AGENCE FRANÇAISE
DE SÉCURITÉ SANITAIRE
DES ALIMENTS

Assessment of the health risks from non-compliance with drinking water parametric values

June 2004 to October 2005

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This document presents the approach proposed to assess health risks from non-compliance with drinking water parametric values and collect the individual information sheets proposed for each chemical substance studied from June 2004 to October 2005.
All files (individual information sheets from June 2004 to April 2007) are collected in the French document which is available on Afssa website: www.afssa.fr.

List of abbreviations

ADI	Acceptable Daily Intake
ATSDR	Agency for Toxic Substance and Disease Registry
BMD	Benchmark Dose
MAC	Maximum Acceptable Concentration
CR	excess lifetime Cancer Risk
CREDOC	Centre de recherche pour l’étude et l’observation des conditions de vie [Research centre for the study of living conditions]
HA	Health Advisories
ERI	Excès de Risque Individuel [excess individual risk]
ERU	Excès de Risque Unitaire [excess unit risk]
INCA	Enquête Individuelle et Nationale des Consommations Alimentaires [French National individual food consumption survey]
IPCS	International Program of Chemical Safety
IRIS	Integrated Risk Information System
JECFA	Joint Expert Committee on Food Additives
LOAEL	Lowest Observed Adverse Effect Level
MCL	Maximum Contaminant Level
MRL	Minimal Risk Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
RfD	Reference Dose
RIVM	RijksInstituut voor Volksgezondheid en Milieuhygiene
SCF	Scientific Committee on Food
SISE-Eaux	Système d'information en Santé-Environnement sur les Eaux [Health-Environment Water Information system]
SF	Slope Factor
TC	Tumorigenic Concentration
TD	Tumorigenic Dose
TDI	Tolerable Daily Intake
UDI	Unité de distribution d’eau - [Water supply system]
US EPA	United States Environmental Protection Agency
TRV	Toxicological reference value
WHO	World Health Organization

Introduction

The Agence française de sécurité sanitaire des aliments [French Food Safety Agency] received a request on 17 April 2003 from the Ministère chargé de la santé [Ministry for Health] for an assessment of the health risks from non-compliance with the parametric values for drinking water.

The question posed involves the determination, for certain physico-chemical parameters, of a concentration in water higher than the regulatory value which would pose no risk to the health of a person consuming this water for a limited period.

- Preamble:

The quality limits of chemical parameters and reference values of indicator parameters set by the French Public Health Code, which transposes Council Directive 98/83/EC, mainly correspond to the guideline values established by the World Health Organization. These guideline values represent "*the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption."* In addition, the World Health Organization specifies in its directives that "*deviations above the guideline values in either the short or long term may not mean that the water is unsuitable for consumption. The amount by which, and the period for which, any guideline value can be exceeded without affecting public health depends upon the specific substance involved*."

When a situation of non-compliance with water quality standards and reference levels occurs, it has to be managed in such a way as to avoid causing any harmful effects to consumer health. However, it must be remembered that the water in the mains supply is also intended for uses other than in the diet (drinking and cooking food), which might have an impact on human health and public safety:

- in the home and within organisations: personal hygiene and domestic uses and for waste disposal;
- in hospitals: used for dialysis, healthcare activities, cleaning equipment;
- in industry and in urban areas: firefighting and cooling systems for a variety of installations.

A suspension of the water supply could, for this reason, pose a risk greater than that from the consumption, for a limited period, of water not in compliance with the parametric values. In such a situation, suspension of the water supply should not be envisaged systematically, as the consequences of such a measure must be assessed on the basis of each individual situation. The possible consequences of a suspension of the water supply are presented in Annex I.

Regulations are in place to cover non-compliances with the parametric values. As a last resort, for substances which are covered by quality limits, a derogation may be granted for a maximum period of three years, renewable, if the following conditions are strictly complied with:

- there are no other reasonable means of maintaining the water supply;
- ingestion of the water does not constitute a potential hazard to human health;

As part of a derogation request, an action plan to improve mains water quality must be prepared by the body responsible for the water supply.

Within this context, the working group undertook a review from the standpoint of food safety, as regards drinking water, and based on two themes. Firstly, the search for a general approach to enable a common system to be proposed for all chemical substances. Secondly, for each substance, the collection and analysis of toxicological and population exposure data to develop recommendations which could be used by the Direction Générale de la Santé to establish management thresholds in the event of a deviation above the parametric values.

- To identify a general approach, the working group examined:
    - how the guideline values were constructed;
    - the estimation, for the different substances, of intake from solid food, water and, where applicable, other exposure routes;
    - the health risk assessment systems proposed by other bodies, designed to determine concentrations in drinking water acceptable for limited periods.

- For each substance, the review was organised around the following points:
    - What is the hazard from this substance (toxicological and epidemiological data)?
    - What are the toxicological reference values?
    - What is the principal source of this substance in water?
    - What treatment processes can be used to remedy the situation?
    - What proportion of the intake is from, firstly, solid food and water, and, secondly, other intake sources?
    - Is there a safety margin? How far can consumer safety be guaranteed when there is a concentration in water above the parametric value for a limited period?

The answers to these questions provide the elements of assessment required by the health authorities to fix values for the action thresholds laid down in the Public Health Code.

Finally, it must be emphasised that this study solely concerns the particular situation of non-compliance with the parametric values covered by the Public Health Code for limited time periods, based on the current state of scientific knowledge. **It does not in any sense seek to call into question the risk assessment carried out by the World Health Organisation, nor the parametric values set by the European and national legislation based on it.**

Context and objectives

1. Regulatory framework laid down by the Public Health Code

Council Directive 98/83/EC[1] on water quality drew extensively on the studies published by the World Health Organization (WHO) in 1994 and 1998[2] when setting new limits for drinking water. The Public Health Code transposed these quality requirements and supplemented them by fixing limits notably for microcystin-LR, barium, turbidity and chlorites.

Drinking water must comply with the following quality requirements at the point at which it emerges from the taps used for human consumption:

- it must be free from any number or concentration of micro-organisms, parasites or any substances which constitute a potential danger to human health;
- it must comply with the **quality limits** set out in the French Public Health Code. These limits are fixed for parameters which, when they are found in water, are likely to produce immediate or long-term effects on consumer health. They are generally based on the current World Health Organization (WHO) recommendations.
- it must comply with the **quality reference levels** set out in the French Public Health Code. These reference levels are indicative values established for the purposes of monitoring water production and supply installations and for assessing the risk to human health. The parameters concerned may be indicators of the presence of other substances in the supply at high concentrations and/or of a malfunction of the treatment plant. The presence of these parameters may also cause discomfort and inconvenience for the consumer.

When there is non-compliance with the quality limits and reference levels, these situations have to be managed in such a way as to avoid causing any harmful effects to consumer health.

The Public Health Code includes regulations specifying the procedures for managing these situations of non-compliance with the quality limits or reference levels, in particular the role of the different stakeholders.

When the corrective measures do not enable rapid remedying of the non-compliance with the water quality limits, a derogation may then be envisaged. The derogation procedure is set out in Council Directive 98/83/EC on the quality of water intended for human consumption.

A derogation satisfies a double objective:

- to manage situations of non-compliance with water quality standards whilst ensuring user health is protected,
- to implement the necessary effective measures to restore mains water quality.

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[1] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption, OJEC of 5.12.98

[2] The Guidelines for Drinking Water Quality are currently being revised by the World Health Organization: http://www.who.int/water_sanitation_health/dwq/guidelines3rd/en/

A derogation may only be granted when there is strict compliance with the two conditions below:

- there are no other reasonable means available to maintain the water supply (treatment, change of supply, implementation of interconnections, pumping station shutdown, etc.);
- the deviation above the quality limit during the derogation period will not have any harmful effects on consumer health;

As part of a derogation request, an action plan to improve mains water quality must be prepared by the body responsible for the water supply.

The derogation is temporary: it may only be granted, following authorisation by the local health authorities, for a period of three years, renewable once. A third derogation may be granted in exceptional circumstances; the decision is then made by the European Commission.

2 Situations of non-compliance with parametric values

2.1 Origin of substances found in water

A number of different origins may explain the presence in water of undesirable substances or substances at unusual levels:

- the geological nature of the catchment area for the water supply used for drinking water production,
- certain activities in the catchment basin (farming, industry, urban areas, etc.),
- certain stages in the treatment process for water intended for human consumption may result in concentrations in the water of:
  - substances used during physico-chemical treatment phases,
  - disinfection by-products,
- interactions between the water and the plant and equipment in the mains network,
- exceptional (meteorological) or accidental situations at different stages in the production of the water (from the original source to the point of use).

A table in Annex II shows the most likely origins of substances which are subject to quality limits or reference levels in the Public Health Code.

The Public Health Code specifies that a report of a non-compliance with these parametric values must trigger an investigation to identify the origin of the presence in the water of the substance concerned and that corrective measures must be implemented as quickly as possible.

Management systems for remedying the non-compliance situation must be adapted according to the source of the contamination, its location (between the catchment point and the point of use) and to which treatment procedures can be implemented.

2.2 Data on mains water quality in France

Information on the quality of mains water in France was extracted from the national database SISE-Eaux [Health-Environment Water Information System] at the Ministry for Health. This database collects data from the mains water tests carried out by each local health authorities. Each year, more than 300,000 samples of water are collected for this purpose, producing over four million different test results.

2.2.1. Organisation of the water supply in France

Almost the entire French population is connected to the public mains supply network. These networks are supplied by approximately 29,300 catchment basins, of which 27,900 (95%) are groundwater and 1,400 surface water. However, in terms of quantity, groundwater accounts for only 64% of production.

Water is supplied by 26,845 "unités de distribution publique (UDI)" [water supply systems]. A water supply system comprises a network managed and operated by a single structure and supplying water to the same quality standard. The number of supply systems varies between one Department and another, from 7 UDI to 875 UDI. Over 60% of the supply systems serve less than 500 inhabitants, while some 2,100 UDI supplying over 5,000 inhabitants serve a total of almost 70% of the French population. *(Source: Ministry for Health, 2004)*

2.2.2. Type of information received as part of the referral

The information collected was analysed with the objective of providing the working group with useful elements for evaluation and not as an exhaustive review of the quality of the water supply in France.

The information sent by the Ministry for Health covered the tests performed at the exit points of production plants and at the UDI for the years 1999 to 2002. For each parameter tested and for each UDI, the following information was provided:

- the population supplied by the UDI;
- the total number of tests carried out on the network and/or performed at the exit points of production plants;
- the number and percentage of non-compliant tests;
- the mean and maximum of the concentrations measured per UDI;
- the mean of the results of the non-compliant tests (concentration higher than the quality limit);
- the value of the 95th percentile and the 50th percentile for all the non-compliant tests.

2.2.3. Processing the data received

Exploitation of the information received from the Ministry for Health enabled:

- estimation of the number of UDI for which data were available and an estimate of the population supplied by these UDI;
- estimation of the number of UDI for which at least one non-compliant result had been recorded and the population concerned;

Moreover, an inventory of the supply units for which a non-compliance with the quality limits or reference levels for several substances has been observed, with identification of the substances concerned, is currently being prepared by Afssa, using data from the SISE-Eaux database.

2.2.4. Representivity of the data

The procedures for conducting test programmes as part of the health inspection framework are now laid down by the French Public Health Code. For the period 1999 to 2003, these procedures were fixed by Decree No. 89-3 of 3 January 1989[1] concerning the quality of water intended for human consumption. Nonetheless, the representivity of the data available is limited for a number of reasons:

- The test programme depends on the size of the population supplied, but it may also be adapted to local conditions. Therefore, when the mains water fails to meet quality standards, this control system can be strengthened. Conversely, for certain substances whose absence from the water source guarantees their absence from the water supplied, the frequency of testing at supply level can be reduced.

  This means that certain parameters were not tested in some UDI during the period under consideration.

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[1] Decree No. 89-3 of 3 January 1989 concerning the quality of water intended for human consumption, excluding natural mineral water, JORF of 04 January 1989

- For each UDI, the tests performed on the supply network and at the exit point of production plant were taken into consideration. It is possible that for certain UDI, the analysis results did not accurately represent the quality of the water actually consumed, in view of the complexity of the modes of supply (mixture of water, interconnection, etc.).

  For example, this situation may be found in the case of a UDI in which the water supplied comes from a mixture within the network of water produced from two different treatment plants, one producing water in compliance and the other supplying non-compliant water, when the mixed water does meet the quality standards. This would cause the UDI in compliance to be declared non-compliant, resulting in an overestimate of the number of non-compliant UDI.

- The data from the SISE-Eaux database enable evaluation of the quality of water in the mains supply: samples are taken either at the exit point of the treatment plant or from a point on the mains network. Before the new regulations came into effect, testing was not intended to highlight non-compliances concerning a breakdown in water quality within the internal networks. Any non-compliances discovered were therefore not recorded in this database. From now on, tests are to be performed at the point of use for certain parameters which are liable to change within the mains network.

2.3 Interpreting the test results

The analytical uncertainty (Cf. Annex III) concerns :

- the level of concentration of the elements in the water
- the analysis method used,
- the type of element and its stability over time.

For each test result, the question arises of how to take into account the analytical uncertainty, notably for the value above which the non-compliance can be considered effective.

Furthermore, sampling fluctuations may become apparent, related to the stability of the parameter in the water mass and over time.

Procedures for taking into account analytical uncertainty and uncertainty related to sampling fluctuations in situations of non-compliance for water were examined by the working group and some proposals were discussed. Dealing with this issue on the ground remains a relatively complex matter, however, and requires more in-depth examination.

Risk assessment

Before presenting the approach adopted for determining a concentration in water (greater than the parametric value) which would present no risk to the health of a person consuming this water for a limited period, it is worth recalling the method used by the World Health Organization to determine the guideline values.

1. Determination of guideline values for chemical substances

The approach varies according to whether or not there is a threshold for the appearance of the undesirable effect induced by the substance under consideration.

- When it is possible to define a threshold dose below which no harmful biological effect is observed, this is described as a compound with a deterministic effect. Above that threshold the effect increases depending on the dose administered.
- Conversely, for certain compounds, it is not considered possible, in principle, to define a no-effect threshold. The effect is then described as probabilistic or stochastic, which is the case for genotoxic carcinogenic substances.

The WHO defines a guideline value (GV) as an estimate of the concentration of a substance in drinking water which does not result in any significant risk to the health of the consumer over a lifetime of consumption. It is expressed in mg/L.

The starting point for fixing a guideline value is the toxicological reference value of the parameter. The toxicological indices or toxicological reference values (TRV) proposed by different bodies (WHO, USEPA, ATSDR, RIVM, etc.) are generally specific to a determined critical effect[1], a route of administration and an exposure period.

Some guideline values are defined on the basis of other considerations, principally acceptability criteria, discussed in Paragraph 1.3.

1.1 Threshold toxic effects

1.1.1 Determining the toxicological reference value

In the case of oral exposure, the toxicological reference value is defined as being the estimate of the quantity of substance to which an individual can theoretically be exposed for a determined period without the occurrence of harmful effects on health. Depending on the organisation, and although similar in type, different terms are used to describe them:

- Reference doses (RfD) by the US EPA,
- Minimal risk levels (MRL) by the ATSDR
- Tolerable Daily Intake (TDI) for the World Health Organization (WHO), the RIVM or Health Canada.

The toxicological reference value is expressed in mass of substance per kilo of body weight and per day (mg/kg b.w./d)

Generally, this TRV is obtained from long term animal studies (more rarely from epidemiological studies in humans), during which the critical dose is determined (NOAEL[2], LOAEL[3], BMD[4]). This value is then divided by uncertainty factors to obtain an acceptable safety level for humans. These uncertainty factors take into account the variability between species and between individuals, and uncertainties related to the experimental protocols.

TRV = Critical dose / uncertainty factors

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[1] *the critical effect is the first adverse effect which occurs when the dose is increased and judged relevant to humans for determination of the TRV (Invs, 2002)*

[2] NOAEL: No Observed Adverse Effect Level

[3] LOAEL: Low Observed Adverse Effect Level

[4] Benchmark dose

It is important to emphasise that this TRV does not represent a toxicity threshold but an exposure level considered acceptable as it does not result in the manifestation of an effect considered undesirable.

Evaluation of the "benchmark dose" (or BMD)[1] is an alternative method for determining the TRV, recommended by the US EPA, which avoids the variability inherent in animal experimentation when using a NOAEL as a critical dose. It is less dependent on the experimental doses selected and can be based on smaller samples.*(Crump, 1984)*

1.1.2 Fixing the WHO guideline value

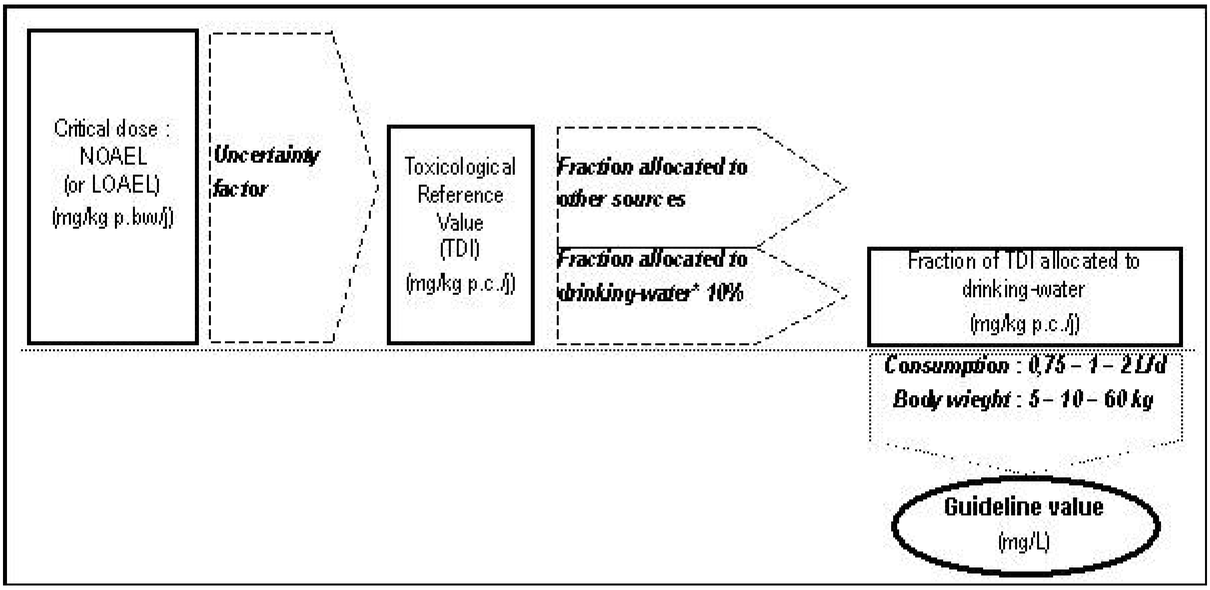
For substances with threshold toxic effects, the guideline value for water is calculated based on the bodyweight and water consumption of the target population:

$$\text{GV} = \frac{\text{TDI} \times b.w. \times P}{C}$$

in which:

- "b.w." is body weight. The reference values used by the WHO are: 60 kg for an adult[2], 10 kg for a child, 5 kg for an infant,
- "C" is the daily consumption of drinking water. The reference values used by the WHO are: 2 litres for an adult[3], 1 litre for a child, 0.75 litre for an infant,
- " P" is the proportion of the TDI attributed to drinking water, as this is not usually the sole source of exposure for humans, so that only part of the TDI is attributable to water intake.

