The case for re-evaluating the upper limit value for selenium in drinking water in Europe

E. Barron, V. Migeot, S. Rabouan, M. Potin-Gautier, F. Séby, P. Hartemann, Y. Lévi and B. Legube

ABSTRACT

Selenium is an essential trace element for life, which can be toxic for humans when intakes reach a certain amount. Therefore, since the margin between healthy intake and toxic intake is narrow, the selenium concentration of tap water is a parameter that must be monitored because of its potential for increased intake. The present work gives an overview of the different approaches used to calculate safe limits for selenium. As recommended by WHO, the guidelines for drinking water form the basis of national legislated standards for drinking water. Before setting a maximum acceptable level in drinking water, it is necessary to take into account the total intake of selenium in both food and beverage. The limit value of $10\,\mu g\,l^{-1}$ for drinking water laid down in the European regulations for all countries should be adapted depending on geographic area, as previously recommended by WHO.

Key words | drinking water, guideline, selenium, standard

E. Barron
V. Migeot (corresponding author)
S. Rabouan
B. Legube
Université de Poitiers, Laboratoire de Chimie et Microbiologie de l'Eau,
UMR CNRS 6008,
40, avenue du Recteur Pineau,
86022 Poitiers Cedex,
France
E-mail: *virginie.migeot@univ-poitiers.fr*

V. Migeot
S. Rabouan
Université de Poitiers,
Faculté de Médecine et Pharmacie,
6 rue de la Milétrie, 86034 Poitiers Cedex,
France

V. Migeot
Université de Poitiers,
Centre Hospitalo-Universitaire de Poitiers,
2 rue de la Milétrie, 86021 Poitiers Cedex,
France

M. Potin-Gautier
Université de Pau et de l'Adour,
Equipe de Chimie Analytique Bio-Inorganique et Environnement,
UMR CNRS/UPPA 5254,
Avenue de l'Université, 64000 Pau,
France

F. Séby
Ultra Traces Analyses Aquitaine,
Hélioparc Pau Pyrénées,
2 avenue du Président Angot,
64053, Pau Cedex 9,
France

P. Hartemann
Département Environnement et Santé Publique,
Université de Nancy, Faculté de Médecine,
INSERM U420,
9 avenue de la Forêt de Haye, BP 184,
54 505 Vandoeuvre-les-Nancy Cedex,
France

Y. Lévi
Université de Paris-Sud XI, Laboratoire Santé Publique Environnement,
Faculté de Pharmacie,
5 rue JB Clément 92296
Chatenay Malabry Cedex,
France

doi: 10.2166/wh.2009.097

INTRODUCTION

Selenium is a trace element whose upper and lower limit values in terms of health risks are currently at the centre of numerous debates (Césarini 2004). On the one hand, selenium has been linked with toxic and even lethal effects when intake is excessive: in animals consuming plants containing high levels of this element (Tinggi 2003) and in humans through consumption or occupational exposure (Helzlsouer *et al.* 1985; Yang *et al.* 1989; Srivastava *et al.* 1995; Thérond *et al.* 1997; Dodig & Cepelak 2004; Hira *et al.* 2004; Reid *et al.* 2004; See *et al.* 2006; Sutter *et al.* 2008). In these cases of selenosis, the clinical signs classically described in humans are anomalies of nails (symmetric thickening and stratifying of fingernails, presence of distinct transverse or longitudinal ridges on the wall of the nails, presence of a white area at the base of the nail wall…) and hair, or even their loss.

On the other hand, selenium is today recognized as an element that is essential to good metabolic function. Its deficiency leads to health problems in humans and animals alike (van Rij *et al.* 1979; Navarro-Alarcon & Lopez-Martinez 2000; Suetens *et al.* 2001; Tapiero *et al.* 2003; Tinggi 2003). In humans, the best known pathological condition is Keshan disease, observed notably in an area of China where the selenium level in the soil is very low (Keshan Disease Research Group 1979). Since 1978, systematic supplementation of the population's diet with sodium selenate has resulted in almost complete eradication of this congestive cardiomyopathy (Simonoff & Simonoff 1991; Césarini 2004).

Selenium is today considered to be an element with a narrow therapeutic margin (Reilly 1998; Schwarz & Foltz 1999). However, there is no international consensus regarding the optimal range of selenium intake for human health.

Across the world, public supplies of drinking water are generally considered to be a negligible source of selenium as they contain concentrations of less than $1\,\mu g\,l^{-1}$ (Santé Canada 1986; Simonoff & Simonoff 1991; Barclay *et al.* 1995; Conde & Sanz Alaejos 1997). In humans, apart from occupational exposure, the principal source of selenium is dietary. The foods with the highest concentration of selenium are those that are rich in protein (meat, poultry, fish) (Diaz-Alarcon *et al.* 1996), whereas foods derived from plants generally have low levels apart from several exceptions (mushrooms, garlic, onions, nuts, cabbage…) (Pappa *et al.* 2006; Ventura *et al.* 2007).

Nevertheless, significant differences in selenium concentration are observed in the same food depending on the soil in which it was grown (Pappa *et al.* 2006). It is not only the selenium content of the soil, which varies as a function of natural abundance and human intervention, that affects the speciation and therefore the amount of bio-available element taken up by the plant, but also various physico-chemical parameters of the soil, such as pH, redox conditions and content of mineral salts and organic matter (Diaz-Alarcon *et al.* 1996; Combs 2001; Malisa 2001; Carvalho *et al.* 2003; Hartikainen 2005; Ashworth & Shaw 2006). In consequence, animals have a selenium intake that varies from one area to another according to the selenium content of the plants they ingest. Therefore humans, at the end of the food chain, ingest very variable amounts depending on the type and source of their nutrition.

Extreme values have been observed between the areas with the lowest levels of selenium (said to be selenium-poor), where intake has been estimated at less than $20\,\mu g\,day^{-1}$, and those with the highest levels (said to be selenium-rich), where intake has been estimated at up to $5{,}000\,\mu g\,day^{-1}$ (Combs 2001). In general, average European intake has been estimated at between 40 and $100\,\mu g\,day^{-1}$. US and Japanese intake is said to be slightly higher at an average of $150\,\mu g\,day^{-1}$ (Rayman 2005, 2008; Dumont *et al.* 2006). In France, the average intake has been estimated at around $50\,\mu g\,day^{-1}$ (Simonoff & Simonoff 1991; Noel *et al.* 2003; Leblanc *et al.* 2005), which would classify this country as an area somewhat poor in selenium (Freschard 1990).

Thus, since the margin between healthy intake and toxic intake is narrow, the selenium concentration of tap water is a parameter that must be monitored because of its potential to increase intake. Water for human consumption must not pose health risks, direct or indirect, to the populations consuming it. With regard to selenium content, the World Health Organization (WHO) proposes a health-based guideline value of $10\,\mu g\,l^{-1}$ in drinking water

(WHO 1996). This value has been adopted and laid down in the European regulations (Directive 98/83/CE, 3 November 1998), which have in turn been translated into French law (Ministère de la Santé et des Solidarités 2007).

