553.

Stout MD, Herbert RA, Kissling GE, Collins BJ, Travlos GS, Witt KL, Melnick RL, Abdo KM, Malarkey DE et Hooth MJ (2009) Hexavalent chromium is carcinogenic to F344/N rats and B6C3F1 mice after chronic oral exposure. *Environmental Health Perspectives* 117, 716-722.

Thomann RV, Snyder CA et Squibb KS (1994) Development of a pharmacokinetic model for chromium in the rat following subchronic exposure: 1. The importance of incorporating long-term storage compartment. *Toxicology and Applied Pharmacology* 128, 189-198.

Thompson CM, Proctor DM, Haws LC, Hebert CD, Grimes SD, Shertzer HG, Kopec AK, Hixon JG, Zacharewski TR et Harris MA (2011) Investigation of the mode of action underlying the tumorigenic response induced in B6C3F1 mice exposed orally to hexavalent chromium. *Toxicological Sciences*.

Trent LK et Thieding-Cancel D (1995) Effects of chromium picolinate on body composition. *Journal Sports Med Phys Fitness* 35, 273-280.

US-EPA (1998a) Toxicological review of hexavalent chromium. United States - Environmental protection agency. Washington, DC.

US-EPA (1998b) Toxicological review of trivalent chromium. United States - Environmental protection agency. Washington, DC.

US-EPA (2005) Supplemental guidance for assessing cancer susceptibility from early-life exposure to carcinogens,. United States - Environmental protection agency. EPA/630/R-03/003F. Washington, DC.

US-EPA (2008) Child-specific exposure factors handbook. United States - Environmental protection agency. EPA/600/R-06/096F. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=199243. Washington, DC.

US-EPA (2010) Toxicological review of hexavalent chromium. United States - Environmental protection agency. Washington, DC.

Warren G, Schultz P, Bancroft D, Bennett K, Abbott EH et Rogers S (1981) Mutagenicity of a series of hexacoordinate chromium(III) compounds. *Mutation Research/Genetic Toxicology* 90, 111-118.

WHO (1996) Aspects sanitaires et nutritionnels des oligo-éléments et des éléments en traces. World Health Organization. Genève.

WHO (2003) Chromium in drinking water: background document for preparation of WHO guidelines for drinking water quality. World Health Organization. Genève.

WHO (2011a) Concise international chemical assessment document for chromium VI - Post consultative group draft. World Health Organization.

WHO (2011b) Guidelines for drinking-water quality, 4rd edition. World Health Organization. Genève.

Wiegand HJ, Ottenwalder H et Bolt HM (1986) Disposition of a soluble chromate in the isolated perfused rat liver. *Xenobiotica* 16, 839-844.

Witmer CM, Harris R et Shupack SI (1991) Oral bioavailability of chromium from a specific site. *Environmental Health Perspectives* 92, 105-110.

Yamamoto A, Wada O et Ono T (1981) A low-molecular-weight, chromium-binding substance in mammals. *Toxicology and Applied Pharmacology* 59, 515-523.

Yoon J, Amy G, Chung J, Sohn J et Yoon Y (2009) Removal of toxic ions (chromate, arsenate, and perchlorate) using reverse osmosis, nanofiltration, and ultrafiltration membranes. *Chemosphere* 77, 228-235.

Zhang JD et Li XL (1987) Chromium pollution of soil and water in Jinzhou. *Zhonghua Yu Fang Yi Xue Za Zhi* 21, 262-264.

Zhitkovich A (2011) Chromium in drinking water: Sources, metabolism and cancer risks. *Chemical Research in Toxicology*, 1617-1629.

Zotter K et Licsko I (1992) Removal of chromium(VI) and other heavy metals from groundwaters in neutral and alkaline media. *Water Science and Technology* 26, 207-216.

Standards

AFNOR NF T 90-043 (1988) Determination of chromium(VI) - molecular absorption spectrometry method.

AFNOR NF EN 1233 (1996) Determination of chromium - atomic absorption spectrometric methods.

AFNOR NF EN ISO 17294-2 (2005) Application of inductively coupled plasma mass spectrometry (ICP-MS).

AFNOR ISO 23913 (2006) Determination of chromium(VI) – method using flow analysis (FIA and CFA) and spectrometric detection.

AFNOR NF EN ISO 18412 (2007) Determination of chromium(VI) - photometric method for weakly contaminated water.