This approach provides a guarantee that the sum of all the sources of intake does not exceed the TDI.



* a default proportion of 10% was attributed by the WHO, however, this may vary, depending on the substances, from 1% (for DDT) to 100% (for chlorine).

Figure 1: Process for determining guideline values used by the WHO for substances with threshold toxic effects.

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[1] The objective of this method is to determine, using a statistical adjustment of all the observation data, the lower limit of the confidence interval at 95% of the dose producing a critical effect with an increase in frequency most often set at 5 or 10%. It is this value which is used as the starting point (critical dose) for applying the safety factors already mentioned for establishing the TRV. *(Crump, 1984)*

[2] certain bodies, such as the US-EPA, use, for adults, a reference weight of 70 kg.

[3] certain bodies, such as the US-EPA or Health Canada, use, for adults, a daily consumption of 1.5 litres.

The WHO generally attributes a proportion of 10% of the TDI to drinking water, whilst stating that " *It is recognized that exposure from various media may vary with local circumstances. It should be emphasized, therefore, that the derived guideline values apply to a typical exposure scenario or are based on default values that may not be applicable for all areas. In those areas where relevant data on exposure are available, authorities are encouraged to develop context-specific guideline values that are tailored to local circumstances and conditions. For example, in areas where the intake of a particular contaminant in drinking-water is known to be much greater than that from other sources (i.e., air and food), it may be appropriate to allocate a greater proportion of the TDI to drinking-water to derive a guideline value more suited to the local conditions. In addition, in cases in which guideline values are exceeded, efforts should be made to assess the contribution of other sources to total intake; if practicable, exposure from these sources should be minimized " (WHO, 1994)*

When determining the guideline values, the WHO generally based them on a daily consumption of 2 litres for a person weighing 60 kg. When toxicological and/or epidemiological data highlight a particular susceptibility in infants or young children, the guideline values were established based on a individual weighing 10 kg consuming a litre of water a day or an individual weighing 5 kg consuming 0.75 litres a day *(WHO, 1994).*

1.2 Non-threshold toxic effects

Non-threshold toxic effects are genotoxic, mutagenic and/or carcinogenic effects[1]."*The major hypothesis is that there is no toxicity threshold; in other words, whatever the intensity of exposure, it is always associated with a probability that the disease will occur." (Invs, 2002)*

This is expressed as excess risk, meaning an increase in the probability of the occurrence of the effect compared with the situation in which there was no exposure to the substance.

1.2.1 Determining the toxicological reference value

The toxicological reference value for these substances can be defined as the dose corresponding to the additional probability, compared with a non-exposed subject, that an individual will develop cancer if he is exposed over a lifetime to one dose unit of the carcinogenic substance.

For substances deemed not to have an effect threshold, the approach used is based on:

- determination of a dose equivalent for humans,
- modelling of the experimental data,
- extrapolation to low doses of effects observed experimentally in animals at high doses.

Over time, different statistical or mechanistic models have been recommended, attempting to better take into account the knowledge acquired on the biology of carcinogenicity *(Invs, 2002)*.

In terms of the mechanistic models, developed from hypotheses on the mechanism of action of carcinogenicity:

- Until recently, extrapolation to low exposure doses was based on the use of a linearised multi-stage model. This originated from the multi-stage theory developed by Armitage and Doll in which a cell must pass sequentially through k stages before becoming cancerous. Each stage may be matched to a linear function of the dose, each being independent of the other, but necessary for the expression of the tumour.
- Since 1996, the EPA has been recommending the use of the MVK (Moolgavkar-Venzon-Knudson) model, sometimes called the two stage clonal expansion model due to its greater relevance to current

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[1] Assessment of the potential carcinogenicity of chemical substances is based generally on long term animal studies, or sometimes on data on carcinogenicity in humans. Based on the data available, the IARC classifies chemical substances in four groups according to their carcinogenic risk *(WHO, 1994)*. The US-EPA has a classification system for chemical substances based on their carcinogenicity. These classifications are shown in Annex IV *(InVs, 2002).*

knowledge of the mechanisms of carcinogenicity and the possibility of integrating time-based data ("time-to-tumor" model) *(US EPA, 1999)*.

An alternative approach is proposed by the US EPA, based on a linear extrapolation described initially by Gaylor and Kodell (1980). *(Gaylor et al., 1999)*

As mentioned above, depending on the organisation, different expressions of the TRV for non-threshold toxic effects can be found:

- The Oral slope factor (Sfo) produced by the US EPA for the oral route,
- Excess unit risk (EUR) used by the WHO,
- Excess lifetime Cancer Risk (CR) used by the RIVM for all exposure routes.

For these three organisations, this indicator is the opposite of a dose and is expressed in (mg/kg b.w./d)$^{-1}$

- The tumorigenic dose or concentration (TD05 or TC05) used by Health Canada. This is the total dose (or concentration) which induces a 5% increase in the incidence of tumours attributable to exposure to a genotoxic compound.

In the particular case of water, the US-EPA also defines a particular TRV entitled the "Drinking Water Unit Risk", expressed as the converse of a concentration (µg/L)$^{-1}$, which enables direct calculation of the risk from the concentration found in drinking water. This value is obtained by multiplying the "oral slope factor" by 70 kg (default weight for an adult) and dividing it by 2 L (default water consumption). It can therefore only be used for risk assessment if these conditions are met.

1.2.2 Fixing the WHO guideline value

In the case of substances considered as having non-threshold toxic effects, the relationship between a level of risk fixed previously and the corresponding guideline value is based on a mathematical model extrapolating the epidemiological or experimental results to low doses.

As a general rule, these guideline values are presented as being the concentration in drinking water associated with an excess lifetime cancer risk[1] of 10^{-5} (one additional case of cancer per population of 100,000 persons consuming drinking water for 70 years containing the substance in question at a concentration equal to the guideline value). It must be emphasised that Council Directive 98/83/EC on the quality of water intended for human consumption, uses, for most substances, an excess cancer risk of 10^{-6}.

To determine the guideline value, the WHO uses the hypothesis of a daily water consumption of 2 litres. It should be noted that in this case determination of the guideline value does not take into account any other intakes.

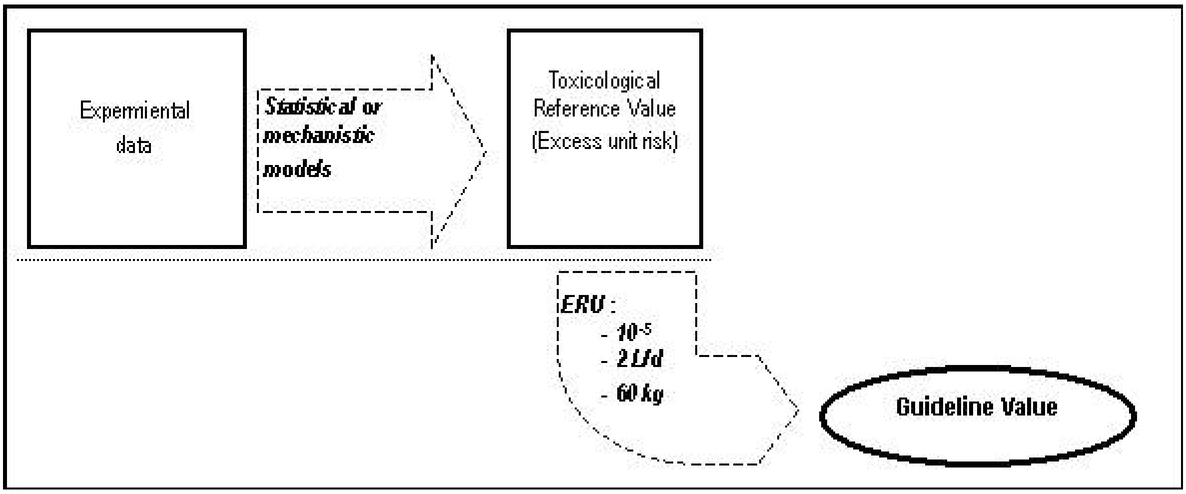

Figure 2 : Process for determining guideline values followed by the WHO for non-threshold toxic effects

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[1] As part of the review of its drinking water guidelines by the World Health Organization, this body is proposing a range of concentrations in drinking water which correspond to an additional cancer risk of 10^{-4}, 10^{-5} and 10^{-6} (http://www.who.int/water_sanitation_health/dwq/guidelines3rd/en/)

1.3 Acceptability criteria

A number of criteria influence consumer acceptance of drinking water. Certain substances for which guideline values have been established by the WHO on the basis of health data may alter the taste and odour of the water at concentrations lower than this value.

For this reason, the World Health Organization proposes specific guideline values for those substances which influence user acceptability of water without, however, having a direct influence on health. *(WHO, 1994).*

2. Approach adopted

In the first place, it must be remembered that the World Health Organization, in its Guidelines on drinking water quality *(WHO, 2004),* stated that "*the exceedance of a guideline value may not result in a significant or increased risk to health. Therefore, deviations above the guideline values in either the short or long term may not mean that the water is unsuitable for consumption. The amount by which, and the period for which, any guideline value can be exceeded without affecting public health depends upon the specific substance involved.*"

This section describes the methodology used by the working group to establish recommendations on non-compliances with the quality limits or reference levels for water intended for human consumption which would be acceptable for limited periods.

Different approaches are described in turn, distinguishing between:

- Substances with a threshold toxic effect,
- Potentially carcinogenic substances,
- Mixtures of substances,
- Pesticides,
- Certain parameters covered by quality reference levels,

These approaches are applied to chemical substances which are the subject of quality reference levels or limits in the Public Health Code[1]. An information sheet, followed by recommendations, has been produced for each parameter.

In addition, the working group also looked at the systems proposed by other bodies for defining levels acceptable in the event of a deviation above the parametric values, notably the US EPA "Health Advisory" programme *(Donohue J.M. et al., 2002; US-EPA, 1989 and 2002)* and the system proposed by Germany.

The approach selected was presented to the "Drinking Water" and "Chemical and Physical Contaminants" Committees of AFSSA.

2.1 Chemical substances with threshold toxic effects

Using the method for calculating the guideline value

$$\text{GV} = \frac{\text{TDI} \times b.w. \times P}{C}$$

and complying with the level selected for the toxicological reference value, it is possible to look again, as the WHO in fact suggests, at the default values with regard to the French situation. As the guideline values were established by the WHO on the basis of a standard exposure scenario, it is interesting to compare them with a more realistic exposure scenario based on national data, where these exist, concerning:

- Drinking water consumption[2],
- The portion of the TRV attributable to drinking water given, notably, the estimated level of dietary intake (generally 10% attributed to water).

The approach described below is therefore intended to find an eventual "available toxicological credit" whilst complying with the toxicological reference value used by the WHO.

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[1] The approach proposed for deviations above the quality reference levels for radioactivity indicators will be presented in the information sheet specific to these substances.

[2] If the values used by the WHO over-estimate national water consumption data, the same proportion of credit could logically be applied for each substance.

2.1.1 Water consumption data

The working group looked at the water consumption data for the mains water supply, which can be ingested in different forms:

- cold water (for drinking),
- heated water (for preparing coffee, tea, etc.),
- water incorporated during food preparation and cooking (rice, pasta, soup, etc.).

Consumption data were provided by the Observatoire des consommations alimentaires *(Afssa, 2003)*. These data, drawn from the INCA 1999 and Sofres 1997 surveys, are shown in Table 1.

Table 1: **Summary of mains water consumption, heated and unheated, for different age groups**
Source: INCA 1999 and Sofres 1997 Surveys – Processed by OCA (Afssa, 2003)

		Whole population		Percentage of water consumers (%)	Consumers of mains water only	
Population	Source	Mean (ml/d)	95th perc. (ml/d)		Mean (ml/d)	95th perc. (ml/d)
Adult (> 15 yrs)	INCA 1999	540	1371	96	560	1377
Children 3 - 14 yrs	INCA 1999	279	761	84	331	807
Children 3 - 4 yrs	INCA 1999	203	610	75	270	627
Children 9 - 11 yrs	INCA 1999	285	718	87	327	727
Babies < 30 mths	SOFRES 1997	96	520	40	238	693

Guide: mean consumption for adults was 539.7 ml of tap water per day. The 5% heaviest consumers consumed over 1371.4 ml/day. Over a week of consumption, 96.3% of the population consumed tap water: for consumers of mains water only, mean consumption was 560.2 ml/day.

- The INCA 1999 survey[1] (individual and national food consumption survey) was conducted with 3003 subjects representative of the French population.

  In this survey, unheated water was represented by tap water consumed directly and heated water corresponded to tap water consumed in the form of tea or coffee. Water incorporated in food was not taken into account and this intake could be as much as 170 to 280 ml per day *(Meyer et al., 1999)*

- The survey conducted by Sofres in 1997[2] on behalf of the Syndicat Français des ALiments de l'enfance et de la diététique (SFAED) [French Association of Children's and Dietetic Foods], covered 658 children aged from 1 to 30 months.

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[1] The INCA 1999 survey (individual and national food consumption survey) was conducted by CREDOC in 1998-99 (CREDOC-AFSSA-DGAL, 2000). Food consumption data were obtained from consumption diaries, completed for a period of 7 consecutive days, with the identification food and portions being facilitated by a book of photographs. The survey covered 3003 subjects (1985 individuals aged over 15 years and 1018 children aged between 3 and 14 years) representative of the French population. National representivity was ensured through stratification (age, sex, individual socio-professional categories and family size).

[2] In the Sofres 1997 survey, the sample studied was 658 infants aged between 1 and 30 months. The sample was representative of families in mainland France with children of the same age from the standpoint of region, size of community and the socio-professional category of the head of the family. The survey was conducted in the field in the first half of 1997, by Sofres and Dijon University Hospital for the Alliance 7 association. The parents of the infant studied recorded all their child's food intake for 7 consecutive days.

This survey refers to "ordinary water" which SFAED defines as tap water. Data for the consumption of heated water are not available.

The major covariables for tap water consumption are the consumption of other drinks, weight, age and region of origin. *(Beaudeau et al, 2003)*

Fluctuations in the quality of water supplied locally are likely to alter user behaviour *(Meyer et al.,1999 ; Gofti-Laroche et al., 2001)* and major regional variations in tap water consumption were reported at the end of the INCA 1999 study. Table 2 shows the disparities which can exist between regions in which high consumption of water is reported (South-west and South-east) and regions where it is lower *(Beaudeau et al, 2003.)*

Table 2: Regional disparities in tap water consumption

	4 – 14 yrs		40 – 64 yrs[1]	
Consumption in L/day	Low consumption region	High consumption region	Low consumption region	High consumption region
50 Percentile	0.20 L/day	0.31 L/day	0.42 L/day	0.61 L/day
95 Percentile	0.78 L/day	1.06 L/day	1.30 L/day	1.69 L/day
99 Percentile	1.21 L/day	1.57 L/day	1.89 L/day	2.38 L/day

Data from recent surveys of mains water consumption habits in the French population indicate that the values for water consumption used as default values by the WHO are similar to those observed in heavy consumers.

It was deemed desirable to retain, whatever the age group concerned, the WHO reference water consumption data.

2.1.2 Relative role played by water compared with other sources of intake

Determination of the proportion of the TRV attributable to drinking water compared with other routes of exposure (dietary in particular) requires a specific approach for each compound. For this reason, data which could estimate the population's exposure to different sources were sought out, in particular those linked to diet, the other routes being, except in specific cases, of minority interest.

These data were drawn from:

- TDS (Total Diet Studies) type studies, mostly based on sampling campaigns for the most heavily consumed foodstuffs ("shopping basket" studies) or duplicated diet (standard meals served in different organisations);
- contamination data for substances in certain foods or beverages (tea, beer, wine, miscellaneous beverages excluding water).

The results of the exposure studies in France or other countries were also taken into account.

The working group took into account the estimates of intakes by other routes of exposure, when these data were available.

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[1] This age group represents the heaviest consumers of heated and unheated mains water in the age group 15 to ≥ 65 years

2.1.3 Work schedule for substances having a threshold toxic effect

For each chemical substance with a threshold toxic effect, listed in the Public Health Code, the following process was followed:

1. a report on the hazards posed by each substance and identification of the most relevant toxicological reference value (TRV),
2. an estimation, within the limits of the available data, of daily dietary intakes in the French, or failing that, the European population,
3. adding intake from solid food and intake from drinking water for different concentrations of this substance in water (with the objective of identifying the proportion of exposure attributable to water),
4. comparing the estimation of intake in water and food and where applicable, from air, with the tolerable daily intake determined from the TRV used and the reference body weight of an individual.

   The working group generally used the WHO criteria, based on a daily consumption of 2 litres by an individual weighing 60 kg. However, when the toxicological and/or epidemiological data highlighted a particular susceptibility in infants or children, this consumption was reduced to 1 litre for a child weighing 10 kg and to 0.75 litre for an infant weighing 5 kg.

When considering the upper limit for intake from solid food, the approach adopted consisted in identifying the proportion of exposure which could be attributed to water; whilst complying with the tolerable daily intake.

The approach is purposely protective through the choice of high values for water consumption and food consumption estimates.

It is clear that it cannot be fully completed without sufficient available data on daily food consumption.

2.2 Chemical substances with non-threshold toxic effects

Genotoxic carcinogenic substances are considered as acting without a threshold and even very low levels of exposure are associated with an excess cancer risk.

The guideline values proposed by the European Union and reflected in the Public Health Code correspond, for the most part[1], to the concentration in drinking water associated with an additional lifetime cancer risk of 10^{-6} (1 excess case per 1,000,000 persons exposed).

Insofar as the consumption of water with a concentration Co (= Parametric value) of a substance with non-threshold toxic effects is associated with an additional cancer risk, it is possible, by using the excess unit risk (EUR) for the latter, to estimate the surplus additional lifetime cancer risk from exposure to water with a concentration (n × Co) over 3, 6 or 9 years.