The objective of this paper is to discuss firstly the guideline value proposed by WHO and secondly its inclusion in the European regulations. In the case of France, this latter discussion is based on the results of an epidemiological study measuring the exposure to selenium of French adults supplied with drinking water containing a concentration of selenium in excess of the upper limit ($10\,\mu g\,l^{-1}$).

GUIDELINE VALUE PROPOSED BY WHO

History (WHO 2004)

In 1958, WHO recommended a maximum level of $50\,\mu g\,l^{-1}$ for selenium in drinking water. In 1963, this value was lowered to $10\,\mu g\,l^{-1}$, while recognizing that selenium is an essential trace element. In 1984, this same guideline value ($10\,\mu g\,l^{-1}$) was retained, with the provision that it should be adapted depending on geographic area: that is, depending on the selenium intake of each population. The guidelines issued in 1993 retained this recommendation.

Method of calculation (WHO 2006)

The guideline value is the result of a calculation based on the no observed adverse effects level or NOAEL. This calculation, described below, is presented in Figure 1, scenario (1). On the basis of human data, WHO estimates the NOAEL at $240\,\mu g\,day^{-1}$ ($4\mu g\,day^{-1}\,kg^{-1}$ of body weight). Then, the intake derived from food on the one hand and drink on the other is estimated on the basis of a percentage allocated to each source, here 90% and 10%, respectively. It is thus estimated that drinks should provide a maximum of 24 μg of selenium per day. Assuming that an individual drinks 2 l of water per day, the maximum concentration permitted in drinking water is therefore calculated at $12\,\mu g\,l^{-1}$. WHO subsequently adjusted this value to $10\,\mu g\,l^{-1}$ in water for human consumption.

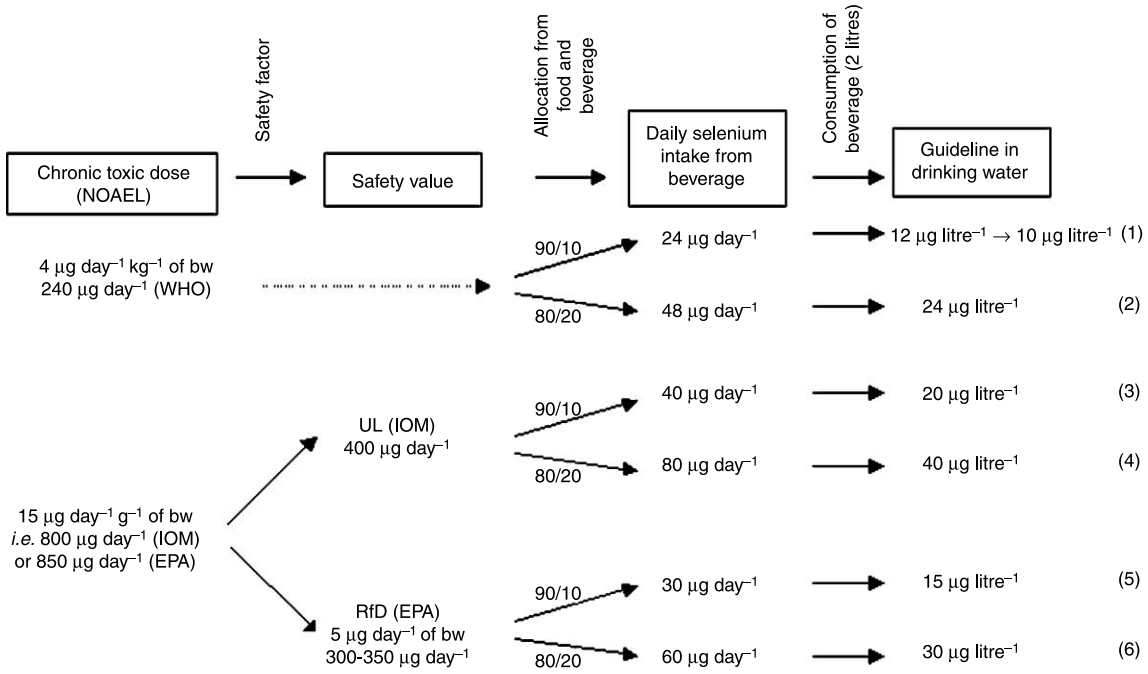

Figure 1 | Scenario currently used by WHO for its proposal for the guideline value for the concentration of selenium in drinking water (scenario 1, in bold) and other possible scenarios depending on the reference values attributed by different organizations (WHO: scenarios 1 and 2; IOM: scenarios 3 and 4; EPA: scenarios 5 and 6) and on the attributed distribution of intake between food and drinks (90/10: scenarios 1, 3 and 5; 80/20: scenarios 2, 4 and 6).

Comments

Recommendations (Goldhaber 2003; Schumann 2006; Renwick *et al.* 2008)

The recommendations for adequate intake on the one hand and upper limit of intake on the other are proposed by panels of experts in different specialities and working in various organizations (WHO, USEPA (US Environmental Protection Agency), American Institute of Medicine (IOM)). Each organization proposes and defines different recommendations.

On the one hand, the 'nutritionists' concentrate on doses necessary to prevent deficiency. With this objective, the IOM proposes four types of increasing dose:

1. EAR: 'estimated average requirement', which is the dose defined as preventing deficiency in 50% of the population
2. RDA: 'recommended dietary allowance', which is the dose defined as providing adequate intake for 97.5% of the population
3. AI: 'adequate intake', which is the recommended dose as determined for an adult population in good health
4. UL: 'tolerable upper intake level', which is the maximum dose that can be ingested on a daily basis by most of the general population without undesirable effects. Although defined among the nutritional doses, this dose is determined from the NOAEL and can in fact be considered equivalent to a toxicity level, the calculation of which is described below

The margin between the RDA and the UL gives the safe range of intake.

These values are generally derived from human data. The RDA is extrapolated from the EAR as a function of the available data concerning the element in question. If the standard deviation of the EAR is known and if the nutritional requirements of the population follow a normal distribution, the RDA is defined as two standard deviations above the EAR. If the standard deviation is not known, a coefficient of variation (CV) is applied at 10%. In this case the addition of twice the CV to the EAR gives the RDA.