AFNOR NF EN ISO 11885 (2009) Determination of selected elements by inductively coupled plasma optical emission spectrometry (ICP-OES).

NF EN ISO 15586 (2004) Determination of trace elements using atomic absorption spectrometry with graphite furnace.

Legislation and Regulations

Council Directive 86/278/EEC of 12 June 1986 on the protection of the environment, and in particular of the soil, when sewage sludge is used in agriculture.

Directive 2000/53/EC of the European Parliament and of the Council of 18 September 2000 on end-of-life vehicles.

Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 (WFD) establishing a framework for Community action in the field of water policy.

Directive 2002/95/EC of the European Parliament and of the Council of 27 January 2003 on the restriction of the use of certain hazardous substances in electrical and electronic equipment.

Directive 2002/96/EC of the European Parliament and of the Council of 27 January 2003 on waste electrical and electronic equipment (WEEE).

Directive 2006/11/EC of the European Parliament and of the Council of 15 February 2006 on pollution caused by certain dangerous substances discharged into the aquatic environment of the Community.

Commission Directive 2008/84/EC of 27 August 2008 laying down specific purity criteria on food additives other than colours and sweeteners.

Commission Directive 2008/128/EC of 22 December 2008 laying down specific purity criteria concerning colours for use in foodstuffs.

Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys.

Commission Regulation (EC) 1048/2005 of 13 June 2005 amending Regulation (EC) No 2032/2003 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market.

Regulation (EC) 166/2006 of the European Parliament and of the Council of 18 January 2006 concerning the establishment of a European Pollutant Release and Transfer Register and amending Council Directives 91/689/EEC and 96/61/EC.

Regulation (EC) 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

Regulation (EC) 219/2009 of the European Parliament and of the Council of 11 March 2009 adapting a number of instruments subject to the procedure referred to in Article 251 of the Treaty to Council Decision 1999/468/EC with regard to the regulatory procedure with scrutiny. Adaptation to the regulatory procedure with scrutiny — Part Two.

Commission Regulation (EC) 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products.

French legislation

Arrêté du 13 janvier 1976 relatif aux matériaux et objets en acier inoxydable au contact des denrées alimentaires.

Arrêté du 29 mai 1997 relatif aux matériaux et objets utilisés dans les installations fixes de production, de traitement et de distribution d'eau destinée à la consommation humaine.

Arrêté du 8 janvier 1998 fixant les prescriptions techniques applicables aux épandages de boues sur les sols agricoles pris en application du décret n° 97-1133 du 8 décembre 1997 relatif à l'épandage des boues issues du traitement des eaux usées.

Arrêté du 2 février 1998 relatif aux prélèvements et à la consommation d'eau ainsi qu'aux émissions de toutes natures des installations classées pour la protection de l'environnement soumises à autorisation.

Arrêté du 17 septembre 2003 relatif aux méthodes d'analyses d'échantillons d'eau et à leurs caractéristiques de performance.

Circulaire DGS/SD7A N° 2003-445 du 17 septembre 2003 concernant les modalités d'application de l'arrêté relatif aux méthodes d'analyses d'échantillons d'eau et à leurs caractéristiques de performance.

Décret 98-638 du 20 juillet 1998 relatif à la prise en compte des exigences liées à l'environnement dans la conception et la fabrication des emballages.

Décret 2005-577 du 26 mai 2005 relatif aux conditions de mise sur le marché et d'emploi du nonylphénol, de l'éthoxylate de nonylphénol et du ciment contenant du chromium hexavalent ou chromium VI, et modifiant le code du travail (deuxième partie: Décrets en Conseil d'Etat).

Décret 2007-1496 du 18 octobre 2007 relatif aux conditions de mise sur le marché et d'emploi des composés de l'arsenic, des sulfonates de perfluorooctane et modifiant le code de l'environnement.

Décret 2010-166 du 22 février 2010 relatif à la sécurité des jouets.

ANNEXES

Annexe I - LEGISLATION ON RESTRICTIONS ON THE USE AND RELEASE OF CHROMIUM

I.1 - Uses

The use of chromium is legally restricted for:

- food supplements and colourings (Directives 2008/128/EC as amended and 2008/84/EC),
- cosmetics (Regulation (EC) 1223/2009),
- toys (Directive 2009/48/EC transposed into French law by Decree 2010-166),
- electrical and electronic equipment (Directive 2002/95/EC),
- wood protection (Regulation (EC) 1048/2005 and Decree 2007-1496),
- vehicles (Directive 2000/53/EC)
- packaging (Decree 98-638).