To be able to include any possible susceptibility of newborn babies and young children, the US-EPA *(US EPA, 2005)* proposes applying an additional factor of 10 for the period of life from birth to 2 years and an additional factor of 3 for the period from 2 to 15 years of age.

The approach proposed enables quantification of the proportion of excess cancer risk associated with exposure during a given time to a concentration higher than the quality limit (n x Co).

Table 3 shows, for genotoxic carcinogenic substances, the increased risk factor associated with a non-compliance situation over 3, 6 and 9 years compared with the estimated risk when there is an immediate return to compliance. The calculations are based on the least favourable case of exposure from the youngest age and applying the additional factors proposed by the US-EPA for newborns and young children.

Table 3: Estimate of the increased risk factor from deviation above a parametric value in water during a given period.

Level of deviation above the guideline value	Conformity after 3 years	Conformity after 6 years	Conformity after 9 years
1.5 x	1.2	1.25	1.3
2 x	1.4	1.50	1.6
2.5 x	1.6	1.75	1.9
3 x	1.8	2	2.2
4 x	2.15	2.5	2.8
5 x	2.55	3	3.4

<u>Guide:</u> if the concentration in water is 5 times the guideline value (for example 50 µg/L for a guideline value of 10 µg/L) and if the return to compliance occurs after 6 years, the excess cancer risk estimated for the area supplied by the UDI is 3 times greater that that expected from an immediate return to compliance.

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[1] This is not the case for arsenic, Benzo[a]pyrene and Bromodichloromethane.

2.3 Non-compliance with the parametric value for several substances

The WHO in its Guidelines (WHO, 2004) states that " *Chemical contaminants of drinking-water supplies are present with numerous other inorganic and/or organic constituents. The guideline values are calculated separately for individual substances, without specific consideration of the potential for interaction of each substance with other compounds present. The large margin of uncertainty incorporated in the majority of the guideline values is considered to be sufficient to account for potential interactions.* " This organisation also emphasises the importance of deciding which measures to take based on local circumstances in situations where contaminants with similar toxicological effects are present at concentrations near or above the guideline values.

In view of the potential interactions between certain substances, it would seem worthwhile to

- make an inventory of those water supply systems in which non-compliances have been observed for several substances in order to identify these parameters and the problems they are likely to cause.
- examine very closely all requests for derogation covering several substances for a single water supply system.

2.4 Specific case of pesticides

As for other chemical substances, the World Health Organization proposed guideline values for pesticides, applying a general methodology based on the nature of the toxic effects.

Council Directive 80/778/EEC of 15 July 1980 relating to the quality of water intended for human consumption fixed, for pesticides, a maximum admissible concentration of 0.1 µg/L per substance and a value of 0.5 µg/L for total substances. The parametric value of 0.1 µg/L was fixed as a precaution, based on the fact that pesticides are not natural constituents of water and that, in consequence, they should not be found there. This value corresponds to the detection thresholds of the test methods available in the early 1970s for pesticides tested for at the time. It is not based on a toxicological approach and therefore has no significance in health terms.

By the end of the 1980s, when developments in analysis methods had enabled an improvement in the conditions for controlling pesticides in drinking water, pesticide levels at or below 0.1 µg/L could be identified.

However, Council Directive 98/83/EC retained the parametric values of 0.1 µg/L[1] for each pesticide, including the metabolites and relevant degradation and reaction products and 0.5 µg/L for total substances. The Public Health Code transposes this Directive and has therefore adopted a similar approach.

Moreover, the Public Health Code sets quality limits for the untreated water used for the production of water intended for human consumption. This water must not contain levels greater than 2 µg/L of water per separate substance.

The proposed approach developed in the information sheet on pesticides takes these considerations as the basis for proposing a limit value for all pesticides.

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[1] With the exception of aldrin, dieldrin, heptachlorine and heptachlor epoxide for which a quality limit is fixed at 0.03 µg/L

2.5 Parameters subject to quality reference levels

The values proposed for the quality reference levels in the Public Health Code are values established on the basis that the substances concerned might be:

- indicators of a malfunction in the treatment plant,
- indicators of the presence in the catchment basin of other substances at a high level,
- the cause of discomfort or inconvenience to the user.

For certain chemical substances, the quality reference level might be lower than the concentration which could be accepted on the basis of toxicological and/or epidemiological data.

Therefore, for these substances, the determination of a situation of non-compliance with quality reference levels might require a specific approach described in the summary information sheets for each substance concerned.

Conclusions and general recommendations

REGULATORY FRAMEWORK FOR WATER INTENDED FOR HUMAN CONSUMPTION

Having regard to the quality limits and reference levels for chemical substances in the Public Health Code;

Having regard to Articles R 1321-26 to R 1321-36 of the Public Health Code concerning corrective measures, restrictions on use, suspension of supply, derogations, information and advice to consumers;

Whereas a derogation from the quality limits may only be granted subject to the following conditions:

- there are no other reasonable means available for maintaining the water supply;
- the deviation above the quality limit during the derogation period will not cause harmful effects on consumer health;

Whereas an action plan to improve the quality of the water supplied must be produced by the body responsible for the water supply;

Whereas the quality limits and reference levels in the Public Health Code are, for the most part, based on the recommendations on drinking water quality which the World Health Organization published in 1994 and 1998;

Whereas the quality limits for pesticides are based on environmental criteria with a view to protecting the quality of water resources;

Whereas the substances subject to a quality reference level may be:

- indicators of a malfunction in the treatment plant,
- indicators of the presence of other substances at high levels in the supply,
- the cause of discomfort and inconvenience to users

and therefore, for some of these substances, the quality reference level may be lower than the concentration which might be accepted on the basis of toxicological and/or epidemiological data;

ORIGIN AND TREATMENT OF SUBSTANCES IN WATER

Whereas for each substance subject to a quality limit or reference level the most probable origin, and where applicable, the sources of contamination of the water intended for human consumption, have been identified;

Whereas for each substance subject to a quality limit or reference level, treatment options enabling a reduction in its levels in water have been identified;

DETERMINATION OF GUIDELINE VALUES

Having regard to the processes adopted by the World Health Organization for determining the guideline values applicable to chemical substances which might be present in water intended for human consumption;

Whereas the World Health Organization states in its Guidelines that "*the exceedance of a guideline value may not result in a significant or increased risk to health. Therefore, deviations above the guideline values in either the short or long term may not mean that the water is unsuitable for consumption. The amount by which, and the period for which, any guideline value can be exceeded without affecting public health depends upon the specific substance involved.*";

Whereas the guideline values proposed by the World Health Organization were calculated for each substance taken individually, without taking account of possible interactions with other substances present;

SCOPE OF APPLICATION OF THE APPROACHES

Whereas for each substance subject to quality limits and reference levels under the Public Health Code the following processes are applied:

- for chemical substances with threshold toxic effects, the proposed approach consists in calculating total intakes from water, solid food and air whenever sufficient information is available and comparing them with the toxicological reference value;
- for chemical substances with non-threshold toxic effects, the approach consists of quantifying the proportion of excess cancer risk associated with exposure during a given period at a concentration greater than the quality reference or limit;

Whereas for some parameters (turbidity, total organic carbon,…) subject to a quality reference level, a specific approach will be used;

Whereas, consequently, it is necessary to provide, for each substance, a specific information sheet followed by recommendations;

Whereas the approach adopted only covers water used for food preparation and for drinking, and for some substances, intake from inhalation or cutaneous contact via water could be considered in the risk assessment;

RISK ASSESSMENT FOR CHEMICAL SUBSTANCES

Having regard to the hazards presented by each substance and the toxicological reference value proposed by the international bodies;

Whereas the results of recent surveys of food consumption habits in the French population show that water consumption in 95% of French consumers drinking French water only is:

- less than 693 mL per day, for infants less than 30 months old,
- less than 1.06 L per day for children aged 4-14 years, in regions where heavy water consumption was reported,
- less than 1.69 L per day for adults aged over 15 years, where heavy water consumption was reported,

and the WHO default values (2 L/d for adults, 1 L/d for children and 0.75 L/d for infants), similar to these values, were used for this assessment;

Having regard to all intakes from water, solid food and air, when relevant data are available;

Having regard to the information concerning mains water supplied in France from the SISE-Eaux (Système d'Information en Santé-Environnement sur les Eaux) national database at the Ministry for Health and more specifically the 95th percentile of the non-compliant analysis results recorded;

Having regard to the results of exposure studies conducted in France or in other countries;

The Agence française de sécurité sanitaire des aliments:

Recommends:

1. In the event of non-compliance with the quality limit or reference level for a parameter, that the management threshold(s) be fixed on the basis of the assessment presented in the information sheet produced for each parameter[1],

2. In view of the potential interactions between several compounds:

- that particular attention be paid to derogation requests concerning several parameters at a single water supply system,
- that an inventory be made immediately of the water supply systems at which non-compliances have been observed for several substances in order to identify these parameters and the problems they are likely to reveal.

Emphasises:

- that the means must be brought to bear which enable the concentration to be lowered to the quality limit or reference level as soon as possible,
- that, where necessary, special measures should be taken as regards activities for which a deterioration in water quality could have consequences for health (haemodialysis centres, food industry, etc.),
- that it is not in any sense questioning the quality limits and reference levels arising from the risk assessment conducted by the World Health Organization.

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[1] The individual information sheets will be completed gradually for all the substances covered by the referral

Individual information sheets

File 1: Assessment of health risks related to exceeding the quality limit for antimony in water destined for human consumption

Main chemical forms used or encountered in the environment:

- antimony (7440-36-0) (Sb)
- antimony trioxide (ATO) (1309-64-4) (Sb_2O_3)
- antimony and potassium tartrate (APT)(28300-74-5) ($KSbOC_4H_4O_6$)
- antimony and sodium tartrate (AST) (34521-09-0) ($NaSbOC_4H_4O_6$)

In aqueous medium, antimony is present in the form of ions or soluble complexes. The predominant form appears to be a pentavalent oxoanion, $Sb(OH_6)^-$ *(Cotton and Wilkinson,1999; Mohammad et al, 1990)*.

1 Origin and sources of contamination:

In water sources:

Antimony is not very abundant in the earth's crust. The most abundant mineral is stibine (SbS_2) which is combined with other sulphide minerals, including galena and pyrite, in platform rocks and is also combined with quartz in hydrothermal veins. It may be present in groundwater in soils with a high sulphide mineral content.

Antimony is used with other metals to increase their hardness. It is used in the manufacture of semi-conductors, plastics and chemicals.

In public water supply systems:

Antimony is present in certain lead-free joints (Sb/Sn) in public supply systems.

2 Treatments reducing the antimony content of water

In accordance with the French drinking water regulation, the use of treatment products is subject to approval from the Minister responsible for health.

The following treatments can reduce antimony content in water, although confirmation is required on an individual case basis that the proposed treatments are approved.

Coagulation – flocculation – separation

Pentavalent antimony (Sb V) reacts with ferric iron and aluminium to give an iron or aluminium antimonate, which is co-precipitable for iron hydroxide.

Acidic pH values promote the reaction of iron with antimony.

Trivalent antimony (Sb III) is not or is very little eliminated and therefore prior oxidation is necessary for this compound.

Decarbonation

Decarbonation with lime or soda is performed at a pH of above 9.

The presence of magnesium improves the efficiency of this treatment.

Selective adsorption

On alumina: fluorides impede the process. The pH must be less than 7.5. Only antimony V is eliminated.

On manganese dioxide: the pH must be less than 8. Antimony III and V are eliminated.

Iron oxyhydroxide gives equivalent results to MnO_2.

Membrane retention

Nanofiltration – low cut-off point (< 200 Daltons) - retains antimony III and V, but is not a specific treatment to be applied.

Reverse osmosis retains antimony III and V.

3 Analysis methods

The decree of 17 September 2003[1] relative to methods for analysis of water samples and their performance characteristics specifies that, in the case of antimony, the accuracy, precision and limit of detection must not exceed 25% of the parametric value (i.e. 1.25 µg/L) and that the limit of quantification must not be more than 5 µg/L.

This can be achieved by analysis methods using absorption or atomic emission spectrometry (ICP, ICP-MS).

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[1] Decree of 17 September 2003 relative to methods for analysis of water samples and their performance characteristics, NOR: SANP0323688A, JORF (Official Journal of the French Republic) of 7 November 2003, p. 19027 to 19033

Standard NF EN ISO 11885 of March 1998, outlines the standardised method for assay of 33 elements, including antimony, by atomic emission spectrometry with inductively coupled plasma.

Uncertainty of measurement

Uncertainty of measurement can be estimated using inter-laboratory tests, determining the reproducibility coefficient of variation (CVR%). *(AGLAE, 2003)*

Table 1.1: Evolution in uncertainty for various concentration ranges of antimony in water using the CVR% estimated by AGLAE, from inter-laboratory tests, all analysis methods combined – Source: AGLAE, 2003

Concentration level in water (µg/L)	5 µg/L	10 µg/L	16 µg/L	20 µg/L	25 µg/L	30 µg/L
CVR %			17.3%	15.8%	14.8%	13.8%
Estimation of uncertainty*			± 5.6 µg/L	± 6.4 µg/L	± 7.4 µg/L	± 8.2 µg/L

* *95% confidence interval (2 × CVR)*

The uncertainty for the parametric value is not currently available but it is probably at least 40%.

4 Exposure

4.1 Exposure routes

In the general population, dietary intake is predominant. The extent of digestive tract absorption depends on the solubility and the chemical form. Intestinal absorption appears to be between 5 and 20% of the dose ingested in animals. For humans, the very rare data available following intoxication suggest an absorption in the region of 5%.

In professional exposure (metal industry, mining, chemical industries, etc.) the respiratory route is the main means of introduction of antimony into the body, mostly in the chemical form of antimony trioxide.

4.2 Contamination of supply water

The regulatory sanitary control programme defined by decree 89-3 of 3 January 1989 did not stipulate systematic analysis of this parameter. In general, this parameter is investigated at the start of exploitation of a catchment.

A study of the data available using the SISE-EAUX database (French Ministry of Health – SISE-Eaux) over a 4-year period (January 1999 to December 2002) shows that the 95th percentile of the results of the 137 analyses (above the quality limit) is 28 µg/L (the 50th percentile is 10 µg/L).

4.3 The proportions of sources of exposure

Apart from specific professional contexts, the antimony dose ingested is significantly higher than the dose inhaled since the latter is, for an urban population, between 60 and 460 ng/day *(Slooff, 1992)*. The total intakes from the various environmental sources (air, soil, food and water) are much lower than potential professional exposure. Table 1.2 sums up the main exposure data found in the literature.

Table 1.2: Estimation of the antimony exposure level for different countries

Source	Study date	Country	Type of study	Estimated intake	Reference
Food	2000-2003	France	Contamination x consumption	Adults (> 15 years) 1 µg/d [a] and 2 µg/d[b] Children (3 to 14 years) 0.8 µg/d [a] and 1.6 µg/d[b]	*Leblanc et al., 2004*
Food	2003	France	Duplicate meal – catering establishment	3 µg/d	*Noël* et al., *2003*
Food	1999	UK	Total diet study Shopping basket	3 µg/d[a] and 4 µg/d[b]	*Ysart et al., 1999*
Food	1986	USA	Shopping basket	18 µg/d	*Merz et al. in WHO, 1996*
Food	1987	USA	Total diet study – shopping basket	4.6 µg/d	*Iyengar et al., 1987*
Air	1992			0.060 to 0.460 µg/d	*Slooff, 1992*
Air	1988			0.04µg/d	*Health Canada*

[a] *Average consumption*

[b] *High food consumers (97.5th percentile)*

Evaluation of intake provided by solid foods:

A maximum value of 20 µg/d has been retained, on the basis of the American study by Merz *et al. (1996)*, which is actually higher than French estimates.

5 Effects on health

5.1 Sub-chronic and chronic toxicity

The toxic potential of pentavalent forms of antimony, which are the predominant forms in water, appears to be lower than that of trivalent forms; antimony in organic form appears to be less toxic than in inorganic form (*Stemmer, 1976*). Soluble antimony salts trigger gastrointestinal irritation after ingestion, leading to vomiting, abdominal cramps and diarrhoea. High doses (several hundred milligrams) can cause cardiac toxicity (modification of repolarization).

Repeated exposure to high doses (medicines containing antimony) is sometimes accompanied by uveitis (non-specific intra-ocular inflammation), oedema of the retina or even optic nerve damage.
Oral toxicity tests conducted using antimony oxide have always demonstrated toxic signs at higher contents, notably due to the lower solubility of antimony oxide.
It is possible that antimony could increase the toxic effects of arsenic (*Gebel,1999*).

5.2 Genotoxicity, mutagenicity and carcinogenicity

Professional exposure to antimony trioxide by the respiratory route has been associated with an increased incidence of lung cancers, but the studies available are not very numerous and the exposure data are fragmentary. By inhalation in animals, exposure to antimony trioxide has been accompanied by an increase in lung cancers.
For the oral route, a few mutagenesis and genotoxicity studies, mainly *in vitro*, have been revealed to be positive but none of the carcinogenesis studies conducted by the oral route in rats or mice have given a positive result.

Classification proposed by the IARC (International Agency for Research on Cancer):

- Antimony trioxide (ATO) is classed as a "possibly carcinogen" for humans (Group 2B)
- antimony trisulphide is not classifiable as to its carcinogenicity to humans (Group 3)

European classification of carcinogens, mutagens and agents which are toxic for reproduction: antimony trioxide is classified as a category 3 carcinogen and the risk phrase R40: carcinogenic effect suspected – insufficient evidence, is attributed to it.

6 Reference values

6.1 Toxicological reference values:

Various international bodies propose toxicological reference values (TRVs) for antimony. These values are presented in table 1.3 and the method of constructing them is detailed hereafter.

Table 1.3: Summary of studies taken into account for construction of TRVs

Source	TRV	Value	Study	Population	Effect
WHO (1994)	TDI tolerable daily intake	0.86 µg/kg b.w./d	1970	Rat	Reduction in longevity
WHO (2003)[1]	TDI tolerable daily intake	6 µg/kg b.w./d	1998	Rat	Weight loss
EPA (1991)	RfD reference dose	0.4 µg/kg b.w./d	1970	Rat	Reduction in longevity
ATSDR (1992)	MRL minimal risk level	not defined[2]	-	-	-
Health Canada (1997)	TDI tolerable daily intake	0.2 µg/kg b.w./d	1998	Rat	Histological changes

[1] Not validated

[2] No MRL has been defined for antimony due to the absence of an appropriate no observed adverse effect level *(ATSDR, 1992).*

<u>Selection criteria of the study by US-EPA in 1991</u>: the study selected is relatively old, *(Schroeder et al., 1970)* concerning chronic intoxication in the rat by antimony and potassium tartrate supplied by drinking water (5 mg/L), absence of no observed effect level but a lowest observed effect level (LOAEL) of 0.35 mg/kg b.w./d. The use of an uncertainty factor of 1000 led EPA to establish a reference dose of 0.4 µg/kg b.w./d.