On the other hand, the 'toxicologists' define different toxic doses (Figure 2):

- LOAEL: 'lowest observed adverse effects level', which is the lowest dose at which an undesirable effect has been observed
- NOAEL: 'no observed adverse effects level', which is the highest dose at which no undesirable effect has been observed

To evaluate the risk of toxicity, the EPA defines an RfD 'reference dose', which represents the daily dose to which

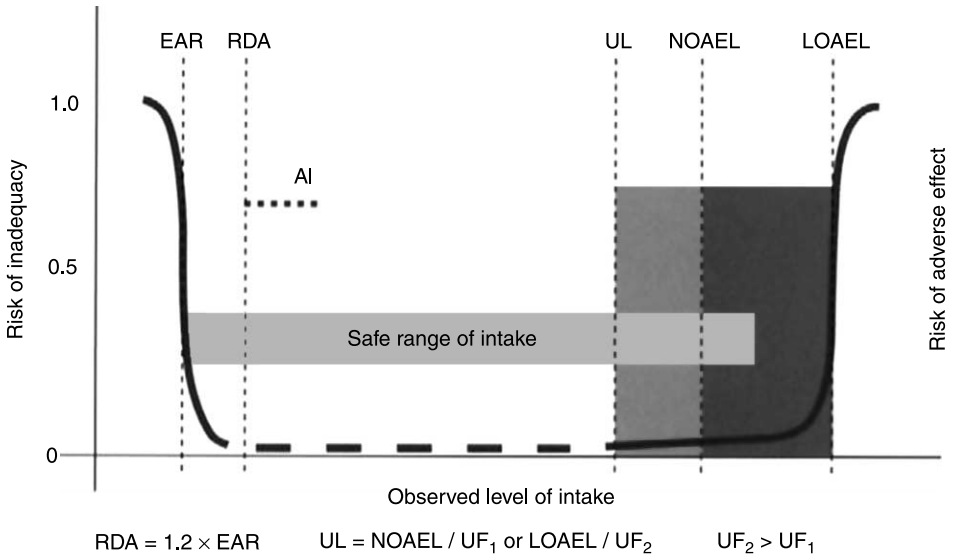

Figure 2 | Commonly used abbreviations in the context of 'dietary reference intakes': EAR = estimated average requirement; RDA = recommended dietary allowance; AI = adequate intake; UL = upper level; NOAEL = no observed adverse effect level; LOAEL = lowest observed adverse effect level (Schumann 2006).

the population can be exposed over a whole lifetime without significant risk of undesirable effects. It is calculated from the NOAEL or the LOAEL, applying higher or lower coefficients of safety (3–10) depending on the type of extrapolation, which in turn depends on the data available (extrapolation from animal to man taking into account inter-individual variability…).

Although defined by different organizations, the UL and the RfD are related and should therefore logically be of the same order of magnitude. In most cases, the reasons why differences can be observed result from the application of different coefficients of safety.

With a similar intent to that of the UL and the RfD, WHO uses the ADI 'acceptable daily intake' to describe a safe level of intake.

In order to define these doses, organizations have recourse to different studies. Since the initial aim of these studies is not necessarily the definition of recommended doses, an extrapolation is generally necessary (Figure 3). Furthermore, the results of these studies can be expressed in $\mu g\,day^{-1}\,kg^{-1}$ of body weight or in $\mu g\,day^{-1}$, and the conversion from one unit to the other therefore depends on the body weight that has been taken to represent an individual. Finally, each organization proposes its values. In the case of selenium, two principal apparent contradictions can be observed.

1. The IOM defined the EAR with the objective of determining the intake necessary to achieve optimal glutathione peroxidase activity (GP, selenoprotein) (i.e. plateau of plasma concentration of this enzyme). The average of the intakes estimated by two studies was adopted as the EAR: that is, $45\,\mu g\,day^{-1}$. Because the data regarding the standard deviation of the EAR were insufficient, the RDA was estimated at $55\,\mu g\,day^{-1}$ using a CV of 10%. Because WHO considered two-thirds of GP activity to be sufficient for good health (Levander & Whanger 1996), its proposed recommendations are lower than those of the IOM and lie between 30 and $40\,\mu g\,day^{-1}$. Certain authors, who no longer look at GP activity but who use instead selenoprotein P expression or the results of epidemiological studies highlighting the protective effects of selenium against cancer, conclude that these recommendations are insufficient (Combs 2001; Rayman 2008). In the light of this, WHO (2006) suggests that the necessary intake should lie between 100 and $300\,\mu g\,day^{-1}$, which explains why this organization is currently in the process of revising its guideline value for selenium.
2. The IOM and the EPA have defined the NOAEL on the basis of studies performed by Yang & Zhou (1994) in a selenium-rich area of China (Figure 3). These authors established upper limits based on the observation of five subjects suffering from selenosis. The LOAEL was established for a plasma selenium concentration of $1{,}054\,\mu g\,l^{-1}$, corresponding to an intake of $910\,\mu g\,day^{-1}$. When these same subjects were examined six years later, they presented an average plasma

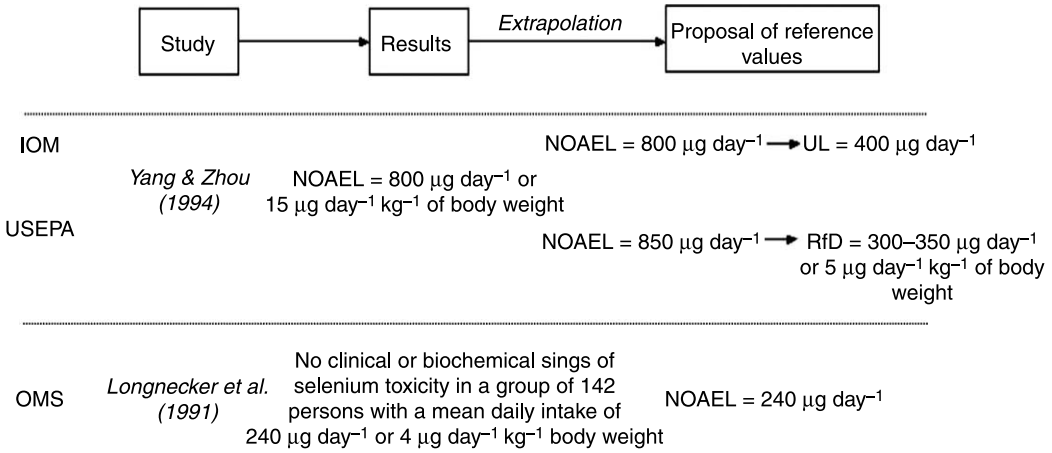

Figure 3 | Steps generally used to propose a reference value; examples for the definition of a safe selenium intake by three organizations (Yang & Zhou 1994; Goldhaber 2003; WHO 2004).

concentration of 968 $\mu g\,l^{-1}$, corresponding to an intake of 819 $\mu g\,day^{-1}$, with no clinical signs of selenosis. The authors then proposed a NOAEL of 800 $\mu g\,day^{-1}$ and 15 $\mu g\,day^{-1}\,kg^{-1}$ of body weight for an individual of around 55 kg. The IOM adopted a NOAEL of 800 $\mu g\,day^{-1}$ and the EPA one of 850 $\mu g\,day^{-1}$. The IOM then applied a safety coefficient of 2 to the NOAEL of 800 $\mu g\,day^{-1}$ to arrive at a UL of 400 $\mu g\,day^{-1}$. A safety coefficient of 3, higher than that of the IOM, was chosen by the EPA to define the RfD. The EPA is actually of the opinion that since the study by Yang and Zhou looked at just five individuals, who were moreover Chinese (i.e. non-American), the inter- and intra-individual factors might be underestimated in their results. Thus, based on the NOAEL of 15 $\mu g\,day^{-1}\,kg^{-1}$ of body weight, the RfD was defined as 5 $\mu g\,day^{-1}\,kg^{-1}$ of body weight, which results in a value between 300 and 350 $\mu g\,day^{-1}$, depending on the individual body weight applied (60 kg (AFSSA 2004) and 70 kg (Goldhaber 2003), respectively).