I.2 - Waste and environmental release

Releases of chromium into the environment are regulated for classified installations for environmental protection (ICPEs) (Order of 2 February 1998), the glass and mineral fibre industry (Order of 12 March 2003), and electrical and electronic equipment (Directive 2002/96/EC).

Regulation (EC) 166/2006 concerns the establishment of a European Pollutant Release and Transfer Register and requires the monitoring of releases of chromium and its compounds above specified thresholds by any facility at which one or more of the activities listed in Annex I of the Regulation takes place.

I.2.1 - Spreading of sludge from wastewater treatment plants

The Order of 8 January 1998 as amended, transposing into French law Directive 86/278/EEC as amended by Regulation (EC) No 219/2009, specifies requirements for spreading of sewage sludge on agricultural soil and especially limit values for chromium in the sludge.

I.2.2 – Water in the environment

Chromium is not one of the WFD's priority substances, but is one of the substances covered by List II of Directive 2006/11/EC, for which Member States must take appropriate measures to reduce water pollution. A provisional environmental quality standard (EQSp) for total chromium, set by the Circular of 7 May 2007 (cited in INERIS, 2011), is based on 3.4 µg/L being added to the geochemical background.

Article R 211-11-1 of the French Environment Code provides for a national programme of action to prevent, reduce or eliminate pollution of inland and territorial surface waters, transitional waters and marine waters especially by chromium(VI).

Annexe II - AVERAGE LEVELS OF TOTAL CHROMIUM IN FOOD

Table II - I. Estimate of the average level of chromium in foods (mg/kg fresh weight) according to the TDS 2 (Anses, 2011a)

Food group	Estimate of the average level of total chromium (mg/kg fresh weight)
Bread and dried bread products	0.22
Breakfast cereals	0.28
Pasta	0.23
Rice and wheat products	0.14
Croissant-like pastries	0.40
Sweet and savoury biscuits and bars	0.31
Pastries and cakes	0.32
Milk	0.12
Ultra-fresh dairy products	0.15
Cheese	0.38
Eggs and egg products	0.22
Butter	0.64
Oils	1.00
Margarine	0.59
Meat	0.30
Poultry and game	0.27
Offal	0.24
Delicatessen meats	0.41
Fish	0.24
Crustaceans and molluscs	0.26
Vegetables (excluding potatoes)	0.12
Potatoes and potato products	0.15
Pulses	0.13
Fruit	0.10
Dried fruits, nuts and seeds	0.27
Ice creams, sorbets and frozen desserts	0.36
Chocolate	0.87
Sugars and sugar derivatives	0.21
Non-alcoholic beverages	0.07
Alcoholic beverages	0.08
Coffee	0.05
Other hot beverages	0.12
Pizzas, quiches and savoury pastries	0.30
Sandwiches and snacks	0.30
Soups and broths	0.006
Mixed dishes	0.24
Dairy-based desserts	0.27
Compotes and cooked fruit	0.12
Seasonings and sauces	0.34
Dietetic foods	0.22

Table II - II. Estimate of dietary intake (excluding water) of total chromium (average, P5 and P95) for the French child and adult population (in µg/day), according to EAT 2 (Anses, 2011a)