<u>Selection criteria of the study by WHO in 1994</u>: on the basis of the same study by Schroeder *et al.* (1970), a reduction in longevity and abnormal findings for blood glucose and blood cholesterol levels were observed in intoxicated animals. A no observed effect level was determined at 0.43 mg/kg b.w./d, the use of an uncertainty factor of 500 led WHO to set a tolerable daily intake of 0.86 µg/kg b.w./d.

<u>Selection criteria of the study by Health Canada in 1997</u>: study by Poon *et al*. *(1998),* a no observed effect level of 0.5 mg/L is equivalent to a mean intake of 0.06 mg/kg b.w./d, the use of an uncertainty factor of 300 led Health Canada to set a tolerable daily intake of 0.2 µg/kg b.w./d.

<u>Selection criteria for the study by WHO in 2003</u>: Poon *et al*. *(1998)* conducted a sub-chronic study (90 days) using the same chemical form and the same method of administration of increasing doses of 0 to 500 mg Sb/L. The animals treated demonstrated few clinical signs, only a reversible reduction in weight was observed in the group treated at the highest dose (500 mg/L). The authors retain a no observed effect level of 0.5 mg/L on the basis of slight histopathological modifications in the thyroid (thickening of the epithelium and reduction in size of thyroid follicles), liver and spleen. These studies are criticised by Lynch *et al. (1999)* who prefer to consider weight loss as the only detrimental effect, the no observed effect level then becomes 50 mg/L i.e. 6 mg/kg/d. It is this last approach that was chosen by WHO in the 2003 revision, applying an uncertainty factor of 1000 (100 for the intra- and inter-species variation and 10 for the use of a sub-chronic study), the TDI is then 6 µg/kg/d. However, the approach used by Lynch *et al.* has been criticised by Valli *et al*. (2000)

The toxicological reference value of 6 µg/kg bw/d proposed by WHO in the context of revision of directives for water quality is retained in the context of this study. However, the criteria for choosing the TDI are still the subject of debate in the scientific community.

6.2 Reference values in drinking water

Concerning supply water, the quality limit is set at 5 µg/L by the French Public Health Code.

Several recommendations and guideline values are found in the literature. These values are summarised in table 1.4 and their construction is detailed in table 1.5. In the context of revision of guidelines for drinking-water quality , WHO propose a new guideline value for antimony : 20 µg/L, on the basis of a TDI of 6 μg/kg b.w./d, a water consumption of 2 litres per day and a body weight of 60 kg *(WHO, 2003).*

Table 1.4: The reference values proposed by various bodies

Value of Directive 98/83/EC Annex IB	WHO guideline value 1994	WHO guideline value 2004	Health Canada (1997 revision 2001)	US EPA (revision 2002)
5 μg/l	*5 μg/l* *(P[1], LOD[2])*	18 μg/L	6 μg/L (P[1]) (Assay limit)	6 μg/L

[1] *Provisional*

[2] *Limit of detection*

Table 8: Details of construction of reference values in water

International body	Critical dose type	Study date	Critical dose value	UF	Type of reference value	Reference value	Drinking water proportion	Value obtained
WHO (1994)	LOAEL	1970	0.43 mg/kg/d	500	TDI	0.86 μg/kg bw/d	10% (60 kg/2L)	2.6 μg/L[1]
WHO (2004)	NOAEL	1999	6 mg/kg/d	1000	TDI	6 μg/kg bw/d	10% (60 kg/2L)	18 μg/L[2]
Health Canada (2001)	NOAEL	1998	0.06 mg/kg/d	300	TDI	0.2 μg/kg bw/d	38% (70 kg/1.5L)	4 μg/L

[1] *rounded up to 5 μg/L for analytical reasons*

[2] *rounded up to 20 μg/L*

7 Comparison of daily intakes with the tolerable daily intake

On the basis of a tolerable daily intake (TDI) of 6 μg/kg b.w./d, table 1.6 presents the proportion of this toxicological reference value provided by consumption of water presenting different antimony contents.

The calculation is made for adults on the basis of a hypothesis of an individual water consumption level of 2 L/d, representative of the water consumption of the highest consumers.

The tolerable daily intake (TDI) of 360 μg/d is defined as the TDI (expressed in μg/kg b.w./d) proposed by WHO multiplied by the reference bodyweight for an adult estimated to be 60 kg.

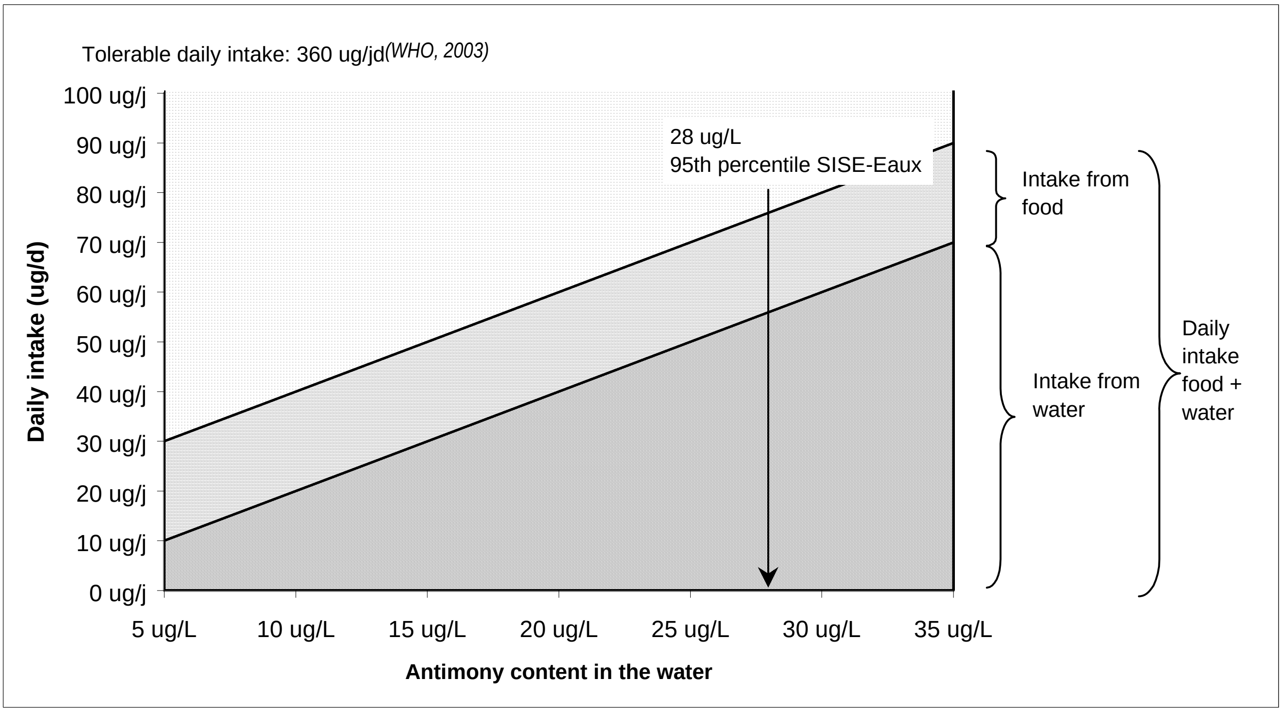
Table 1.6: Proportion of the TDI provided by drinking water for various antimony concentrations in drinking water

Concentration in water	Quantity provided by water	TDI proportion (WHO 2003)
5 μg/L	10 μg/d	2.8%
10 μg/L	20 μg/d	5.5%
20 μg/L	40 μg/d	11.1%
30 μg/L	60 μg/d	16.6%
35 μg/L	70 μg/d	19.4%

The sum of the intakes from solid food and the intakes from drinking water presenting increasing antimony concentrations is presented in graph 1.1.

The hypotheses formulated are as follows:

- the studies available in the literature made it possible to estimate that the antimony intake provided by food for adults is less than 20 μg/d.
- calculation of intake from drinking water is performed for adults on the basis of a hypothesis of an individual water consumption of 2 L/d, representative of the water consumption of the highest consumers.



Graph 1.1: Antimony intake via water and food for an increasing concentration in drinking water – adult individual consuming 2 L/d water.

Thus, it appears that at the concentration of 28 μg/L antimony in drinking water (95th percentile of non-conforming analyses registered in SISE-Eaux), the total water and solid food intakes are less than the tolerable daily intake of 360 μg/d for an adult individual.

8 Opinion

After consulting the “Water” Expert Committee on 4 May and 8 June 2004 and the “Expert Panel on Contaminants" on 7 May 2004, Afssa issues the following opinion:

Considering the quality limit in annex 13-1-I-B. of the French Public Health Code of 5 micrograms per litre for antimony;

Considering the following elements:

- that antimony may be naturally present in water sources and that it may be present in public water supply systems;
- that the hydrosoluble compounds in antimony are non-genotoxic substances possessing a toxic effect threshold;
- that it is possible that antimony may increase the toxic effects of arsenic;
- that the toxicological reference value of 6 micrograms per kilogram of bodyweight and per day proposed as a tolerable daily intake by WHO in the framework of revision of recommendations relative to the quality of drinking water undertaken in 2003 is estimated to be the most appropriate for conduct of this assessment;
- that diet (solid food and drinking water) is the main source of exposure to antimony, outside specific professional contexts;
- that the results of the surveys available in the literature make it possible to estimate that solid dietary intakes for the general French population are less than 20 micrograms per day;
- that the data from the SISE-Eaux base demonstrate that 95% of the non-compliant analysis results registered between 1999 and 2002 are lower than the value of 30 micrograms per litre;
- that the treatment processes authorised by the French Ministry of Health can be applied to reduce antimony contents in water,

Afssa (French Food Safety Agency) :

Reiterates that the means required to bring antimony concentrations to the quality limit must be implemented as rapidly as possible,

Observes that ingestion of water with an antimony concentration of close to 30 micrograms per litre (95th percentile of values above the quality limit, registered in the SISE-Eaux database), does not expose an individual to a level higher than the tolerable daily intake proposed by WHO, taking into account other dietary intakes,

Draws attention to the potential synergetic effects of antimony with arsenic.

File 2: Assessment of health risks related to exceeding the quality reference for chlorites in water destined for human consumption

The quality reference limit is 200 µg/L for chlorite. However, it is also specified that the *"lowest value must be sought without compromising disinfection"*. In its recommendations of 1994, the World Health Organisation stipulates that the value of 0.2 mg/L *"This guideline value is designated as provisional because use of chlorine dioxide as a disinfectant may result in the chlorite guideline value being exceeded, and difficulties in meeting the guideline value must never be a reason for compromising adequate disinfection."* *(WHO, 1996)*. This warning is repeated in the WHO 2003 draft file *(WHO, 2003)*.

1 Origin of their presence in water:

The presence of chlorites in water is related to the use of chlorine dioxide in the pre-oxidation or pre-disinfection phase and in the disinfection phase for water destined for human consumption.

The main redox reactions occurring when chlorine dioxide ClO_2 is added generally lead to the formation of chlorite ions (50%), chloride ions (40%) and chlorate ions (10%).

2 Analysis methods

The decree of 17 September 2003[1] relative to methods for analysis of water samples and their performance characteristics specifies that, in the case of chlorites, the limit of quantification must not be more than 0.1 mg/L.
Standardised method:

Standard NF EN ISO 10304-4 of June 1999, (ISO 10304-4:1997 of December 1997) outlines the method for assay of anions dissolved by ionic liquid chromatography and, notably, in part 4 presents assay of chlorate, chloride and chlorite ions in water with low contamination levels.

3 Exposure:

The main route of exposure is drinking water *(WHO, 1994, 2003).*

3.1 Contamination of supply water

The chlorite concentration in water destined for human consumption depends on the chlorine dioxide concentration used during the pre-oxidation step and/or during the disinfection step and certain intermediate treatment steps (particularly the ozonation step).
The formation of chlorite ions from chlorine dioxide occurs, on average, within 30 to 60 minutes. The proportion of chlorites formed is between 50 and 70% of the dioxide having reacted. For water with a high humic substance content, this percentage may reach 80% *(Drout N. et al., 2000).*
Usual practices in France for using chlorine dioxide are presented in tables 2.1 and 2.2.

Table 2.1: Assessment of chlorine dioxide concentrations used during pre-oxidation for a panel of 70 sites *Source: Drout N. et al., 2000*

ClO_2 conc. mg/L	Number of water treatment stations	Theoretical chlorite concentration (mg/L)*
2 to 3	10	0.8 to 1.8
1 to 2	28	0.4 to 1.2
0.5 to 1	28	0.2 to 0.6
0.2 to 0.5	4	0.08 to 0.3

** assuming that 40 to 60% of chlorine dioxide is converted into chlorite*

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[1] Decree of 17 September 2003 relative to methods for analysis of water samples and their performance characteristics, NOR: SANP0323688A, JORF (Official Journal of the French Republic) of 7 November 2003, p. 19027 to 19033

Table 2.2: Assessment of chlorine dioxide concentrations used during disinfection for a panel of 175 sites

Source: Drout N. et al., 2000

ClO_2 conc. mg/L	Number of water treatment stations	Theoretical chlorite concentration (mg/L)*
> 1	4	> 0.4 - 0.6
0.4 to 1	91	0.16 to 0.6
0.1 to 0.4	80	0.04 to 0.24

** assuming that 40 to 60% of chlorine dioxide is converted into chlorite*

The regulatory sanitary control programme defined by decree 89-3 of 3 January 1989 did not stipulate systematic analysis of this parameter. Thus, data are currently non-existent in the SISE-EAUX database.

3.2 Dietary sources

Chlorine dioxide, chlorites and chlorates can be present in certain foodstuffs which are made using flour. These substances are used in certain processes *(WHO, 2003)*:

- chlorine dioxide is used in the production of certain types of flour as an agent to bleach carotene and other natural pigments;
- sodium chlorite is used as a bleaching agent in food preparations containing modified starch and as an additive in the production of paper used for the packaging of foodstuffs;
- sodium chlorate is used as a defoliant, siccative and fungicide in agriculture.

At the current time, the bibliographic searches have not made it possible to quantitatively estimate the exposure of the population via dietary sources.

4 Effects on health

Chlorites are rapidly absorbed by the gastrointestinal tract, distributed throughout the entire body and eliminated predominantly by urinary excretion. There does not appear to be any bioconcentration towards a specific organ, a small part remains in unchanged form but the majority is converted into chlorides.

4.1 Sub-chronic and chronic toxicity

The principal effect of chlorites is characterised by the formation of methaemoglobin in the blood. This effect is observed in cats and monkeys as well as in humans exposed to high doses (accidental exposure). *(WHO, 2003)*

Studies conducted in zones where water has been disinfected with chlorine dioxide have not revealed any harmful effects, either in adults or in newborns *(U.S. EPA, 2000).* Some studies suggest a possible link between exposure to chlorine dioxide and chlorites and harmful effects on development or reproductive functions but this is debated owing to methodological biases.

A certain number of effects in animals identified in the literature are summarised by the US EPA. *(U.S. EPA, 2000)*:

- Several studies in animals have revealed impaired neurone development (brain weight and behavioural change). Reproduction studies in rats have demonstrated an impact on spermatozoids (mortality and modification of mobility). However, these effects appear at higher doses than those for which effects on development appear.
- Delayed development has been observed in animals following *in utero* and post-natal exposure due to ingestion of chlorine dioxide and chlorites, which suggests to the US EPA that babies and children may be the most susceptible *(U.S. EPA, 2000).*

4.2 Mutagenicity and carcinogenicity

Carcinogenesis studies in mice and rats have not revealed any significant increase in the number of tumours in treated groups. IARC has classified chlorites as group 3.

5 Reference values

5.1 Toxicological reference values

The toxicological study on two generations of rats conducted by the Chemical Manufacturers Association (CMA) is the critical study used by the EPA to determine its reference dose (RfD)*(Gill. Et Al., 2000)*. From this study, the CMA calculates a NOAEL (no observed adverse effect level) for haematological toxicity equal to 6 mg/kg b.w./d and a NOEL (no observed effect level) for neurotoxicity equal to 28.6 mg/kg b.w./d chlorites.

The US EPA, retaining auditory changes and a reduction in brain weight as critical effects in rats, retains a NOAEL of 2.9 mg/kg b.w./d and a LOAEL (lowest observed adverse effect level) of 5.9 mg/kg b.w./d. An uncertainty factor of 100 (10 for inter- and intra-species variations) is applied to the NOAEL, the TDI (tolerable daily intake) determined by the US EPA is equal to 30 µg/kg b.w./d.
The toxicological value selected by WHO of 30 µg/kg b.w./d is determined from this same study, using a similar approach.
Table 2.3 summarises the method of construction of the toxicological reference values proposed by these various bodies.

Table 2.3: Summary of toxicological reference values proposed by various bodies

Source	Reference value		Effect	Study
WHO, 1996	TDI	10 µg/kg b.w./d	Reduction in glutathione concentrations (rats) NOAEL of 1 mg/kg b.w./d Safety factor of 100 inter- and intra-species variations	*Heffernan, 1979 in WHO, 1996*
US EPA, 2002	RfD Reference Dose	30 µg/ kg b.w./d	Auditory impairment and reduction in brain weight (rats) NOAEL of 2.9 mg/kg b.w./d Safety factor of 100 inter- and intra-species variations	*Gill. Et Al., 2000* *CMA, 1996 in US-EPA, 2000*
WHO, 2003	TDI	30 µg/kg b.w./d	Auditory impairment and reduction in brain weight (rats) NOAEL of 2.9 mg/kg b.w./d Safety factor of 100 inter- and intra-species variations	*Gill. Et Al., 2000* *CMA, 1996 in WHO, 2003*
ATSDR, 2002	MRL	0.1 mg/kg b.w./d	Effect on neurodevelopment (rats) NOAEL of 2.9 mg/ kg b.w./d and an LOAEL of 5.7 mg/ kg b.w./d Safety factor of 30	*Gill. Et Al., 2000* *CMA, 1996 in ATSDR, 2002*

NOAEL: No observed adverse effect level; LOAEL: Lowest observed adverse effect level;
MRL: Minimal risk level

The toxicological reference value of 30 µg/kg bw/d proposed by WHO in the context of revision of directives for water quality is retained in the context of this study.