WHO defined the NOAEL as 4 $\mu g\,day^{-1}\,kg^{-1}$ of body weight (corresponding to 240 $\mu g\,day^{-1}$ since it considers individual body weight as 60 kg) (WHO 1996). This value, much lower than that defined by the other organizations, is based on the study by Longnecker *et al.* (1991). This study looked at 142 American subjects living in a selenium-rich area. No clinical or biological sign of selenium toxicity was observed in any of these subjects who had an average intake of 240 to 724 $\mu g\,day^{-1}$.

WHO has not calculated a safe level of intake based on this NOAEL. Thus, there exists a more than threefold disparity between the NOAEL defined by IOM-EPA and that defined by WHO. It just so happens that the maximum guideline value for the selenium concentration recommended in drinking water has been calculated on the basis of the NOAEL established by WHO (scenario 1 of Figure 1). Using an identical calculation method on the basis of the NOAEL defined by the IOM, this upper limit of concentration would have been 40 $\mu g\,l^{-1}$. However, when considering a safety margin, it is more appropriate to base the calculation on the UL or the RfD. These would give upper limits of selenium concentration in drinking water of 20 and 15 $\mu g\,l^{-1}$, respectively (scenarios 3 and 5 in Figure 1).

These apparent contradictions remind us that it is important to know and to take into account the context and method of calculation of these recommended values. Their variability from one organization to another corroborates the fact that they cannot be regarded as an absolute upper limit but rather as a reference value. This point has already been made in a workshop on RfDs and RDAs (Goldhaber 2003). Guidelines from WHO are non-mandatory and should be seen in the light of local circumstances.

However, in some countries, the guideline value for selenium in drinking water is applied, as for other substances, as the maximum acceptable limit, above which water is considered legally as failing to comply with the standard for water for human consumption.

Distribution of intake between drinks and food

The percentage of total selenium intake derived from drinks depends principally on the selenium concentration of drinking water. In its calculation of the guideline value, WHO considered that 10% of intake is derived from drinks. In Australia this percentage has been defined as 20%. Thus, on the basis of the Australian model, the guideline value might have been proposed at 24 $\mu g\,l^{-1}$ (scenario 2 in Figure 1).

Rounding of the guideline value

Despite the fact that the calculation of the guideline value results in a concentration of 12 $\mu g\,l^{-1}$, WHO proposed a value of 10 $\mu g\,l^{-1}$, to avoid indicating an amount of certainty that is scientifically justified. It must be regarded as a reference value and not as an absolute upper limit. Thus if WHO recommendations are strictly considered as standards and not only as guidelines, it results in a very restrictive upper limit of concentration for selenium in European drinking water. Drinking water treatment plants are thus obliged, in the absence of a special dispensation granted on a temporary basis, to institute an additional treatment process once its water passes the upper limit of 10 $\mu g\,l^{-1}$. The cost of this is then borne by the local community.

In the US in 1979, Lafond and Calabrese considered the selenium upper limit of 10 $\mu g\,l^{-1}$ then in force as

inappropriate and too low (Lafond & Calabrese 1979). Since 1992, the EPA has proposed a maximum permitted concentration of 50 $\mu g l^{-1}$ (EPA 2003).

THE SITUATION IN FRANCE

As stated in the Introduction, the value for the standard for French drinking water is based on European regulations, themselves based on the WHO proposal. Ever since 1984, WHO has been at pains to point out that the guidance value should be adapted depending on geographic area: that is, depending on the population's level of intake of selenium from food.

In the case of France, the average daily intake of selenium has been estimated at around 50 $\mu g\ day^{-1}$ (Simonoff & Simonoff 1991; Noel *et al.* 2003; Leblanc *et al.* 2005) and therefore well below the NOAEL. In these estimations, the intake derived from water has been considered negligible, because in France the majority of water sources have a selenium concentration below 10 $\mu g l^{-1}$, respecting the regulatory standard. However, several French geographic areas are supplied with drinking water that has a selenium concentration above the standard (Figure 4).

In these areas, it would be useful to know the concentration and bio-availability of selenium in the soil or, better still, to measure directly the population's exposure to selenium (total intake) and then to make an informed decision concerning the maximum acceptable limit for selenium in drinking water.

This is why we paid particular attention to the department of the Vienne, situated in the west of France (department 86 in Figure 4). The repeated observation of selenium concentrations in excess of 10 $\mu g l^{-1}$ at some points of distribution of water in this department led in 1997 to the instigation of a large-scale sampling campaign. This demonstrated selenium levels in excess of the standard in 13 sources, 12 of which serve 8 distribution units in the

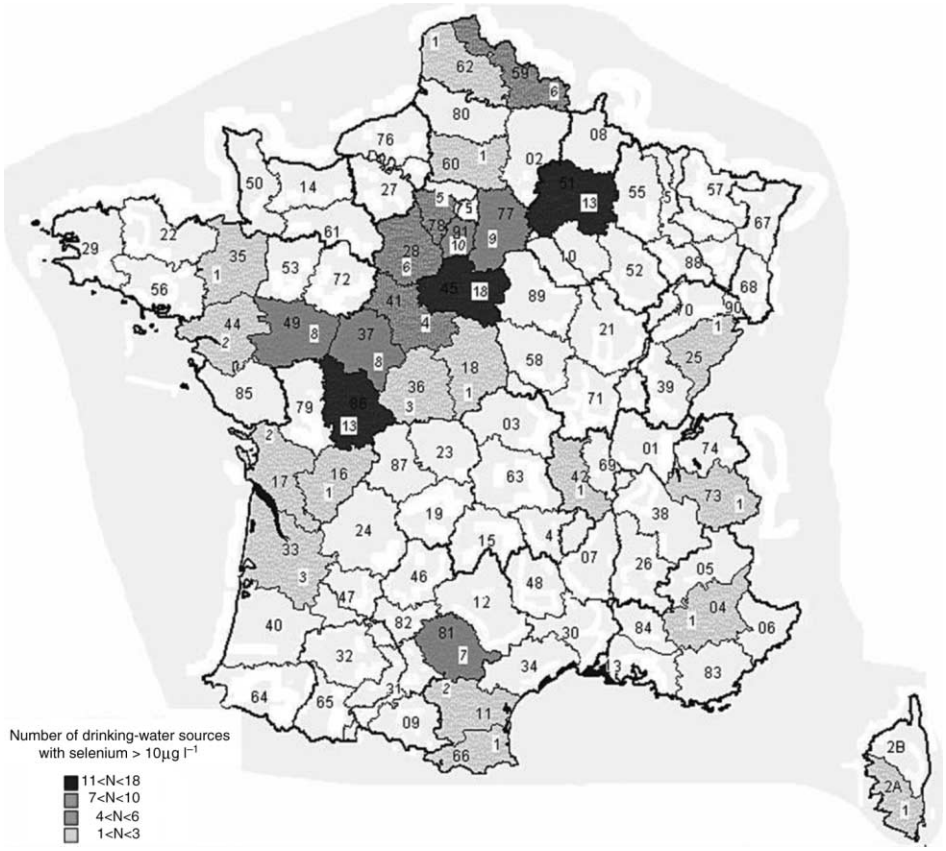

Figure 4 | Water sources used for the production of drinking water in France that have maximum selenium levels greater than 10 $\mu g l^{-1;}$ data from the SISE-Eaux database.