	Child population (3 to 17 years old)			Adult population		
Food group	Average	P5	P95	Average	P5	P95
Bread and dried bread products	10.58	1.31	30.00	22.31	3.35	54.08
Breakfast cereals	4.09	1.02	19.23	0.94	1.02	24.75
Pasta	13.66	4.28	38.06	12.16	2.38	38.06
Rice and wheat products	5.75	0.87	21.00	6.37	0.87	26.06
Croissant-like pastries	6.87	2.12	30.27	4.13	2.14	29.91
Sweet and savoury biscuits and bars	5.40	0.54	21.14	2.92	0.42	19.95
Pastries and cakes	9.58	1.83	34.96	9.99	2.04	37.49
Milk	19.97	2.49	57.16	9.92	1.04	52.35
Ultra-fresh dairy products	10.37	1.80	29.17	10.73	1.41	34.94
Cheese	6.82	1.08	20.96	11.17	1.76	32.40
Eggs and egg products	2.09	0.97	10.37	3.20	1.25	12.75
Butter	5.42	0.65	15.69	7.62	1.09	24.96
Oils	7.13	1.11	23.46	10.79	1.55	32.86
Margarine	1.47	0.44	10.27	2.73	0.83	18.71
Meat	10.24	2.38	27.73	13.25	3.15	34.92
Poultry and game	4.45	1.21	15.37	6.87	1.89	26.19
Offal	0.12	0.88	4.88	0.34	1.18	7.38
Delicatessen meats	6.92	1.02	20.95	9.03	1.49	25.97
Fish	2.91	1.07	10.79	3.10	0.77	14.16
Crustaceans and molluscs	0.33	0.27	6.00	0.89	0.49	7.85
Vegetables (excluding potatoes)	7.36	0.86	20.61	12.55	1.92	30.95
Potatoes and potato products	7.95	1.74	20.51	8.55	1.74	23.14
Pulses	0.74	0.91	8.96	0.82	0.95	10.20
Fruit	6.21	0.85	20.33	13.24	1.35	45.30
Dried fruits, nuts and seeds	0.30	0.13	5.02	0.74	0.30	8.79
Ice creams, sorbets and frozen desserts	3.62	2.34	24.99	2.81	2.34	24.58
Chocolate	7.26	0.92	29.26	4.49	0.74	32.61
Sugars and sugar derivatives	2.20	0.34	8.80	4.72	0.34	16.80
Non-alcoholic beverages	10.76	1.23	33.83	7.81	1.14	37.76
Alcoholic beverages	0.17	0.17	13.48	14.29	1.44	67.87
Coffee	0.24	0.37	14.39	9.72	0.61	38.70
Other hot beverages	2.77	0.23	23.93	3.75	0.34	24.17
Pizzas, quiches and savoury pastries	4.63	1.59	22.99	4.99	3.17	29.60
Sandwiches and snacks	3.25	2.18	25.38	3.64	3.42	37.62
Soups and broths	2.95	0.78	20.86	5.73	1.17	39.61
Mixed dishes	9.37	2.13	32.14	8.99	2.14	43.04
Dairy-based desserts	7.07	2.20	31.79	5.03	2.20	37.33
Compotes and cooked fruit	2.01	1.03	11.77	1.58	1.03	14.22
Seasonings and sauces	3.51	0.44	12.81	5.18	0.73	17.01
Dietetic foods	0.00	0.63	0.63	0.01	1.59	16.17

Annexe III - CHARACTERISATION OF THE HEALTH RISK ASSOCIATED WITH INGESTION OF DRINKING WATER

The health risk associated with the ingestion of chromium in DW was characterised using assumptions about the proportion of chromium(VI):

- at the current parametric value of 50 µg/L,
- at the maximum concentration proposed provisionally of 6 µg/L (Section 3.10),
- at the concentrations measured in DW (data processed according to scenario S2 - Section 3.5.2).

These estimates use the human toxicity values and the data mentioned in Section 3.9 (daily consumption of water: 2 L, body weight: 60 kg, share of TDI allocated to water exposure for non-carcinogenic effects: 20%).

III.1 - Non-carcinogenic effects of chromium(VI)

The chromium(VI) concentration corresponding to the share of TDI attributable to water is **6 µg/L**.

Table III – I gives the share of the TDI attributable to water consumed by the concentration of chromium(VI) in DW based on assumptions about the proportion of chromium(VI) at the current parametric value for chromium, at the maximum concentration proposed provisionally and at total chromium concentrations measured in DW.

At the current parametric value, it is found that:

- with 1% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 8% of the TDI attributable to water;
- with 100% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 833% of the TDI attributable to water.

At the maximum concentration proposed provisionally, it is found that:

- with 1% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 1% of the TDI attributable to water;
- with 100% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 100% of the TDI attributable to water.

At the average concentrations measured, it is found that:

- with 1% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 0.5% of the TDI attributable to water;
- with 100% of chromium found in the form of chromium(VI), the chromium(VI) intake corresponds to 42% of the TDI attributable to water.