5.2 Reference values in water

Concerning water supply, the quality reference set by the French Public Health Code is 200 µg/L.

Several recommendations and guideline values are found in the literature. These values are summed up in table 2.4 and their construction is detailed in table 2.5. In the context of revision of the guidelines for drinking-water quality, WHO may propose a new guideline value for chlorites equal to 700 µg/L, on the basis of a TDI of 30 µg/kg b.w./d, a water consumption of 2 litres per day and a bodyweight of 60 kg, considering that 80% of chlorite intake is provided by water *(WHO, 2003).*

Table 2.4: Reference values proposed by the various bodies

Value of directive 98/83/EC Annex IB	*WHO guideline value 1994*	WHO guideline value 2004	Health Canada	US EPA (2000)
/	*200 µg/L*	700 µg/L	/	800 µg/L (Guideline) 1000 µg/L

Table 2.5: Details of construction of reference values in water

International body	Critical dose type	Study date	Critical dose value	UF	Type of reference value	Reference value	Drinking water proportion	Value obtained
WHO (1994)	*NOAEL*	*1979*	*1 mg/kg/d*	*100*	*TDI*	*10 µg/kg bw/d*	*80%*	*240 µg/d*
WHO (2004)	NOAEL	1996	2.9 mg/kg/d	100	TDI	30 µg/kg bw/d	80%	720 µg/L**
US-EPA	NOAEL	1996	2.9 mg/kg/d	100	RfD	30 µg/kg bw/d	80%	840 µg/L*

** the weight of an adult is 70 kg in the calculations of the US EPA*
*** rounded up to 700 µg/L*

6 Comparison of daily intakes with the tolerable daily intake

The data available do not make it possible to estimate the daily chlorite intake via solid foods and water.

7 Opinion

After consulting the “Water” Expert Committee on 4 May and 8 June 2004 and the “Expert Panel on Contaminants" on 7 May 2004, Afssa issues the following opinion:
Considering the quality reference in annex 13-1-I-B. of the French Public Health Code of 200 micrograms per litre for chlorites; that the lowest value must be sought without compromising disinfection of the water supply;

Considering the following elements:

- that the results of surveys available in the literature do not make it possible to estimate daily chlorite intakes related to diet in the general population;
- that the main route of exposure to chlorites is ingestion of water;
- that chlorites possess a toxic effect threshold;
- that the toxicological reference value of 30 micrograms per kilogram of bodyweight and per day proposed as a tolerable daily intake by WHO in the framework of revision of recommendations relative to the quality of drinking water undertaken in 2003 is estimated to be the most appropriate for conduct of this assessment;

Afssa (French Food Safety Agency):

Reiterates that the means required to bring chlorite concentrations to the quality reference level must be implemented as rapidly as possible,
Considers that, on the basis of the hypotheses formulated by the World Health Organisation, the consumption of water presenting a concentration greater than the quality reference and less than or equal to 700 micrograms per litre does not expose an individual to a dose higher than the tolerable daily intake,
Recommends that a summary of national data be compiled to enable estimation of the levels and frequencies for exceeding of the reference quality for this parameter.

File 3: Assessment of health risks related to exceeding the quality limit for fluorides in water destined for human consumption

The dominant chemical forms in water are:

- Sodium fluorides (NaF), potassium fluorides (KF), calcium fluorides (CaF_2)
- Hydrofluoric acid (HF)

Fluorides can be presented in the form of complexes with silicium, boron or aluminium.

1 Origin and sources of contamination

Natural origins:

Apart from mineral waters in which fluorine may have a deep origin (magmatic), the highest values in groundwater are associated with fluorite (CaF_2) and, particularly, with apatite [$Ca_5 (PO_4)_3$ (F, Cl, OH)]. Fluorine can also be present in substitution in micas and amphiboles. In the case of sedimentary rocks, it is often the result of secondary deposits produced by leaching of igneous or metamorphic rocks. Fluorine can also be bound to clays. The highest contents are found in waters with a low calcium content.

Anthropic sources:

Fluorine is used in the production of glass, ceramics, enamel, bricks, pottery, cement, aluminium, steel, in casting, surface treatments, welding and brazing of metals and also in the production of fluorinated chemicals. Sodium fluoride is used in the manufacture of various pesticides and can be present as an impurity in phosphate fertilisers.

2 Treatments reducing the fluoride content in water

In accordance with the French drinking water regulation, the use of treatment products is subject to approval from the Minister responsible for health.

The following treatments can reduce fluoride content in water, although confirmation is required on an individual case basis that the proposed treatments are approved.

Selective adsorption on apatite or activated alumina; pH plays an important role.

Decarbonation

In the presence of phosphates, formation of fluoroapatite.

Membrane treatments

Reverse osmosis retains fluorides.

In the presence of calcium, formation of CaF_2 which can be retained by nanofiltration.

3 Analysis methods

The decree of 17 September 2003[1], relative to methods for analysis of water samples and their performance characteristics specifies that, in the case of fluorides, the accuracy and precision must not exceed 10% of the parametric value and the limit of detection must not exceed 3% of the parametric value (i.e. 45 µg/L). In addition, the limit of quantification must be 200 µg/L.

Water samples for determination of fluorides must be collected in a polyethylene bottle given the risks of contamination of the sample by glass bottles.

Fluorides can be tested for in water using spectrophotometric methods, but especially using potentiometric methods and by ionic chromatography. The standardised methods for determination of fluorides in water are as follows:

- NF T90-004 (August 2002): Water quality – determination of the fluoride ion – Potentiometric method.
- NF EN ISO 10304-1 (June 1995): Water quality – Determination of dissolved fluoride, chloride, nitrite, orthophosphate, bromide, nitrate and sulphate ions, using liquid chromatography of ions – Part 1: method for water with low contamination.
- ISO 10359-2 (October 1994): Water quality – Determination of fluoride – Part 2: Determination of inorganically bound total fluoride after digestion and distillation.

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[1] Decree of 17 September 2003 relative to methods for analysis of water samples and their performance characteristics, NOR: SANP0323688A, JORF (Official Journal of the French Republic) of 7 November 2003, p. 19027 to 19033

The uncertainty of the measurement can be estimated using inter-laboratory tests, determining the reproducibility coefficient of variation (CVR%). *(AGLAE, 2003)*

Table 3.1: Evolution in uncertainty for various concentration ranges of fluorides in water using the CVR% estimated by AGLAE, from inter-laboratory tests, all analysis methods combined – Source: AGLAE, 2003

Concentration level in water (mg/L)	0.4	0.5	0.6	0.7	0.8	0.9
CVR %	12.4%	11.7%	11.4%	11.1%	10.9%	10.7%
Estimation of uncertainty* (mg/L)	± 0.1	± 0.12	± 0.14	± 0.16	± 0.18	± 0.2

* *95% confidence interval (2 × CVR)*

4 Exposure

4.1 Route of exposure

Exposure to fluorides is mainly by the oral route. Fluorides are rapidly absorbed in the gastrointestinal tract, mainly in the duodenum. Absorption is dependent on gastric pH, the nature of the fluoride salt ingested, the presence of potential complexants (*Al, Ca, Mg and Cl reduce absorption whereas* PO_4^{2-} *and* SO_4^{2-} *increase it*) and the physiological condition of subjects. The fluorides absorbed are distributed by the blood stream and carried to the storage organs (teeth and bone tissues mainly); plasma only contains around 10% of the body's total status. Kinetics studies have highlighted the strong potential of blood homeostasis; serum fluoride levels only reflect the dose absorbed in the event of prolonged ingestion of water containing more than 6 mg F/L. *(Cerklewski, 1997)*. Fluorides are eliminated primarily in the urine (50-60% of the dose ingested).

4.2 Control and level of contamination of water

The regulatory sanitary control stipulated analysis of fluorides at the drawing point for surface water (1 to 12 times per year) and after treatment for groundwater and surface water (0 to 1 time per year). Analysis of the data in the SISE-EAUX base for the 4-year period (January 1999 to December 2002) shows that 50th percentile of the results of the 1106 analyses[31] (above the quality limit) is 1.85 mg/L.

4.3 Sources of exposure

For the general population, the main sources of exposure to fluorides are foods (mainly tea and fish), water, dental health products and, to a lesser extent, the air. Tea is the food with by far the highest fluoride content, along with sea fish, while meat, milk and eggs provide few fluorides. Certain mineral waters are naturally rich in fluorides (several milligrams per litre). The contribution of vegetables is low, but more variable. The bioavailability of fluorides depends on the dietary matrix in which they are found. In addition, in the presence of calcium, the formation of a complex makes fluorides only very slightly bioavailable. In subjects working in agricultural environments (use of fertilisers) or industrial environments, an additional source can be air contaminated by fluorine particles.

Depending on the country and the application of a policy of fluorination of the water supply, fluoride intake from drinking water ranges from 0.3 to 1.9 mg/d *(Arnaud, 2001)*. Tables 3.2 and 3.3 present estimates of respective daily fluoride intakes for different countries and different age groups.

Table 3.2: Estimate of fluoride exposure levels for different countries

Country	Type of study	Total daily intake (mg/d)	Comment	Source
Netherlands	Estimated dose : water and food Level supplied by solid foods and water lower for children BUT swallow more toothpaste	1.4 - 6.0 > 3.5	80-85% by solid foods	*WHO 2003*
UK	Contamination of food × food consumption Total Diet Study 1997	1.2 0.94^b to 2^c	85 % provided by drinks (tea)	*FSA COT UK 2000*
Canada	Daily intake: air, soil, food and toothpaste (apart from water)	Children 7 months to 4 years (10 kg): 0.42 to 0.83 Adults 20 years and over (60 kg): 1.87 to 1.88		*Health Canada, 1997*
World	All intakes combined	0.46 to 3.6-5.4	Marked variations depending on geographic zones	*WHO 1996*

a General population
b Adult population average consumption
c Adult population high consumption

Table 3.3: Estimate of fluoride exposure level for different age groups
source: Committee on toxicity of chemicals in food, consumer products and the environment, 2000

Age group (years)	Study date	Daily intake in mg/kg bw/d	
		Mean	97.5th percentile
1 ½ to 4 ½	2000	0.023 (0.30 mg/d)	0.053 (0.69 mg/d)
4-6	1995	0.031 (0.84 mg/d)	0.060 (1.62 mg/d)
7-10	1995	0.024 (0.65 mg/d)	0.047 (1.27 mg/d)
11-14	1995	0.017 (0.97 mg/d)	0.037 (2.1 mg/d)
15-18	1995	0.015 (1.5 mg/d)	0.034 (2.38 mg/d)
Adults	1990	0.016 (1.12 mg/d)	0.033 (2.31 mg/d)

Intake provided by fluorinated table salt: The quantity of salt actually consumed by households is estimated to be 2 to 3 g/day/person and it is on this basis that fluoride intake from salt is determined. The prevalence of fluorinated salt (containing 250 mg/kg fluorides in the form of potassium fluoride) being around 35% in France, it is calculated that the maximum daily intake is 0.75 mg/person[32].

Fluoride supplementation in children

Supplementation in children can be provided firstly by fluorinated table salt, the actual intakes of which are not known, and, secondly, in the form of fluorinated medicines; the recommended quantities are 0.25 mg/day under the age of 2 years, 0.50 mg/day from 2 to 4 years, 0.75 mg/day from 4 to 6 years and 1 mg/day over the age of 6 years. Fluorinated medicines are presented in the form of tablets or oral solutions. They provide calcium fluoride or sodium fluoride *(Afssaps, 2002)*.

The total quantity of fluorides ingested daily is difficult to accurately assess. A value of between 1 and 2 mg/day is retained in this study.

5 Effects on health

5.1 Requirements and recommended intakes

Fluorine does not play an essential metabolic role in animals and humans, but it plays a fundamental role in the formation of fluoroapatite in the teeth and bones *(Arnaud, 2001)*

To be of good quality, dental enamel must contain a certain amount of fluoroapatite. Fluorine must be available in sufficient quantities during mineralization of the tooth buds of the permanent teeth, some of which replace the milk teeth. The topical action of fluorine by adsorption on the surface of the enamel exists, but its effect is limited. According to WHO *(2003)*, a minimum concentration in water of 0.5 mg/L is necessary for development of the protective effect. Unfortunately the quantity of fluorides ingested causing the first tooth damage (aesthetic effects) is relatively close to the optimum quantity for mineralization of the enamel.

Fluorine is bound mainly in the skeleton and contributes to its solidity. The detrimental effects only appear at doses much higher than those causing dental fluorosis.

The Upper intake level corresponds to lifetime daily ingestion of a quantity not causing harmful consequences for the health in the current state of knowledge.

In practice, when the quantity of fluorides contained in water actually ingested (tap water and/or mineral water) is low (for example, less than 0.5 mg/L), it is recommended that fluorine supplements be given to children, in the form of fluorinated table salt or fluorinated medicines (*Afssaps, 2002)*.

Fluorine is an ambivalent element, with beneficial effects for moderate intakes and harmful effects on human health following excessive or prolonged intake.

Table 3.4: Recommended intakes and fluorine Upper intake level for different age groups *Source: Arnaud, 2001.*

Age - Sex	*Recommended dietary allowance (RDA in mg/day)*	*Upper intake level (mg/day)*
Children 0 – 6 months	0.1	0.4
Children 6 – 12 months	0.2	0.5
Children 1 – 3 years	0.5	0.7
Children 4 – 8 years	1	2.2
Boys and girls 9 – 13 years	1.5	4
Adolescents 14 – 18 years	2	4
Adult men	2.5	4
Adult women	2	4
Healthy elderly subjects	2 (women), 2.5 (men)	4

5.2 Effects on humans

Acute toxicity

The ingestion of critical doses of fluorides can cause digestive disturbances (nausea, vomiting, abdominal pain, diarrhoea), a state of fatigue with drowsiness, or even convulsions, coma or cardiac arrest. With respect to biology, coagulation disorders (due to formation of calcium and iron complexes) may develop.

In adults, the lethal dose is 2 to 4 grams of fluorides. The minimum dose of 1 mg/kg b.w. is identified as the minimum dose not leading to signs of acute intoxication with fluorides. *(Health Canada, 1997; Cerklewski, 1997; WHO, 1988-2003)*

Chronic toxicity and carcinogenicity

Dental fluorosis

The excessive ingestion of fluorides can have effects on dental enamel (brownish discoloration) and lead to gingival and alveolar damage; it can cause the development of dental fluorosis. In general, in temperate regions dental fluorosis appears at concentrations in the region of 1.5-2.0 mg F/L water. *(WHO, 2003)*

Dental fluorosis is due to an overdosage of fluoride during several months or year in the period of mineralization of teeth : from the third months of life in utero (for milk theet) to 12 years old (for permanent theet) *(Afssaps, 2002)*.

It seems to be unlikely that a daily fluoride intake of less than or equal to 122 µg/kg b.w./d for children aged between 22 and 26 months (maximum risk period) could lead to dental fluorosis in the permanent front teeth. (*Health Canada, 1997*)

In a review of the literature concerning 214 studies, *McDonagh et al.* (*2000*) stress the beneficial role of fluorination of drinking water but also observe a significant relationship between the fluoride content of drinking water and the prevalence of dental fluorosis. For a concentration of 1 mg fluorides per litre, the prevalence of dental fluorosis is 48% (CI95= [40; 57]).

Bone fluorosis

In a review of the literature, Jones *et al.* (*1999*) stress that fluorination of water supplies, as currently practised in certain country (1 mg fluorides per litre), does not significantly increase the risk of bone fluorosis or spontaneous fracture.

Bone fluorosis, with modification of bone structure and mineralization, is observed for water concentrations ranging from 3 to 6 mg/L. (*WHO, 2003*)

Deforming skeletal fluorosis has been reported for concentrations in water of 10 mg/L. The US EPA considers that 4 mg/L is a water concentration which is protective against paralysing bone fluorosis.

On the basis of studies conducted in China and India, the IPCS (*2002*) indicates that (i) for exposure to a level of 14 mg/d, there is a recognised excess risk of bone fluorosis (ii) there is evidence of an excess risk of effects on the skeleton for a total fluorine exposure of above 6 mg/d.

However, a significant increase in the prevalence of bone fractures is observed in a population of 8266 Chinese subjects regularly drinking water containing between 4.3 and 7.9 mg F/L *(Li et al., 2001).*

5.3 Sensitive population sub-group

The highest deposition rate in calcified tissues (bone, teeth) has been observed in children, due to their high skeletal growth rate (*Health Canada, 1997*). The critical impact of fluorine on mineralization of dental buds of permanent teeth makes very young children a particularly sensitive population to even slightly excess levels. Since fluorine is eliminated principally by the urinary route, particular attention must be paid to subjects suffering from kidney impairment.

6 Reference values

6.1 Toxicological reference values

Various international bodies propose toxicological reference values (TRVs) for fluorides. These values are presented in table 3.5 and their method of construction is detailed hereafter.

Table 3.5: Toxicological reference values proposed by various bodies

Source	Study	TRV	Reference value	Population	Effect
Health Canada	1996		122 µg/kg bw/d	22 to 26 months	Dental fluorosis
US EPA (IRIS 2001)	1950	RfD	60 µg/kg bw/d	Children	Dental fluorosis
ATSDR 2003	2001	MRL	50 µg/kg bw/d	Chineese adults	Increase in the number of non-vertebral fractures
Health Canada	LCPE 1993		200 µg/kg bw/d (12 mg/d)	Adults	Skeletal fluorosis
ANC report	2001	Upper intake level	0.4 to 4 mg/d	Infants to adults	
WHO	IPCS 2002		6 mg/d	Adults	Skeletal fluorosis

Position of the US EPA (IRIS, 2002):

The reference dose (RfD) by the oral route set by the US EPA is defined as follows: **RfD = 60 µg/kg bw/day**

- Critical effect: dental fluorosis (aesthetic effect)
- Source: epidemiological study in children aged 12-14 years (1950). The no observed effect level was 1 mg/L fluorides. Assuming that a child with an average body weight of 20 kg drinks 1 L of water per day and that food provides 0.01 mg/kg b.w./d, then the global intake of 0.06 mg/kg b.w./d is considered to be without any harmful effect, without using a safety factor since the population studied is the target population.

Position of the ATSDR (2001):

The MRL reference dose (*Minimal Risk Level*) by the oral route set by the ATSDR is defined as follows: **MRL = 50 µg/kg bw/day**

- Critical effect: bone density changes leading to an increase in non-vertebral fracture rates.
- Source: This MRL is based on a NOAEL of 0.15 mg fluoride/kg/day and a LOAEL of 0.25 mg fluoride/kg/day for skeletal effects (increased fracture rate) (Li et al. 2001). The MRL was derived by dividing the NOAEL by an uncertainty factor of 3 to account for human variability.