east of the department. These units were supplying 40,000 to 55,000 inhabitants and contained up to 40 $\mu g l^{-1}$ of selenium, the origin of which is likely to be geological in the absence of any site likely to cause selenium pollution in an area with no glass industry or industrial carbon combustion. This selenium may result from leaching from Jurassic and Turonian rock, as demonstrated by studies on the sources ([Se] $\approx$ 50–60 $\mu g l^{-1}$) feeding the spa of La Roche-Posay located in the region in question (Figure 5) (Renaudin 1999). This thermal water supplies the spa exclusively, which is reputed for the treatment of dermatological conditions (Pinton *et al.* 1995). It is used for treating patients not only in the form of shower, bath or spray but also as a curative drink. By contrast, the tap water of La Roche-Posay issues from different ground water that conforms to the selenium standard.

In order to supply their populations with water that complies with the standard, the local authorities looked for solutions for these 12 sources. Four of them have been closed. The water issuing from four others has been diluted with water from other existing or new sources. However, neither of these solutions has been possible for the remaining four sources, because the new sources were either high in nitrates or had an insufficient flow rate. The communities (around 10,000 inhabitants) supplied from these four sources issuing drinking water with a concentration of selenium in excess of 10 $\mu g l^{-1}$ are situated in two geographic areas around 50 km apart (Figure 5).

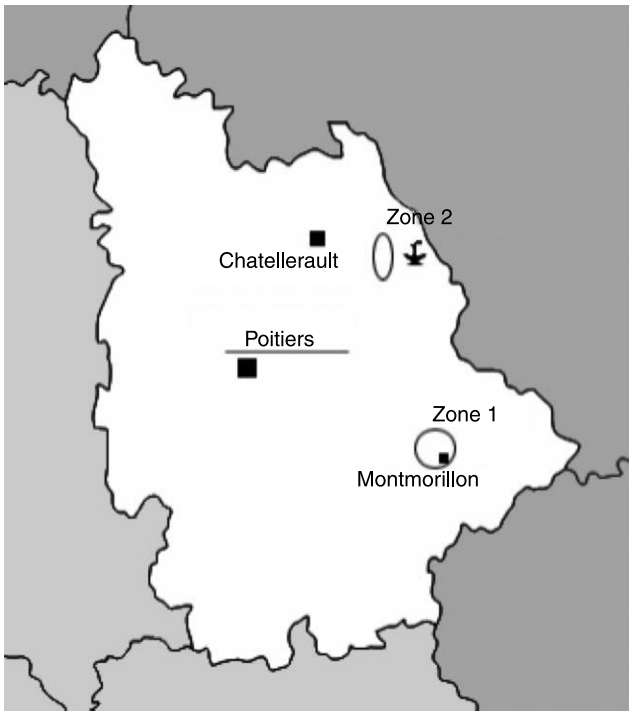

Figure 5 | Geographic location of the areas in the Vienne with a drinking water selenium concentration higher than the standard (10 $\mu g l^{-1}$) and of the spa of La Roche-Posay (represented by a fountain), which has a selenium concentration of 50–60 $\mu g l^{-1}$.

Experiments with various treatments have been performed (coagulation-flocculation, nanofiltration, adsorption, ion exchange resin), of which only nanofiltration and ion exchange resin resulted in effective elimination. However, the investment, the cost of management and personnel, together with difficulties relating to waste disposal, make the instigation of these treatments difficult for units that previously carried out nothing beyond simple chlorination. While waiting for an acceptable solution to be identified, the town councils concerned requested a special dispensation from the prefecture, as provided for in the legislation (AFSSA 2004) (Circulaire du 15 décembre 2004).

In this context we conducted an epidemiological study reported elsewhere (Barron 2007) to assess the level of exposure to selenium of the people living in those communities supplied with drinking water containing a selenium concentration exceeding the maximum acceptable limit (Figure 6). The selenium intake of adults was evaluated by three different approaches: direct measurement of selenium ingested by the duplicate portion method, reconstitution from a food intake questionnaire and use of a biological marker, namely the selenium content of toenail clippings. These approaches were complemented by analysis of some locally produced foodstuffs to determine their selenium content.

Forty apparently exposed subjects (i.e. living in the communities in question) and 40 non-exposed subjects (i.e. living outside the communities in question) were selected to participate in this study. The cohort of exposed subjects was representative of the general population resident in these communes in terms of age, sex and socio-professional category. The subjects in both groups, exposed and non-exposed, were matched according to the same criteria. The participants responded to a pre-inclusion questionnaire (socio-demographic data), four food questionnaires (one per season) and a health questionnaire, and provided

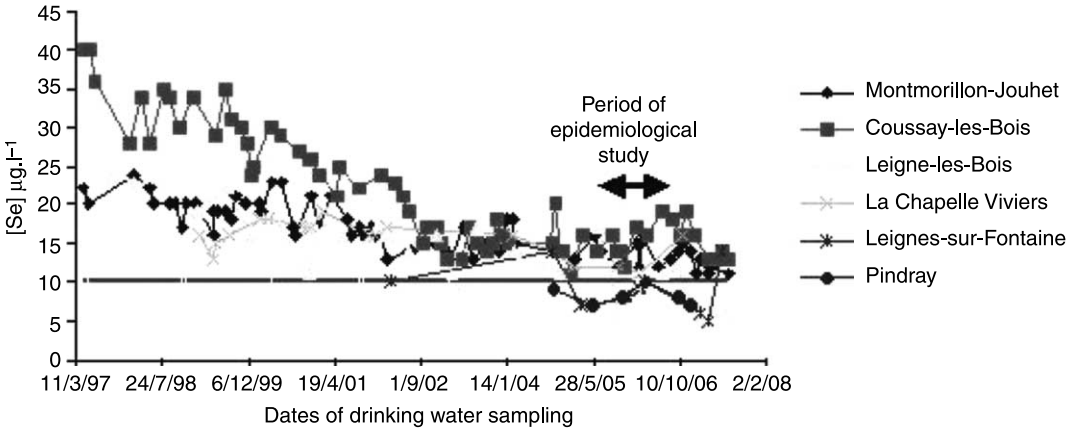

Figure 6 | Selenium concentrations measured in the drinking water of the communities studied since 1997 (data from the Direction Départementale des Affaires Sanitaires et Sociales).

samples of their toenail clippings twice. In addition, the exposed participants provided a duplicate of what they had eaten and drunk over two days per season. The study was well received by the subjects with a compliance rate of more than 90%.