Table III - I. Characterisation of the risk associated with non-carcinogenic effects (share of the TDI attributable to water consumed) according to the proportion of chromium(VI) in DW at the parametric value and at the measured concentrations processed under scenario S2

Proportion of chromium(VI) [Cr(VI)]/[total Cr]	Current parametric value	Maximum concentration proposed provisionally	Average concentration	P95 of concentration
	50 µg/L	6 µg/L	2.5 µg/L	5 µg/L
1%	8%	1%	0.5%	1%
50%	417%	50%	28%	42%
100%	833%	100%	42%	83%

III.2 - Carcinogenic effects of chromium(VI)

The chromium(VI) concentration associated with an individual excess risk level of 10^{-5} is **0.6 µg Cr(VI)/L**.

Characterisation of the excess risk associated with the carcinogenic effects of chromium(VI) is based on the slope factor of 0.5 $(mg/kg\ bw/d)^{-1}$, without taking into consideration the susceptibility of newborns and children (US-EPA, 2005).

The individual excess risk associated with the carcinogenic effects of chromium(VI) is presented in Table III - II. Characterisation of the individual excess risk (IER) according to the proportion of chromium(VI) in DW at the parametric value and at the measured concentrations processed under scenario S2 according to assumptions about the proportion of chromium(VI) in DW at the current parametric value, at the maximum concentration proposed provisionally and at the concentrations measured in DW.

At the current parametric value, it is found that:

- with 1% of chromium found in the form of chromium(VI), the individual excess risk level is $8.10^{-6;}$
- with 100% of chromium found in the form of chromium(VI), the individual excess risk level is 8.10^{-4}.

At the maximum concentration proposed provisionally, it is found that:

- with 1% of chromium found in the form of chromium(VI), the individual excess risk level is $1.10^{-6;}$
- with 100% of chromium found in the form of chromium(VI), the individual excess risk level is 1.10^{-4}.

At the average concentrations measured, it is found that:

- with 1% of chromium found in the form of chromium(VI), the individual excess risk level is between 3.10^{-8} and $8.10^{-7;}$
- with 100% of chromium found in the form of chromium(VI), the individual excess risk level is between 3.10^{-5} and 8.10^{-5}.

Table III - II. Characterisation of the individual excess risk (IER) according to the proportion of chromium(VI) in DW at the parametric value and at the measured concentrations processed under scenario S2

Proportion of chromium(VI) [Cr(VI)]/[total Cr]	Current parametric value	Maximum concentration proposed provisionally	Average concentration	P95 of concentration
	50 µg/L	6 µg/L	2.5 µg/L	5 µg/L
1%	8.10^{-6}	1.10^{-6}	4.10^{-7}	8.10^{-7}
50%	4.10^{-4}	5.10^{-5}	2.10^{-5}	4.10^{-5}
100%	8.10^{-4}	1.10^{-4}	4.10^{-5}	8.10^{-5}

Annexe IV - ACRONYMS AND ABBREVIATIONS

ANSES: French Agency for Food, Environmental and Occupational Health & Safety
ARS: Regional Health Agency
ATSDR: Agency for Toxic Substances and Disease Registry (USA)
BMD: Benchmark Dose
CES: Expert Committee
Cr: Chromium
DGS: French Directorate General for Health
DROM-COM: French overseas territories
EFSA: European Food Safety Authority
FDA: Food and Drug Administration (USA)
HRA: Health Risk Assessment
IARC: International Agency for Research on Cancer
ICPE: Classified Installation for Environmental Protection
ICP-MS: inductively coupled plasma mass spectrometry
ICP-OES: inductively coupled plasma optical emission spectroscopy
IER: Individual Excess Risk
INERIS: French National Institute for Industrial Environment and Risks
LOAEL: Lowest Observed Adverse Effect Level
LoQ: Limit of quantification
MRL: Minimal Risk Level
NOAEL: No Observed Adverse Effect Level
NTP: National Toxicology Program
OEHHA: Office of Environmental Health Hazard Assessment (California, USA)
PDW: Product in Contact with Drinking Water
PRI: Population Reference Intake
RfD: Oral Reference Dose
RIVM: National Institute for Public Health and the Environment (Netherlands)
SF: Slope Factor
SMR: Standardised Mortality Ratio
TDI: Tolerable Daily Intake
TDS: Total Diet Studies
UDI: Distribution Unit
US EPA: United States - Environmental Protection Agency
WG: Working Group
WHO: World Health Organization
DW: Water Intended for Human Consumption (drinking water)