According to the recommendations of AFSSA[1] and the "Apports Nutritionnels Conseillés pour la Population Française" ("Recommended Dietary Allowances for the French Population") report (ANC, 2001), the Upper intake level for children (babies) and adults are, respectively, 0.4 and 4 mg F/day. The maximum safety level proposed by the French Conseil supérieur d'hygiène publique (Public Health Council), for adults has been set at 4 mg/d with the aim of not encouraging excessive fluorine supplementation. That is why, for adults, the value of 6 mg/d proposed by the WHO has been retained in the context of this assessment. Children represent a sensitive population.

6.2 Reference values in water

The French Public Health Code quality limit is set at 1.5 mg/L. Several recommendations and guideline values are found in the literature. These values are summarised in table 3.6 and their construction is detailed in table 3.7.

In its 2004 recommendations (WHO, 2004), the World Health Organisation proposes a fluorine guideline value of 1.5 mg/L for a consumption of 2 litres of water per day, considering that " *There is no evidence to suggest that the guideline value of 1.5 mg/litre set in 1984 and reaffirmed in 1993 needs to be revised. Concentrations above this value carry an increasing risk of dental fluorosis, and much higher concentrations lead to skeletal fluorosis ".* The recent revision (WHO, 2004) proposes to confirm this guideline value.

Table 3.6: Reference values proposed by various bodies

Value of directive 98/83/EC Annex IB	WHO guideline value 2004	Health Canada 1996	US EPA 2002
1.5 mg/L	1.5 mg/L	1.5 mg/L	4 mg/L (MCL*) 2 mg/L (SDWR**)

** Maximum Contaminant Level*

*** Secondary Maximum Contaminant Level*

Table 3.7: Details of construction of reference values in water

International body	Study date	UF	Type of reference value	Reference value	Drinking water proportion	Body-weight	Water consumption	Value obtained
Health Canada1996	1996	1	Tolerable daily intake	0.122 mg/kg bw/d	50%	13 kg	0.8 L/d	1 mg/L
WHO*								1.5 mg/L

* construction method specified in the previous paragraph.

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[1] Afssa, opinion dated 10 July 2001 relative to the proposal to set limit values for certain bottled natural mineral water ingredients and supplementing the opinion of 21 March 2001 relative to the proposal to set limit values for certain bottled natural mineral water ingredients

7 Comparison of daily intakes with the tolerable daily intake

The risks of dental fluorosis are, theoretically, linked to global exposure of the population to fluoride, notably via dietary sources.
Short-term exposure, even for under 3 months, to excessive fluorine levels can have a lasting effect if it occurs during the dental bud mineralization period in children.

7.1 Children and infants

- On the basis of water consumption of 0.75 L/d for babies, the ingestion of water with a fluoride content of 1.5 mg/L leads to exceeding of the Upper intake level proposed for children aged from 1 to 3 years (0.4 to 0.7 mg/d).
- On the basis of a Upper intake level of 2.2 mg/d for children aged between 4 and 8 years, table 3.8 presents the proportion of this Upper intake level that can be attributed to exposure of the population via water, with different fluoride contents.

  The calculations are made on the basis of a hypothesis of an individual water consumption of 1L/d, representative of the water consumption of the highest consumers.

Table 3.8: Proportion of the Upper intake level provided by drinking water for different fluoride concentrations – child of 4 to 8 years

Concentration in water	Quantity provided by water	Proportion of the child Upper intake level
1.5 mg/L	1.5 mg/d	68%
2 mg/L	2 mg/d	90%
2.5 mg/L	2.5 mg/d	114%

Thus, for children under the age of 9 years, the levels provided by water with a fluoride content close to the quality limit (1.5 mg/L) are in the region of or greater than the Upper intake level proposed in the ANC report (*2001*). To this intake can be added intakes from food and toothpaste.

7.2 Adult population

On the basis of a WHO recommendation of 6 mg/d, table 3.9 presents the proportion of this tolerable daily intake which can be attributed to exposure of the population via water, with different fluorine contents.
The calculations are made on the basis of a hypothesis of an individual water consumption of 2 L/d, representative of the water consumption of the highest consumers.

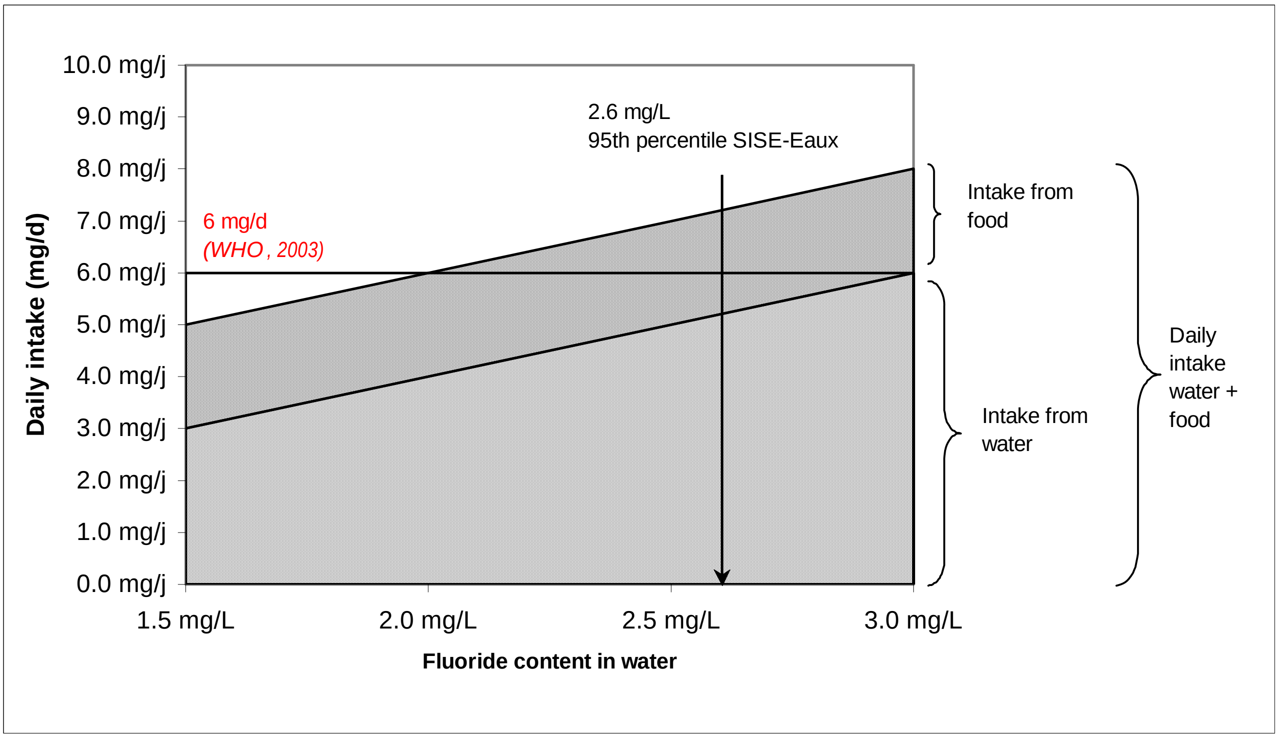
Table 3.9: Proportion of the tolerable daily intake provided by drinking water for different fluoride concentrations

Concentration in water	Quantity provided by water	Proportion of TDI Adults
1.5 mg/L	3 mg/d	50%
2 mg/L	4 mg/d	67%
2.5 mg/L	5 mg/d	83%
3 mg/L	6 mg/d	100%

The sum of the intakes from solid foods and the intakes from drinking water presenting increasing fluoride concentrations is presented in graph 3.1.
The hypotheses formulated are as follows:

- the studies available in the literature led to estimation of fluorine intake from food for adults of less than 2 mg/d.
- calculation of intakes from drinking water is performed for adults on the basis of a hypothesis of individual water consumption of 2 L/d, representative of the water consumption of the highest consumers.

Thus, it appears that at the concentration of 2 mg/L fluorides in drinking water, the total intakes from water and solid food are equivalent to the tolerable daily intake of 6 mg/d for an adult individual.



Graph 3.1: Fluoride intake via water and food for an increasing concentration in drinking water – adult individual consuming 2 L water /d

8 Opinion

After consulting the “Water” Expert Committee on 4 May and 8 June 2004 and the “Expert Panel on Contaminants" on 7 May 2004, Afssa issues the following opinion:

Considering the quality limit in annex 13-1-I-B. of the French Public Health Code of 1.5 milligrams per litre for fluorides;
Considering the opinions of Afssa dated 21 March 2001 and 10 July 2001 relative to the proposal to set limit values for certain ingredients in bottled natural mineral waters;

Considering the following elements:

- that the origin of the fluorides present in water sources may be natural or related to anthropic activities on the water catchment area;
- that the data in SISE-Eaux base demonstrate that 95% of non-compliant analysis results registered are less than the value of 2.6 milligrams per litre;
- that fluorides are substances possessing a toxic effect threshold;
- that the Upper Intake Level of 0.4 to 2.2 milligrams per day proposed by the Agence française de sécurité sanitaire des aliments [French food safety agency] for children under the age of 8 years, are considered to be the most appropriate for conduct of this evaluation in children;
- that the toxicological reference value of 6 milligrams per day taking into account bone fluorosis as a target effect, proposed for adults by WHO, is considered to be the most appropriate for conduct of this evaluation in adults;
- dental fluorosis is due to an overdosage of fluoride during several months or year in the period of mineralization of teeth : from the third months of life in utero to 12 years old;
- that the recommended fluoride intakes range from 0.1 milligrams per day for children aged between 0 and 6 months and 2.5 milligrams per day for healthy elderly men;
- that food represents one of the main sources of exposure to fluorides and that these intakes can be estimated at close to 1 to 2 milligrams per day;
- that the toxicological and epidemiological data have made it possible to identify babies and children as the sensitive population;
- that the treatment processes authorised by the Ministry of Health can be used to reduce the fluoride contents of water,

Afssa (French Food Safety Agency):

Reiterates that the means required to bring fluoride concentrations to the quality limit level must be implemented as rapidly as possible,

Observes that the ingestion of water containing 2 milligrams per litre of fluorides exposes an adult individual to a dose equivalent to the tolerable daily intake of 6 milligrams per day, taking into account other dietary intakes,

Considers:

- that the consumption of water with a concentration higher than the quality limit is not acceptable for water intake for babies and children up to 12 years old,
- that in the event that the quality limit is exceeded, the population must be informed of the need to reduce their fluoride intake from non-water sources,

Specifies that it in no way calls into doubt the quality limit resulting from the risk assessment conducted by the World Health Organisation,

File 4: Assessment of health risks related to exceeding the quality limit for lead in water destined for human consumption

The evolution of lead in aqueous medium is determined by several factors: pH, temperature, total alkalinity and stagnation duration of the water in domestic pipes.
In aqueous medium, lead is present in the form of ions or complexes.

1 Origin and sources of contamination:

In water sources:

Lead is one of the primary deposits in eruptive and metamorphic rocks, where it is then present mainly in sulphide form (galena). It is redistributed *via* alteration into all rocks in the form of carbonate (cerusite), sulphate (anglesite) and can replace potassium in silicaceous rocks and phosphates. However, it is a metal, the compounds of which are not very water-soluble and demonstrate weak geochemical mobility. Contents in groundwater are consequently very low, apart from in mining areas where the pH of the water can be very acidic. It is also immobilised in sediments.

Since lead was removed from petrol, the contents present in rainwater coming from roads have fallen greatly. Industries using lead are the biggest source of waste but this waste is generally in the form of fine dust, from which the lead is not easily dissolved.
In water supply systems, lead can be dissolved from pipes, joints or system connections.

2 Treatments reducing lead contents in water

Compliance with the quality limit of 25 µg/L then 10 µg/L involves wide-scale systematic replacement of lead pipes, and even those made of materials known to release lead, present in the private domestic systems. Given the cost and the time required, it is essential to implement corrective measures, particularly centralised treatment of water, in order to limit its corrosive effect. This may include increasing the pH and the total alkalinity, or even the use of orthophosphate treatments[1,2].

3 Analysis methods:

The decree of 17 September 2003[3] relative to methods for analysis of water samples and their performance characteristics specifies that, in the case of lead, the accuracy, precision and limit of detection must not exceed 10% of the parametric value (i.e. 1 µg/L) and that the limit of quantification must not be more than 5 µg/L.
Standard NF EN ISO 11885 of March 1998, outlines the standardised method for assay of 33 elements, including lead, by atomic emission spectrometry with inductively coupled plasma.

French standard FD T90-112 of July 1998, outlines the standardised method for assay of 8 metal elements (Mn, Fe, Co, Ni, Cu, Zn, Ag, Pb) by flame atomic absorption spectrometry.

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[1] Opinion of the Conseil supérieur d'hygiène publique de France of 9 December 2003 relative to corrective measures to be implemented to reduce the dissolution of lead in water

[2] Opinion of the Agence française de sécurité sanitaire des aliments of 10 December 2003 on the drafting of guidelines for authorisation to use orthophosphate treatments for water destined for human consumption.

[3] Decree of 17 September 2003 relative to methods for analysis of water samples and their performance characteristics, NOR: SANP0323688A, JORF (Official Journal of the French Republic) of 7 November 2003, p. 19027 to 19033

Analytical uncertainty

The uncertainty of the measurement can be estimated using inter-laboratory tests, determining the reproducibility coefficient of variation (CVR%). *(AGLAE, 2003)*

Table 4.1: Evolution in uncertainty for various concentration ranges of lead in water using the CVR% estimated by AGLAE, from inter-laboratory tests, all analysis methods combined – Source: AGLAE, 2003

Level of concentration in water (µg/L)	10	15	20	25
CVR %	10.8%	11.8%	12.5%	12.8%
Estimation of uncertainty (µg/L)	± 2.2	± 3.4	± 5	± 6.4

* *95% confidence interval (2 × CVR)*

In the case of lead, the sampling variability is much higher than the analytical uncertainty.

4 Exposure

4.1 Routes of exposure

Ingestion is the main route of exposure to lead. Inhalation and the cutaneous route are negligible for the adult general population. Inhalation is of particular significance in professional environments where lead is handled.

With respect to children, the dust present in old housing in poor condition (< 1948) or from industrial contamination of the environment can become the main route of exposure to lead and lead to the toxicological reference value being exceeded. To this is added exposure from fruit and vegetables contaminated by dust deposits with a high lead content, the consumption of contaminated water and, sometimes, the consumption of scales of paints with a high lead content (“pica” phenomenon).

Absorption by the gastrointestinal route is estimated to be 10% of the quantity ingested in adults, 30 to 50% in children. On an empty stomach, absorption can reach 60 to 80%.

4.2 Contamination of supply water

The surface and underground sources used for the production of water destined for human consumption have been the subject of 27,748 sanitary control analyses on 11, 274 catchments over the period January 1999-October 2002. Lead contents of less than or equal to 10 µg/L represent 98.5% of the total number of analyses performed over this period. Lead concentrations of between 10 and 25 µg/L only concerned 1.1% of analyses. Only 0.4% of the analyses were above 25 µg/L.

Since 25 December 2003, the lead content of water must be monitored in surface sources and in supply water, i.e. at the consumer’s tap. The Public Health Code defines the sampling method to be adopted in the context of sanitary control [1].

Assessment of lead contents of water at the consumer’s tap has been the subject of several specific studies conducted by the Ministry of Health.

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[1] Decree of 31 December 2003 relative to the sampling conditions to be used to measure lead, copper and nickel in water destined for human consumption in application of article R. 1321-20 of the Public Health Code NOR: SANP0420086A.

4.3 Proportion of exposure sources

Table 4.2 reveals the significance of the proportion that can be attributed to water in overall lead intakes for babies (50%), justifying construction of the guideline value by WHO.

Table 4.2: Contribution of different sources to lead intakes in France (%), *(Hartemann, 1995).*

Medium	Concentration	Babies (3 months)	Children (2 years)	Adults (60 kg)
Air	0.1-1.0 µg/m^3	1.6-6.9	1.8-8.2	2.6-11.3
Water	10-25 µg/l	49.0-51.9	22.4-25.6	26.4-28.4
Food	variable	32.5-37.9	44.8-48.8	56.7-66.1
Dust	180-310 µg/g	8.6-11.8	21.3-26.9	3.5-4.8

For children and adults, food represents the main route of exposure to lead. However, one must not overlook intake due to inhalation or ingestion of dusts under specific exposure conditions: old housing or industrial environment.

Table 4.3: Summary of exposure to lead from food in France

Study date	Study type	Estimated intake	Route	Reference
2000-2003	Total Diet Study (TDS)	Adults (> 15 years) 18.4 µg/d [a] and 30 µg/d[b] Children (3 to 14 years) 12.8 µg/d [a] and 20.8 µg/d[b]	Food + water	Leblanc *et al.*, 2004
1998-1999	Duplicate portion meal – catering establishment	34 µg/d[a]	Food	Noël *et al.*, 2003
1998-1999	Duplicate portion meal – catering establishment	52 µg/d of which14 µg from water[b]	Food + water	Leblanc *et al.*, 2000
	Duplicate portion meal – catering establishment	43 µg/d	Food	Biego, 1999
1990-1993	Contamination x Consumption	68 µg/d	Food	Decloître, 1998
1992	Duplicate portion meal – catering establishment	73 µg/d	Food + water	DGS (French Government Department of Health), 1995

[a] Average consumers

[b] High consumers (95th percentile)

[c] 2 glasses = 7 µg Pb per main meal (2/3 L)

The daily lead intake from food can be estimated to be less than 40 µg/d.

5 Effects on health

Toxicological characteristics: **Cumulative toxin** with generalised effects.
The effects in humans are summarised below.

Acute toxicity:

The acute toxic effects of lead identified in the literature are as follows, for various targets

- Digestive disorders: colic associated with abdominal cramps (epigastric pains) and vomiting
- Renal disorders: proximal tubulopathy, in exceptional cases oligoanuric renal failure and, in children, Fanconi's syndrome
- Haematological disorders: anaemia
- Neurological disorders: saturnine encephalopathy preceded by headaches, ideo-motor retardation, clumsiness, ataxia, insomnia, irritability, memory disturbances; a severe condition combining impaired consciousness or even coma, convulsions.