The estimation of dietary selenium intake by questionnaire showed comparable levels for the 39 exposed and 39 non-exposed group (respectively 0.70 $\mu g\,day^{-1}\,kg^{-1}$ of body weight (± 0.18) vs. 0.74 $\mu g\,day^{-1}\,kg^{-1}$ of body weight (± 0.25), $p = 0.53$), whereas that from water was higher in the exposed group than the non-exposed group (respectively, 0.24 $\mu g\,day^{-1}\,kg^{-1}$ of body weight (± 0.13) vs. 0.028 $\mu g\,day^{-1}\,kg^{-1}$ of body weight (± 0.011), $p < 0.0001$). The results of the estimations of exposure levels showed that the exposed subjects were not ingesting levels of selenium considered to be toxic. In fact, the average daily selenium intake of the participants, as estimated by the duplicate portion method, corresponded to French recommendations ($\approx 1\,\mu g\,day^{-1}\,kg^{-1}$) (Martin 2000). The maximum value (2.73 $\mu g\,day^{-1}\,kg^{-1}$ of body weight) was well below the NOAEL proposed by WHO (4 $\mu g\,day^{-1}\,kg^{-1}$ of body weight) (WHO 1996). The selenium content of locally produced foodstuffs was within the range of concentrations found in France (Simonoff & Simonoff 1991; Noel *et al.* 2003; Leblanc *et al.* 2005). As for levels in the body, the exposed subjects presented nail concentrations statistically higher than those of the non-exposed subjects (on average 613 ± 117 $\mu g\,kg^{-1}$ vs. 532 ± 100 $\mu g\,kg^{-1}$, $p < 0.005$). However, this difference of 81 $\mu g\,day^{-1}$ does not have any clinical repercussions: there are no significant differences in health status between the exposed and non-exposed group, as evaluated by the Duke health profile. Furthermore, the highest value was lower than those found in selenium-rich areas whose inhabitants presented no signs of toxicity (average 1,950 $\mu g\,kg^{-1}$ (Longnecker *et al.* 1991)).

DISCUSSION

Because of its antioxidant properties, selenium would seem to protect against cancer and cardiovascular disease, among other pathologies (Rayman 2005; Brinkman *et al.* 2006; Ingle & Limburg 2006; Marshall *et al.* 2006; Navas-Acien *et al.* 2008). In this context, more and more authors suggest that total daily intake should lie between 100 and 300 $\mu g\,day^{-1}$ (Combs 2001; WHO 2006). In addition, speciation would seem to be an important factor to take into account (Rayman 2008; Rayman *et al.* 2008), if a link were to be established between these beneficial effects and populations with high selenium intake. However, until the time of writing there has been little data on this subject (Rayman *et al.* 2008).

If a protective effect against certain pathologies were to be demonstrated, appropriate steps to optimize intake could be envisaged individually or collectively (Rayman 2008; Rayman *et al.* 2008). On an individual level, it is possible to eat more food that is naturally rich in selenium (e.g. Brazil nuts or fish) or enriched in selenium during its production. Food supplements, some of which contain selenium

(recommended dose mostly between 30 and 100 $\mu g\,day^{-1}$) are sold in chemist's shops without prescription and can thus be taken freely.

On the collective level, it is possible to increase the population's intake by using selenium in agriculture. On the one hand, the use of selenium-enriched fertilizers on the fields would increase the content of crops. On the other hand, farm animals could be given selenium supplements, either directly by injection or orally (for example by addition of selenite or selenate to water or to salt blocks, or the use of slow-release tablets) or indirectly through enrichment of their pastures (Oldfield 1992; Tinggi 2003).

But this beneficial effect of selenium on health must not make us forget that, depending on dose, it can equally be toxic. Furthermore, recent studies point to the possible dangers of taking supplements in the long term, in particular an increase in the risk of developing type 2 diabetes (Stranges *et al.* 2007).

The preventive health strategy to adopt regarding selenium levels has been a public health issue in most countries of the world and especially in Europe for several years. Certain countries, such as Finland, have, since 1984, chosen to increase their populations' selenium intake through the general use of selenium-enriched fertilizers (Ekholm *et al.* 1990, 2007; Hartikainen 2005). As a result of this policy, the average Finnish intake stands today at around 100–200 $\mu g\,day^{-1}$, whereas it was 30–40 $\mu g\,day^{-1}$ in the middle of the 1970s (Sandstrom 1998).

In France, the average intake is lower than the range recommended today to benefit from the beneficial effects of selenium. At nearly 150 l per year per person, the amount of bottled water represents only 20% of drinking water (Vigouroux & Pointet 2007) consumed. In those areas of France supplied with water containing higher concentrations of selenium than the standard, and provided that intake is not excessive in relation to the recommendations, drinking this water could thus help to increase the selenium intake of their residents. In this context, reconsidering raising the maximum acceptable limit for selenium in drinking water is a major issue that the authorities must address.

To be appropriate, this new value would have to take into account not only the average dietary intake of the French, as recommended by WHO in 1984, but also the possible consumption of dietary supplements. Indeed, the widespread media coverage of these products might lead to an increase in their consumption over the next few years (Rock 2007).

Thus, with a maximum concentration of 20 $\mu g\,l^{-1}$ for selenium in drinking water, a French person drinking 2 l of water per day would have a total intake of 100 $\mu g\,day^{-1}$, including the 60 $\mu g\,day^{-1}$ derived from food. Such an intake would lie at the bottom end of the recommendations, leaving a safety margin and allowing each individual to decide whether or not to take a food supplement.

CONCLUSION

As recommended by WHO, the guidelines for drinking water form the basis of national legislated standards for drinking water. Therefore it is necessary to take into account the total intake of selenium from both food and beverage before setting a maximum acceptable level in drinking water. The European situation is contrasted between France (60 $\mu g\,day^{-1}$ by foods) and Finland (100–200 $\mu g\,day^{-1}$ after general use of selenium-enriched fertilizers). The limit value of 10 $\mu g\,l^{-1}$ for drinking water laid down in the European regulations for all countries should be adapted depending on geographic area, as previously recommended by WHO. Thus it could be proposed to increase this limit value (20 $\mu g\,l^{-1}$ in France, which is a concentration without harm effect), particularly since the USEPA has proposed a maximum permitted concentration of 50 $\mu g\,l^{-1}$. Finally, this new standard should also be continually re-evaluated in the light of the evolution of our knowledge about selenium.