Chronic toxicity:

The chronic toxic effects of lead identified in the literature are as follows:

- Neurological disorder (critical effect): in **children (target population)** from blood lead levels of 100-300 µg/L: behavioural disturbances, stagnation or regression of intellectual development; in adults from levels of 400-700 µg/L lead in the blood: fatigue, clumsiness, irritability, memory disturbances, but neurological impairment can occur for lower lead levels. Damage to the peripheral nervous system.
- Renal disorders: chronic kidney failure
- Cardiovascular disorders: an effect on high blood pressure is suggested but not demonstrated
- Haematological disorders: inhibition of the enzymatic activity of haeme synthesis, explaining the anaemia, which is not generally very severe
- **Carcinogenicity**: Lead and its inorganic derivates have been classified by IARC (1987) in group 2B (potentially carcinogenic in humans) and by the EPA (1993) (group B2). Its carcinogenicity has been demonstrated in animals but insufficiently demonstrated in humans.

The carcinogenic potential of inorganic lead and its organic compounds has been re-assessed. IARC proposes to review the classification as follows *(IARC, 2004)*:

- Lead and its inorganic derivatives are *probably carcinogenic* to humans (Group 2A),
- Organic lead compounds are *not classifiable as to their carcinogenicity* to humans (Group 3).

6 Reference values

6.1 Toxicological reference values

Various international bodies propose toxicological reference values (TRVs) for lead. These values are presented in table 4.4 and the construction method used by WHO is detailed hereafter.
WHO criterion: **neurotoxic effect** (reduction in IQ in children). In 1987, the JECFA set a provisional tolerable weekly intake (PTWI) of 25 µg/kg b.w./d for babies and children, considering that lead has cumulative toxic effects and that it is important to prevent it accumulating in the body. This value is the result of various studies which appear to show that, in children, below levels of 4 µg/kg b.w./d, no increase in serum lead levels is observed, that an increase can occur from 5 µg/kg bw../d *(Ziegler et al., 1978; Rye et al., 1983).* Initially attributed to babies and young children (1987), this value has since been applied to the general population (1993), and maintained at the last re-assessment in 1999 *(IPCS, 2000)*.

Table 4.4: Summary of toxicological reference values proposed by various bodies

Source	TRV	Value	Study	Effect
WHO, 1996	PTWI provisional tolerable weekly intake	25 µg/kg b.w./week	1987	Neurotoxic effect in children
EPA	RfD reference dose	not defined[1]	-	-
ATSDR	MRL minimal risk level	not defined[2]	-	-
Health Canada (1992)	ADI acceptable daily intake	3.5 µg/kg b.w./d	WHO	
RIVM (2001)	MPR maximum permissible risk	25 µg/kg b.w./week	WHO	

[1] It appears that certain effects of lead, particularly changes in blood levels of certain enzymes and the effects on the neuro-behavioural development of children, appear at very low lead levels, apparently without a threshold. The EPA working group studied the possibility of defining an RfD for inorganic lead (and its compounds) at two meetings (07/08/1985 and 07/22/1985) and considered that it was not appropriate to define an RfD *(IRIS EPA, 2003).*

[2] No MRL has been defined for lead due to the absence of a clearly defined threshold for some of the most sensitive effects in humans *(ATSDR, 1999).*

6.2 Reference values in water

The quality limit in drinking water for lead is set by the French Public Health Code at 25 µg/L until 2013 then at 10 µg/L thereafter.
Several recommendations and parametric values are found in the literature. These values are presented in table 4.5 and the details of their construction in table 4.6.

In the context of revision of quality directives for drinking water, WHO does not propose a new guideline value for this substance.

Table 4.5: reference values proposed by different bodies

Value of directive 98/83/EC Annex IB	WHO guideline value 1996	Health Canada (1992)	US EPA (1991)
10 µg/L from 2013 25 µg/L from 2003 to 2013	10 µg/L	10 µg/L MAC*	15 µg/L “Action Level”

**MAC: maximum acceptable concentration*

Table 4.6: details of construction of the reference value proposed by WHO

Nature of critical dose	Study date	Value of critical dose	Uncertainty factor	Type of reference value	Reference value	Drinking water proportion	Value retained
NOAEL	1987	4 µg/kg b.w./d	-	PTWI	25 µg/kg b.w./week	50% babies	10 µg/L

7 Comparison of daily intakes with the toxicological reference value

On the basis of a PTWI of 25 µg/kg b.w./d, table 4.7 presents the proportion of this toxicological reference value that can be attributed to exposure of the population via drinking water, with different lead contents.
The calculation is made for babies on the basis of the following hypotheses:

- an individual water consumption equal to 0.75 L/d, representative of the water consumption of the highest consumers,
- A reference body weight for babies of 5 kg.

Table 4.7: proportion of the PTWI that can be attributed to water depending on the lead content, for babies.

Concentration in water	Quantity provided by water	Proportion of the PTWI
10 µg/L	10.5 µg/kg b.w./week	42%
15 µg/L	15.8 µg/kg b.w./week	63%
20 µg/L	21 µg/kg b.w./week	84%
25 µg/L	26.2 µg/kg b.w./week	104%

Table 4.7 shows that consumption of water containing 25 µg/L leads to the PTWI for babies being exceeded, without taking into account intake from food or from other potential sources (air, dust).

8 Opinion

After consulting the “Water” Expert Committee on 4 May and 8 June 2004 and the “Expert Panel on Contaminants" on 7 May 2004, Afssa issues the following opinion:

Considering the quality limit in annex 13-1-I-B. of the French Public Health Code of 25 micrograms per litre for lead applicable until 25 December 2013;

Considering the following elements

- that lead can be present in water sources and that it can be present in the pipes and joints of public and domestic supply systems;
- that the toxic effect of lead is cumulative;
- that the provisional tolerable weekly intake of 25 micrograms par kilogram of body weight proposed by WHO for infants has since been applied to the general population;
- that toxicological and epidemiological data have made it possible to identify infants and young children as the sensitive population;
- that corrective measures authorised by the ministry for health can be implemented to limit lead contents in water;

Afssa (French Food Safety Agency):

Reiterates that the means required to bring lead concentrations to the level of the quality limit must be implemented as rapidly as possible,
Considers:

- that the consumption of water with a concentration higher than the quality limit currently in force (25 micrograms per litre) is detrimental to the health of infants and young children,
- that, due to the cumulative nature of lead and, in particular given the resorption of osseous lead during pregnancy, the same reservation is valid for the adult population.

File 5: Assessment of health risks related to exceeding the quality limit for arsenic in water destined for human consumption

In water, arsenic is present mainly in inorganic form (90%).

- in water full of oxygen, the arsenate form (As V – $H_2AsO_4^-$ and $HAsO_3$) predominates.
- in reducing medium, the arsenite form (As III – H_3AsO_4) predominates.

An increase in pH can increase the arsenic content dissolved in water.

Methylated types, MMAA (methyl arsenic acid) and DMAA (dimethylarsinic acid), can also be present in water.

1 Origin and sources of contamination

Natural sources
Arsenic is present in more than 200 minerals, with mispickel (FeAsS), the most abundant mineral form being mainly associated with seams of sulphurated minerals. Present in eruptive and metamorphic rocks, it is redistributed by alteration processes in sedimentary terrains and can be concentrated in clayey rocks. It may be trapped in alluvia by adsorption on iron oxides and hydroxides and micas but also in the form of carbonate. In groundwaters, the contents are low, apart from in soils with a high sulphide content or in certain alluvial formations. To redox conditions which prevail in aquifers have a major influence on its availability.

Anthropic sources
Arsenic and its compounds have a very large number of industrial applications (production of alloys, non-ferrous metal foundries, microelectronics, textiles) or agricultural applications.

2 Treatments reducing the arsenic content in water

In accordance with the French drinking water regulation, the use of treatment products is subject to approval from the Minister responsible for health.

The following treatments can reduce arsenic content in water, although confirmation is required on an individual case basis that the proposed treatments are approved.

Coagulation – flocculation – separation

Arsenic reacts with ferric iron to give an iron arseniate co-precipitable by ferric hydroxide.

OH^- ions interfere. pH plays an important role; it must be less than 7.5. Only arsenic V is eliminated. Prior oxidation is required for arsenic III.

Decarbonation

Decarbonation with lime or soda is performed at a pH of 9 or above 9. In the presence of magnesium, this treatment is very effective.

Selective adsorption

On activated alumina, fluorines interfere. The pH must be less than 7.5. Only arsenic V is eliminated.

On manganese dioxide (MnO_2): the pH must be less than 8. Both valences of arsenic are eliminated.

On iron oxyhydroxide, the pH must be less than 8. Both valences of arsenic are eliminated. However, arsenic III is retained in slightly lower quantities: half those of arsenic V.

Membrane retention

Nanofiltration must have a cut-off point of less than 200 Daltons.

Reverse osmosis retains arsenic III and V but it is not a specific treatment.

3 Analysis methods:

The decree of 17 September 2003[1] relative to methods for analysis of water samples and their performance characteristics specifies that, in the case of arsenic, the accuracy, precision and limit of detection must not exceed 10% of the parametric value (i.e. 1 µg/L) and that the limit of quantification must not be more than 10 µg/L.

The methods outlined below are those which are standardised and which have a quantification limit of less than 10 µg/L. *(Thomas, 2002)*

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[1] Decree of 17 September 2003 relative to methods for analysis of water samples and their performance characteristics, NOR: SANP0323688A, JORF (Official Journal of the French Republic) of 7 November 2003, p. 19027 to 19033

- Atomic absorption spectrometry with electrothermal atomisation with a $Ni(NO_3)_2$ matrix modifier. The limit of detection is 1 µg/L.
- Atomic absorption spectrometry with hydride generation. The limit of detection is 0.05 µg/L
- Atomic fluorescence spectrometry after hydride generation. This method differs from the previous one through its final detection system, which uses an atomic fluorescence spectrometer; it is less sensitive to interference. The limit of detection is 0.05 µg/L. It is currently being standardised (listed in the programme of the CEN/TC 230/WGI working group).
- Atomic emission spectrometry by argon plasma (ICP-AES). This method does not have a good limit of detection (35 µg/L*(EPA cited in ATSDR 2000)*) but can be improved using a hydride generator; in this case, the limit of detection is reduced to 0.2 µg/L.
- Mass spectrometry coupled to argon plasma (ICP-MS). Limit of detection 0.4 µg/L *(EPA cited in ATSDR 2000)*

Analytical uncertainty

The uncertainty of the measurement can be estimated using inter-laboratory tests, determining the reproducibility coefficient of variation (CVR%). *(AGLAE, 2003)*

Table 5.1: Evolution in uncertainty for various concentration ranges of arsenic in water using the CVR% estimated by AGLAE, from inter-laboratory tests, all analysis methods combined – Source: AGLAE, 2003

Level of concentration in water (µg/L)	5	10	15	20	25	30
CVR %	19.5%	15.7%	14.4%	13.8%	13.4%	13.1%
Estimation of uncertainty* (µg/L)	± 2	± 3.2	± 4.4	± 5.6	± 6.6	± 7.8

* *95% confidence interval (2 × CVR)*

4 Exposure data

4.1 Route of exposure

For the general population, the main route of exposure to arsenic is the oral route via water and food. Exposure to air is generally less than 1 µg/d *(WHO 2003)*

4.2 Contamination of supply water

The regulatory sanitary control programme stipulated analysis of this parameter at the drawing point before treatment of surface water (2 to 12 times per year) and after treatment for groundwater and surface water (once yearly to once every 5 years). For sources and production installations with a daily output of less than 100 m^3/day, no annual analysis frequency has been set.

A study of the data available from the SISE-EAUX data base (Ministry of Health – SISE-Eaux) for a 4-year period (January 1999 to December 2002) shows that the 50th percentile of the results of 2069 analyses[40] (higher than the quality limit) registered is equal to 20 µg/L.

4.3 Proportion of exposure sources

For the general population, the total exposure to arsenic varies considerably depending on their diet. The majority of the data available concern total arsenic and do not reflect possible variations in exposure levels to the most toxic forms of arsenic, which are mainly inorganic forms. Table 5.2 presents estimates of arsenic intakes from food for different countries.

Table 5.2: Estimation of level of exposure to arsenic for different countries

Country	Study type	Estimated intake	Route	Reference
France	Total diet study	Adults (> 15 years) 1 µg/d [b] and 2 µg/d[c] Children (3 to 14 years) 0.8 µg/d [b] and 1.6 µg/d[c]	Food and water	*Leblanc et al., 2004*
France	Duplicate portion meal – catering establishment	147 µg/d Total As 15 µg/d Inorg As	Food	*Noël et al., 2003*
France	Duplicate portion meal – catering establishment	109 µg/d Total As	Food	*Leblanc et al., 2000*
Canada, Poland, USA, UK		16.7 to 129 µg/d (adult) 1.26 to 15.5 µg/d (children)	Food – adults Food - children	*Health Canada 1989*
UK Total Diet Study	Total diet study	65 µg/d[a] 120 µg/d[b] to 420 µg/d[c]	Food	*Ysart et al, 1999*

[a] *General population, without contribution of water*
[b] *mean consumption*
[c] *High consumers 97.5th percentile*

Seafoods (shellfish and fish) and **meat** are the main sources of exposure to arsenic via food. It is difficult to compare the arsenic intake from food with that from drinking water since the form and biological availability of arsenic are not the same in these matrices.

For example, a high proportion of organic arsenic in fish is found in forms which are not very toxic, such as arsenobetaine and trimethylarsine, and rapidly excreted *(ATSDR 2000*, *Health Canada, 1992)*.

WHO indicates that there are limited data available stipulating that 25% of total arsenic could be in inorganic form in food. The data of the French study *(Noel et al. 2000)* suggest a value of 10% for fished products. However, the value of 15 µg/d inorganic arsenic proposed by the abovementioned study is equivalent to the concentration proposed (12-14 µg/d) in a North American study cited by WHO (*Yost et al. 1998 in WHO 2003*).

Assessment of intakes from solid foods:

In view of the literature, a maximum value of intakes from solid foods of 15 µg/d inorganic arsenic has been retained.

5 Effects on health

Mineral forms of arsenic are more toxic than organic forms. Arsine (AsH_3) is considered to be the most toxic form, followed by arsenites (As III), arseniates (As V) then organic compounds. Inorganic arsenic is metabolised in the body, mainly in the liver. The metabolised forms are monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). These forms are excreted in the urine. However, reactive intermediates can be formed. Absorbed As (V) is rapidly reduced in the blood in the form of As(III), which implies an increase in its toxicity. There is a marked difference in the metabolisation of arsenic between various mammal species *(Wang et al. 2002)*, population groups or individuals *(Loffredo et al. 2003)*. Methylated forms of AsIII (especially MMA^{III}) induced by ingestion of inorganic arsenic may contribute to the toxicity observed; this point is still to be clarified *(Vahter, 2002)*.

In addition, it is possible that antimony may increase the toxic effects of arsenic *(Gebel, 1999)*

Chronic toxicity and carcinogenicity:

The most documented critical effects are certain types of cancer. The International Agency for Research into Cancer (IARC) has classified inorganic arsenic in group 1, on the basis of sufficient evidence of carcinogenicity with an increased risk of cancer of the bladder, lungs and skin in humans *(IARC 2002).*

Following prolonged exposure to arsenic, by ingestion of contaminated water, the most common symptoms are skin lesions (minimum exposure period of 5 days). Skin cancer develops later on and generally takes 10 years to appear. Effects on the cardiovascular system have been observed in children having consumed water contaminated with arsenic (mean concentration of 0.6 mg/L, mean duration 7 years).

Studies on exposure to arsenic have reported hypertension, cardiovascular diseases, diabetes mellitus and foetal malformations. The symptoms triggered by arsenic appear to differ depending on the individual, population group and geographic zone. Thus, “black foot disease” has been widely studied in Taiwan but has not been observed in other countries (*IPCS, 2002*). Studies conducted in several countries have nonetheless demonstrated that arsenic may cause other less severe forms of peripheral vascular disorders. In humans, inorganic arsenic does not appear to cross the blood-brain barrier; however, placental migration has been reported *(Gibson, Gage, 1982 in WHO 2003)*.

6 Reference values

6.1 Toxicological reference values

The international bodies propose various toxicological reference values:

- **For non-carcinogenic cutaneous effects**

  The US-EPA proposes an Rfd of 0.3 µg/kg b.w./d (1993). This TRV takes into account the two main sources of exposure to inorganic arsenic for the general population: water (drinking water and water for food preparation) and food. This value was set on the basis of two epidemiological studies taking into consideration “black foot disease” and hyperpigmentation or keratosis. From these studies, an NOAEL of 9 µg/L was determined, converted into 0.8 µg/kg b.w./d *(Tseng, 1977, Tseng et al., 1968 in ATSDR 2000)*. The uncertainty factor of 3 takes into account both the absence of data concerning reproduction toxicology and intra-species variation.

  For chronic exposure by the oral route, the ATSDR proposes an MRL of 0.3 µg/kg b.w./d (2000). This value is established on the basis of the same studies as the RfD of the US EPA (IRIS) *(Tseng, 1977, Tseng et al., 1968 in ATSDR 2000)* applying an uncertainty factor of 3 which takes into account the intra-species variability.

- **For cutaneous carcinogenic effects**

  The US-EPA has set a TRV for carcinoma-type skin cancers (baso-cellular carcinomas, spino-cellular carcinomas, Bowen’s disease). The TRV is expressed in EUR (excess unit risk) and is equal to 1.5 10^{-3} (µg/kg b.w./d)$^{-1}$, i.e. for a total consumption of 2 L/d, a unit risk value of 5.10^{-5} (µg/L)$^{-1}$. This value was set on the basis of the summary report compiled by the US EPA in 1988. The studies having provided values for establishment of a dose-effect relationship are those by Tseng *et al.* *(1968 in ATSDR 2000)* and Tseng *(1977 in ATSDR 2000)*. A linearised multi-stage model based on prediction of the development of skin cancers as a function of dose and age was used.

  WHO proposes a provisional tolerable weekly intake (PTWI) by the oral route of 15 µg/kg **b.w./week**(*WHO, 1996*).

- **For other carcinogenic effects**

  In its new recommendations *(WHO, 2003)*, WHO specifies that there is currently still a great deal of uncertainty as to the risks at low concentrations. According to the National Research Council (NRC, 2001) the data available do not make it possible to provide a biological base for the use of either a linear model or a non-linear model.