ACKNOWLEDGEMENTS

The authors wish to thank Monsieur J.C. Parnaudeau, Public Health Engineer at the Direction Départementale des Affaires Sanitaires et Sociales of the Vienne, for his commitment and support throughout the course of this study. We thank him in particular for drawing up the map in Figure 4. We thank Marian Green for providing the English translation.

REFERENCES

AFSSA (Agence Française de Sécurité Sanitaire des Aliments) 2004 Evaluation des risques sanitaires liés aux situations de dépassement des limites et références de qualité des eaux destinées à la consommation humaine. Available at: www.echlorial.com/index.php?preaction=joint&id_joint=46234 (accessed July 2008).

Ashworth, D. J. & Shaw, G. 2006 Soil migration, plant uptake and volatilisation of radio-selenium from a contaminated water table. *Sci. Total Environ.* **370**, 506–514.

Barclay, M. N. I., MacPherson, A. & Dixon, J. 1995 Selenium content of a range of UK foods. *J. Food Compos. Anal.* **8**, 307–318.

Barron, E. 2007 *Mesure de l'exposition au sélénium: évaluations chimique et épidémiologique auprès de sujets alimentés par une eau potable à teneur élevée*. Thèse de l'Université de Poitiers, France.

Brinkman, M., Buntinx, F., Muls, E. & Zeegers, M. P. 2006 Use of selenium in chemoprevention of bladder cancer. *Lancet Oncol.* **7**, 766–774.

Carvalho, K. M., Gallardo-Williams, M. T., Benson, R. F. & Martin, D. F. 2003 Effects of selenium supplementation on four agricultural crops. *J. Agric. Food Chem.* **51**, 704–709.

Césarini, J. P. 2004 *Le sélénium: actualités*. Pathologie science formation, Montrouge, France.

Combs, G. F., Jr 2001 Selenium in global food systems. *Brit. J. Nutr.* **85**, 517–547.

Conde, J. E. & Sanz Alaejos, M. 1997 Selenium concentrations in natural and environmental waters. *Chem. Rev.* **97**, 1979–2004.

Diaz-Alarcon, J. P., Navarro-Alarcon, M., Lopez-Garcia de la Serrana, H. & Lopez-Martinez, M. C. 1996 Determination of selenium in cereals, legumes and dry fruits from southeastern Spain for calculation of daily dietary intake. *Sci. Total Environ.* **184**, 183–189.

Dodig, S. & Cepelak, I. 2004 The facts and controversies about selenium. *Acta Pharmaceut.* **54**, 261–276.

Dumont, E., Vanhaecke, F. & Cornelis, R. 2006 Selenium speciation from food source to metabolites: a critical review. *Anal. Bioanal. Chem.* **385**, 1304–1323.

Ekholm, P., Ylinen, M., Koivistoinen, P. & Varo, P. 1990 Effects of general soil fertilization with sodium selenate in Finland on the selenium content of meat and fish. *J. Agric. Food Chem.* **38**, 695–698.

Ekholm, P., Reinivuo, H., Mattila, P., Pakkala, H., Koponen, J., Happonen, A., Hellström, J. & Ovaskainen, M. L. 2007 Changes in the mineral and trace element contents of cereals, fruits and vegetables in Finland. *J. Food Compos. Anal.* **20**, 487–495.

EPA (Environmental Protection Agency) 2003 National Primary Drinking Water Standards, Office of Water, 4606M EPA 816-F-03–016. Available at: http://www.epa.gov/safewater/consumer/pdf/mcl.pdf (accessed November 2007).

Freschard, V. 1990 *Le sélénium: Rôle physiologique et influence sur la santé humaine. Discussion de la supplémentation éventuelle du sujet sain dans certains pays d'Europe*. Thèse de l'Université de Nancy 1, France.

Goldhaber, S. B. 2003 Trace element risk assessment: essentiality vs. toxicity. *Regul. Toxicol. Pharm.* **38**, 232–242.

Hartikainen, H. 2005 Biogeochemistry of selenium and its impact on food chain quality and human health. *J. Trace Elem. Med. Biol.* **18**, 309–318.

Helzlsouer, K., Jacobs, R. & Morris, S. 1985 Acute selenium intoxication in the United States. *Fed. Proc.* **44**, 1670.

Hira, C. K., Partal, K. & Dhillon, K. S. 2004 Dietary selenium intake by men and women in high and low selenium areas of Punjab. *Public Health Nutr.* **7**, 39–43.

Ingle, S. B. & Limburg, P. J. 2006 Can selenium supplementation prevent colorectal cancer? *Gastroenterology* **131**, 1646–1647.

Keshan Disease Research Group 1979 Chinese academy of medical science: epidemiological studies on the etiologic relationship of selenium and Keshan disease. *Chinese Med. J (Engl.)* **92**, 477–482.

Lafond, M. G. & Calabrese, E. J. 1979 Is the selenium drinking water standard justified? *Med. Hypotheses* **5**, 877–899.

Leblanc, J. C., Guerin, T., Noel, L., Calamassi-Tran, G., Volatier, J. L. & Verger, P. 2005 Dietary exposure estimates of 18 elements from the 1st French total diet study. *Food Addit. Contam.* **22**, 624–641.

Levander, O. A. & Whanger, P. D. 1996 Deliberations and evaluations of the approaches, endpoints and paradigms for selenium and iodine dietary recommendations. *J. Nutr.* **126**, 2427S–2434S.

Longnecker, M. P., Taylor, P. R., Levander, O. A., Howe, M., Veillon, C., McAdam, P. A., Patterson, K. Y., Holden, J. M., Stampfer, M. J., Morris, J. S. & Willet, W. C. 1991 Selenium in diet, blood, and toenails in relation to human health in a seleniferous area. *Am. J. Clin. Nutr.* **53**, 1288–1294.

Malisa, E. P. 2001 The behaviour of selenium in geological processes. *Environ. Geochem. Health* **23**, 137–158.

Marshall, J. R., Sakr, W., Wood, D., Berry, D., Tangen, C., Parker, F., Thompson, I., Lippman, S. M., Lieberman, R., Alberts, D., Jarrard, D., Coltman, C., Greenwald, P., Minasian, L. & Crawford, E. D. 2006 Design and progress of a trial of selenium to prevent prostate cancer among men with high-grade prostatic intraepithelial neoplasia. *Cancer Epidemiol. Biomar.* **15**, 1479–1484.

Martin, A. 2000 *Apports nutritionnels conseillés pour la population française*, 3ème édition. Éditions Tec&Doc, Paris.

Ministère de la Santé et des Solidarités 2007 Code de la Santé Publique, R. 1321–2, Décret n° 2007–49 du 11 janvier 2007 relatif à la sécurité des eaux destinées à la consommation humaine, à l'exclusion des eaux minérales naturelles.

Navarro-Alarcon, M. & Lopez-Martinez, M. C. 2000 Essentiality of selenium in the human body: relationship with different diseases. *Sci. Total Environ.* **249**, 347–371.

Navas-Acien, A., Bleys, J. & Guallar, E. 2008 Selenium intake and cardiovascular risk: what is new? *Curr. Opin. Lipidol.* **19**, 43–49.

Noel, L., Leblanc, J. C. & Guerin, T. 2003 Determination of several elements in duplicate meals from catering establishments using closed vessel microwave digestion with inductively coupled plasma mass spectrometry detection: estimation of daily dietary intake. *Food Addit. Contam.* **20**, 44–56.

Oldfield, J. E. 1992 Risks and benefits in agricultural uses of selenium. *Environ. Geochem. Health* **14**, 81–86.

Pappa, E. C., Pappas, A. C. & Surai, P. F. 2006 Selenium content in selected foods from the Greek market and estimation of the daily intake. *Sci. Total Environ.* **372**, 100–108.

Pinton, J., Friden, H., Kettaneh-Wold, N., Wold, S., Dreno, B., Richard, A. & Bieber, T. 1995 Clinical and biological effects of balneotherapy with selenium-rich spa water in patients with psoriasis vulgaris. *Brit. J. Dermatol.* **133**, 344–347.

Rayman, M. P. 2005 Selenium in cancer prevention: a review of the evidence and mechanism of action. *Proc. Nutr. Soc.* **64**, 527–542.

Rayman, M. P. 2008 Food-chain selenium and human health: emphasis on intake. *Br. J. Nutr.* **100**, 254–268.

Rayman, M. P., Infante, H. G. & Sargent, M. 2008 Food-chain selenium and human health: spotlight on speciation. *Br. J. Nutr.* **100**, 238–253.

Reid, M. E., Stratton, M. S., Lillico, A. J., Fakih, M., Natarajan, R., Clark, L. C. & Marshall, J. R. 2004 A report of high-dose selenium supplementation: response and toxicities. *J. Trace Elem. Med. Biol.* **18**, 69–74.

Reilly, C. 1998 Selenium: a new entrant into the functional food arena. *Trends Food Sci. Technol.* **9**, 114–118.

Renaudin, C. 1999 *Sélénium: action, toxicité et utilisation en thérapeutique*. Thèse pour le doctorat de Pharmacie de Poitiers de l'Université de Poitiers, France.

Renwick, A. G., Dragsted, L. O., Fletcher, R. J., Flynn, A., Scott, J. M., Tuijtelaars, S. & Wildemann, T. 2008 Minimising the population risk of micronutrient deficiency and over-consumption: a new approach using selenium as an example. *Eur. J. Nutr.* **47**, 17–25.

Rock, C. L. 2007 Multivitamin-multimineral supplements: who uses them? *Am. J. Clin. Nutr.* **85**, 277S–279S.

Sandstrom, B. 1998 Toxicity considerations when revising the Nordic nutrition recommendations. *J. Nutr.* **128**, 372S–374S.

Santé Canada 1986 *Documentation pour la qualité de l'eau potable au Canada–Documentation à l'appui–Le sélénium*. Available at: http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/water-eau/selenium/selenium-fra.pdf

Schumann, K. 2006 Dietary reference intakes for trace elements revisited. *J. Trace Elem. Med. Biol.* **20**, 59–61.

Schwarz, K. & Foltz, C. M. 1999 Selenium as an integral part of factor 3 against dietary necrotic liver degeneration 1951. *Nutrition* **15**, 255.

See, K. A., Lavercombe, P. S., Dillon, J. & Ginsberg, R. 2006 Accidental death from acute selenium poisoning. *Med. J. Australia* **185**, 388–389.

Simonoff, M. & Simonoff, G. 1991 *Le sélénium et la vie*. Masson, Paris.

Srivastava, A. K., Gupta, B. N., Bihari, V. & Gaur, J. S. 1995 Generalized hair loss and selenium exposure. *Vet. Hum. Toxicol.* **37**, 468–469.

Stranges, S., Marshall, J. R., Natarajan, R., Donahue, R. P., Trevisan, M., Combs, G. F., Cappuccio, F. P., Ceriello, A. & Reid, M. E. 2007 Effects of long-term selenium supplementation on the incidence of type 2 diabetes: a randomized trial. *Ann. Intern. Med.* **147**, 217–223.

Suetens, C., Moreno-Reyes, R., Chasseur, C., Mathieu, F., Begaux, F., Haubruge, E., Durand, M. C., Neve, J. & Vanderpas, J. 2001 Epidemiological support for a multifactorial aetiology of Kashin-Beck disease in Tibet. *Int. Orthop.* **25**, 180–187.

Sutter, M. E., Thomas, J. D., Brown, J. & Morgan, B. 2008 Selenium toxicity: a case of selenosis caused by a nutritional supplement. *Ann. Intern. Med.* **148**, 970–971.

Tapiero, H., Townsend, D. M. & Tew, K. D. 2003 The antioxidant role of selenium and seleno-compounds. *Biomed. Pharmacother.* **57**, 134–144.

Thérond, P., Malvy, D. & Favier, A. 1997 Toxicité du sélénium à doses pharmacologiques par voie orale. *Nutr. Clin. Metabol.* **11**, 91–101.

Tinggi, U. 2003 Essentiality and toxicity of selenium and its status in Australia: a review. *Toxicol. Lett.* **137**, 103–110.

van Rij, A. M., Thomson, C. D., McKenzie, J. M. & Robinson, M. F. 1979 Selenium deficiency in total parenteral nutrition. *Am. J. Clin. Nutr.* **32**, 2076–2085.

Ventura, M. G., Do Carmo Freitas, M., Pacheco, A., Van Meerten, T. & Wolterbeek, H. T. 2007 Selenium content in selected Portuguese foodstuffs. *Eur. Food Res. Technol.* **224**, 395–401.

Vigouroux, P. & Pointet, T. 2007 Boire de l'eau du robinet ou l'eau en bouteille. *Geosciences* **5**, 80.

WHO 1996 *Guidelines for Drinking-Water Quality: Health Criteria and Other Supporting Information*, 2nd edition. Vol. 2. World Health Organization, Geneva.

WHO 2004 *Guidelines for Drinking-water Quality: Recommendations*, 3rd edition. Vol. 1. World Health Organization, Geneva.

WHO 2006 *Expert Consultation for 2nd Addendum to the 3rd Edition of the Guidelines for Drinking-water Quality*, WHO/SDE/WSH/06.05. World Health Organization, Geneva.

Yang, G., Yin, S., Zhou, R., Gu, L., Yan, B., Liu, Y. & Liu, Y. 1989 Studies of safe maximal daily dietary selenium intake in a seleniferous area in China II. Relation between Se-intake and the manifestation of clinical signs and certain biochemical alterations in blood and urine. *J. Trace Elem. Elect. Health Dis.* **3**, 123–130.

Yang, G. & Zhou, R. 1994 Further observations on the human maximum safe dietary selenium intake in a seleniferous area of China. *J. Trace Elem. Electrolytes Health Dis.* **8**, 159–165.

First received 9 September 2008; accepted in revised form 27 December 2008. Available online July 2009