  The National Research Council and the US EPA *(OEHHA, 2004)* considered that assessment of the risks of lung and bladder cancers should be the basis for drafting of standards for arsenic in drinking water. Analysis of various studies conducted in Chile, Taiwan and Argentina shows that the critical effects to be taken into account in terms of cancer, associated with the ingestion of arsenic, are lung and bladder cancers. Modelling of data from these studies made it possible to estimate, for the American population exposed to water with a concentration of 10 µg/L arsenic, that the excess risks for the onset of bladder and lung cancers are, respectively, 12 and 18 per 10,000 in the female population and 23 and 14 per 10,000 in the male population *(InVS, 2002; WHO, 2003; NRC,2001).*

It is important to note that several levels of uncertainty exist with respect to these assessments. Assessment of exposure is mainly the result of studies conducted in a population in Taiwan, where the drinking water can contain other substances with effects that are synergetic with those of arsenic *(IRIS, 1998)*. Extrapolation to low levels of dose-response curves from linear models is probably not appropriate to the case of arsenic *(IRIS, 1998)*. A recent study *(Bates et al. 2004)* demonstrates the absence of any link between the consumption of drinking water (for 40 years) containing arsenic and the development of bladder cancer in Argentina. However, despite these limits, the US-EPA has maintained its position, establishing its TRV for skin cancers.

Table 5.3 summarises the toxicological reference values proposed by different bodies.

Table 5.3: Summary of TRVs proposed by international bodies

Source	Study date	Exposure route	Reference value	Critical effect
US EPA	1993	Oral	RfD=0.3 µg/kg /d UF= 3	"black foot disease"
ATSDR	2000	Oral	MRL=0.3 µg/kg/d UF=3	"black foot disease"
JECFA	1988	Oral	PTWI = 15 µg/kg (Provisional value)	Skin cancer
US EPA	1998	Oral	Oral Slope Factor 1.5 $(mg/kg/d)^{-1}$ Drinking Water Unit 5.10^{-5} $(µg/L)^{-1}$	Skin cancer

6.2 Reference value in water

The quality limit in drinking water is set by the French Public Health Code at 10 µg/L. Several recommendations and parametric values, presented in table 5.4, are found in the literature.

WHO justifies the guideline value of 10 µg/L as being close to the practical assay limit and the measures to be implemented to reduce the concentration in water to below this value are complex.

Table 5.4: Reference values proposed by different bodies

Value of directive 98/83/EC Annex IB	Guideline value WHO 2003	Health Canada (1989 revised 1992)	US EPA (2001)
10 µg/l	10 µg/l (Assay limit)	25 µg/l (provisional)	10 µg/l MCL

7 Assessment of the risk level associated with exceeding the quality limit

Based on the unit risk value of 1.5 10^{-3} $(µg/kg\ b.w./d)^{-1}$, proposed by the US-EPA and also used by WHO, for skin cancers, the risk level associated with consuming drinking water with an arsenic concentration of 10 µg/L, would be in the region of 6.10^{-4} for lifetime exposure (2 L, 70 kg, 70 years).
Based on another approach proposed by the US-EPA *(US-EPA, 2003)* which takes into account the susceptibility of children and infants:

- the risk level associated with consuming drinking water with an arsenic concentration of 10 µg/L, would be in the region of 2.10^{-3} for lifetime exposure.
- table 5.5 presents the excess unit risk associated with exposure over a determined period at a concentration above the quality limit (10 µg/L) and exposure to a concentration equal to the quality limit for the remainder of the subject's lifetime.

Table 5.5: Estimation of risk related to exceeding the quality limit for arsenic in water for a given period[1].

Concentration	**Non compliance duration**		
	3 years	**6 years**	**9 years**
15 µg/L	2.4 10^{-3}	2.5 10^{-3}	2.6 10^{-3}
20 µg/L	2.8 10^{-3}	3 10^{-3}	3.2 10^{-3}
30 µg/L	3.6 10^{-3}	4 10^{-3}	4.4 10^{-3}
40 µg/L	4.4 10^{-3}	5 10^{-3}	5.6 10^{-3}
50 µg/L	5.1 10^{-3}	6 10^{-3}	6.8 10^{-3}

8 Opinion

After consulting the “Water” Expert Committee on 4 May and 8 June 2004 and the “Expert Panel on Contaminants" on 7 May 2004, Afssa issues the following opinion:

Considering the quality limit in annex 13-1-I-B. of the French Public Health Code of 10 micrograms per litre for arsenic;

Considering the following elements:
- that the results of the studies available in the literature make it possible to estimate daily arsenic intakes related to food in the general population;
- that the level of arsenic ingested is significantly higher than the level inhaled, apart from specific professional contexts;
- that arsenic is a substance which does not possess a toxic effect threshold;
- that the International Agency for Research on Cancer (IARC) has classified inorganic arsenic in group 1, on the basis of sufficient evidence of carcinogenicity, with an increased risk of cancer of the bladder, lungs and skin in humans;
- that the risk level associated with the quality limit of 10 micrograms per litre is in the region of 6.10^{-4} based on the toxicological reference value proposed by the US Environmental protection agency for skin cancers and adopted by the World Health Organisation;
- that the inorganic forms of arsenic predominantly present in drinking water are more toxic than the organic forms present in food;
- that the results of most of the studies available in the literature make it possible to estimate that daily intakes of inorganic arsenic via food are less than 15 micrograms;
- that, for the general population, the other routes of exposure are negligible;
- that corrective measures authorised by the ministry for health can be implemented to reduce arsenic contents in water;

Afssa (French Food Safety Agency):

Reiterates that the means required to bring arsenic concentrations to the lowest possible level must be implemented as rapidly as possible,

Considers:
- that the excess cancer risk associated with the quality limit of 10 micrograms per litre is significant and that, consequently, ingestion of water presenting a concentration higher than the quality limit does not appear to be acceptable,
- it is the responsibility of the health authorities to examine situations characterized by slight, temporary exceeding of the limit, on the basis of the associated risk level,

Draws attention to the potential synergetic effects of antimony with arsenic.

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[1] These figures correspond to a high range, taking into account a potential susceptibility in infants and children.

File 6 : Assessment of health risks due to exceeding the quality limit for selenium in water intended for human consumption

Quality limit: 10 µg/L

Chemical forms:
- Elemental selenium (insoluble in water)
- Selenium ion (Se^{2-})
- Seleniate (SeO_4^{2-})
- Selenites (SeO_3^-)

Usually present in water in the form of seleniate (SeO_4^{2-}) or selenite (SeO_3^-).

1 – Origin and sources of contamination:

In the water source:

Natural origins:
Selenium is present in very small amounts in the earth's crust and is a constituent of very rare minerals. It is present alongside sulphide containing minerals in bedrock and is associated with minerals formed by silver, copper, lead and nickel. It is present in sedimentary soil in certain formations which are rich in organic material. Release of selenium into water is determined by variations in the Redox potential and is usually seen in captive naps, as it is soluble under oxidising conditions.

Human-derived sources:
Selenium is used in the electronics (semi-conductors) and photographic industries, chemical for the production of catalysts, rubber, pigments and metallurgy pigments and additives, ironworks, and in the pharmaceutical and textile industries.

2 – Treatments reducing selenium content in waters

In accordance with the French drinking water regulation, the use of treatment products is subject to approval from the Minister responsible for health.

The following treatments can reduce selenium content in water, although confirmation is required on an individual case basis that the proposed treatments are approved.

Coagulation – flocculation – separation

Selenium IV co-precipitating with iron.

Pre-polymerised aluminium salts are ineffective.

OH^- ions interfere in this co-precipitation reaction and the pH, which plays an important role, must be maintained below 7.5.

A preliminary reduction phase is required to remove selenium VI.

Decarbonation

Lime or soda decarbonation is performed at a pH above 9.

For selenium, the IV valency is well removed (approximately 90%) whereas removal of the VI valency is approximately 20%.

Selective adsorption

Manganese dioxide, activated alumina and iron oxihydroxide all retain selenium efficiently. As OH^- ions interfere, pH plays an important role and must be maintained below 7.5. Selenium VI is retained ten times less than selenium IV.

Ion exchange resins

Anionic exchange resins retain the different anionic forms of selenium although this process is not selective for this element and also removes the major anions in water. Exchange occurs preferentially with chlorides.

Membrane treatments

A cut off of less than 200 Daltons is needed for nanofiltration.

Reverse osmosis is effective.

These are demineralisation processes.

3 – Analytical methods

The decree of 17 September 2003[1] on analytical methods for water samples and their performance characteristics states that in the case of selenium, accuracy, imprecision and the limit of detection must not exceed 10% of the set value, (i.e. 1 µg/L) and the limit of quantification must not be greater than 5 µg/L.

Presentation of norm-based methods :

- NF EN ISO 11885, March 1998, Water quality – Assay of 33 elements by atomic emission spectroscopy with induction coupled plasma.
- ISO 9965:1993, July 1993, Water quality. Assay of selenium. Atomic absorption spectrometric method (hydride technique).

Analytical uncertainty

Uncertainty of measurement can be estimated from inter-laboratory studies assessing the coefficient of variation of reproducibility (CVR%). *(AGLAE, 2003)*

Table6.1: Evaluation of uncertainty for different concentration ranges of selenium in water from the CVR% estimated by AGLAE, from inter-laboratory studies, all analytical methods combined – Source: AGLAE, 2003

Concentration in water (µg/L)	5 µg/L	10 µg/L	15 µg/L	20 µg/L	25 µg/L	30 µg/L	35 µg/L	40 µg/L
CVR%	21.0%	20.4%	20.2%	20.1%	20.1%	20.1%	20.0%	20.0%
Estimation of analytical uncertainty*	± 2 µg/L	± 4 µg/L	± 6 µg/L	± 8 µg/L	± 10 µg/L	± 12 µg/L	± 14 µg/L	± 16 µg/L

* *95% confidence interval (2 × CVR)*

4 - Evaluation of exposure:

4. 1 Water: data obtained from the SISE-Eaux database (prior to 2004)

The regulatory programme for health control defined in the French drinking water regulation requires analyses to be conducted for this parameter at the extraction point for surface waters (from 1 to 12 times per year) and after treatment for groundwater and surface waters (at least once every 5 years). Analysis of data available from the SISE-EAUX database (Ministry of health– SISE-Eaux), for a 4 years period (January 1999 to December 2002) shows that :

- analyses[2] are available for 28.5% of water distribution units (i.e. 8584 water distribution units serving 46.1 million people) ;
- at least one over-limit result[3] was found in 0.38% of these water distribution units serving a maximum of 862,000 people ;
- the 95th percentile of the results of the 1113 analyses[3] (above the quality limit) was close to 31 µg/L (50th percentile = 15 µg/L).

4.2 Air

The selenium content in air (often bound to particles) ranges from 0.1 to 10 ng/m^3 in urban areas : higher concentrations may be seen locally *(WHO, 2003).*

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[1] Rule dated 17 September 2003 relating to analytical methods for water samples and their performance characteristics, NOR : SANP0323688A, JORF dated 7 November 2003, pages 19027 to 19033

[2] Analyses conducted on samples taken either from production or from distribution.

4.3 Foods

Apart from occupational exposure in which air and skin contact may be of particular importance, diet is the major source of exposure to selenium *(WHO, 2003).* Food constitutes more than 98% of dietary intake and water appears to be a negligible source *(Health Canada, 1993).*

The total exposure of the French population to selenium is low, and intake appears to be suboptimal for the entire population *(Recommended dietary intake – Apports nutritionnels conseillés, 2001).*

Table 6.2: Summary of nutritional exposure to selenium in different countries

Country	Type of study	Estimated intake			Reference
		Population	Mean intake	Maximum intake or high percentile	
France	Total diet study	Adults (> 15 years old)	42 µg/d (with water)	70 µg/d (97.5 percentile with water)	Leblanc *et al.*, 2004
		Children (3 to 14 years old)	31 µg/d (with water) 28 µg/d (hors eau)	55 µg/d (97.5 percentile with water) 50 µg/d (97.5 percentile excluding water)	from Leblanc *et al.*, 2004
		Children (1 to 2.5 years old)	26 µg/d (97.5 percentile excluding water)	40 µg/d (97.5 percentile excluding water)	OCA(Afssa) from Leblanc *et al.*, 2004
France	Duplicated meals - community restaurant services		66 µg/d		Noël *et al.*, 2003
Germany	Duplicated meals	Children 1.5 to 5.5 years old	Median: 19 µg/d Mean: 22.6 ± 18 µg/d	40 µg/d (95 percentile excluding water)	Wilhelm *et al.*, 2003
Ireland	Duplicated meals	General population° 18 to 64 years old	50 µg/d		Murphy *et al.*, 2002
		men	44 µg/d		
		women	60 µg/d		
USA	Total diet study	Children < 2 years old	13-56 µg/d		FDA Total Diet Study Egan *et al.*, 2002
		Children < 10 years old	71-93 µg/d		
		Men	110-126 µg/d		
		Women	74-87 µg/d		
UK	Total diet study		37.8- 40.2 µg/d		2000 UK Total Diet Study - COT, 2003
Spain			60 – 106 µg/d		Torra *et al,1997.* in Barceloux, 1999
UK	Total diet study	General population	39 µg/d		1997 UK Total Diet Study - Ysart *et al.*, 2000
		Adults	54 µg/d	100 µg/d	
Greece and Finland			95 – 110 µg/d 110 µg/d		Anttolainen *et al.,* 1996 in Tinggi, 2003 Bratakos *et al.*, 1996 in Tinggi, 2003
UK	Total diet study	General population	43 µg/d		1994 UK Total Diet Study Ysart *et al.*, 1999
		Adults	57 µg/d	100 µg/d	
Belgium	Duplicated meals		28.4 to 61.1 µg/d		Robberecht *et al.*, 1994
France			40-50 µg/d		Simonoff & Simonoff, 1991 in ANC report, 2001

A number of studies conducted in European countries showed that selenium intake is relatively low compared to other regions in the world *(Tinggi, 2003).*

For children, estimates in a recent French study (Leblanc et *al.*, 2004) show that selenium intake is 50 µg/d or less in 97.5% of children in the age band 3 to 15 years old. Combining consumption data obtained from the survey conducted by Sofres in 1997 on behalf of the Syndicat Français des Aliments de l'Enfance et de la Diététique (SFAED) (French Syndicate for Foods in Childhood and Dietetics) with food contamination data from the study of Leblanc et *al, 2004* that selenium intake is 40 µg/d or less in 97.5% of children in the age band from 1 to 2.5 years old. These estimates are consistent with results of a recent German study (Wilhelm et *al.*, 2003) which showed selenium intake to be 40 µg/d or less in 95% of children in the 1 to 4 year old age band and an average of 22.6 ± 18 µg/d for children under 7 years old.

In adults, estimates of daily selenium intake in the diet in the European countries ranges from 28 to 110 μg/d depending on the country and evaluation strategy.

Evaluation of intake in solid foods :
In children : based on the French study (Leblanc *et al.*, 2003) a value of 40 μg/d is found for children under 3 years old and 50 μg/d for children under 15 years old.
In adults : the maximum of 100 μg/d was found based on the English study by Ysart *et al. (2000)*. This Total Diet Study is greater than the French estimates (40-50 μg/d, 66 μg/d and 70μg/d).

5 – Effects on health

5.1 Essential requirements

Selenium is an essential element which can be substituted for sulphur in sulphur-containing amino acids through complex enzyme systems, to form analogous selenium-containing compounds, selenomethionine and selenocysteine, which are the predominant forms of dietary selenium.

Selenium has different biological roles : it is needed for the activity of glutathione peroxidase in its protective action against oxidative stress (the decomposition of hydrogen peroxide), in the metabolism of thyroid hormones (deiodase) and it interferes with the toxicity of arsenic, cadmium, mercury and lead.
Optimal intake is difficult to define but the recommended intake is 1 μg/kg bw/d (optimisation of plasma glutathione peroxidase) (*Recommended dietary intake – apports nutritionnels conseillés 2001*). The recommended dietary intakes by age band are summarised in table 6.3 for children and adolescents.

Table 6.3: Recommended selenium intake for different age bands

Source : Recommended dietary allowance, 2001

Age	*Recommended dietery allowance** *(RDA in μg/day)*
0 – 6 months 7 – 12 months	15 20
1 – 3 years old 4 – 6 years old 7 – 9 years old	20 30 30
10 – 13 years old	40
14 – 18 years old	50
Adults	50 to 80 (1 μg/kg bw/d)

* defined as the intake allowing the physiological requirements of almost every individual of the population (97.5%) to be covered

5.2 Toxic Effects

Toxic mechanisms of action of selenium : interference with the oxidation-reduction cycles in the cell, depletion of glutathione, inhibition of protein synthesis, depletion of S-adenosyl-methionine, (SAM) which is essential for methylation of certain substrates and particularly DNA.
The most toxic forms of selenium are the selenites, seleniates and selenomethionine which are soluble and well absorbed.

Chronic toxicity : selenium is a cumulative toxic . Selenosis (lesions of the nails and skin) may occur from doses of 0.9 mg/day and above following prolonged exposure.

Effects have been found on reproduction in some species of animal, although limited data are available in humans *(Vinceti et al., 2000)*

Carcinogenesis :

Except for selenium sulphite which is not found in water, selenium and its compounds are classified by the IARC into group 3 “The agent is not classifiable as to its carcinogenicity to humans"”.

6 – Reference values

6.1 Review of toxicological reference values :

It is difficult to set a toxicity threshold for selenium as this depends on the amount and nature of the proteins present in the diet and on the presence of vitamin E.

Presentation of critical studies:

- **Yang et *al*., 1989 : study of clinical selenosis in 349 Chinese**

Individual selenium intake was calculated for the inhabitants of regions with low, moderate and high selenium concentrations. Whilst no correlation was found between blood selenium and the development of clinical signs of selenosis (morphological change in the nails), chronic selenosis developed in 5 people who had high blood selenium concentrations (1.054 to 1.854 mg/L). The authors estimated that these concentrations were equivalent to a selenium intake of 0.91 mg/d and considered this level to indicate mild selenium toxicity.

In addition, the prothrombin time rises significantly when the selenium intake is greater than 0.85 mg/d, although it is possible that the values seen are within the natural variation of selenium in these populations. The authors suggest a maximum safety level of 0.4 mg/d (safety factor of 2).

- **Longnecker et *al*., 1991: clinical follow up of 142 people for 2 years.**

Inhabitants of Dakota and Wyoming (USA) who had a mean selenium intake of 239 µg/d were followed up for 2 years. An association was found between serum alanine aminotransferase activity and selenium intake, although this was not statistically significant.

Table 6.4: Summary of reference toxicological values proposed by different organisations

Source	Reference value		Population	Critical effect	Details of construction	Study
US EPA, 2002 in Golhaber, 2003	RfD Reference Dose	5 µg/kg b.w./d 300 µg/d	Adults	Selenosis	NOAEL* of 0.85 mg/d of 3 full individual variation. Weight of a Chinese person 55 kg	Yang *et al.*, 1989
FSA 2003 Expert group on vitamins and minerals	SUL Safe upper level	7,5 µg/kg b.w./d 450 µg/d	Adults	Selenosis	NOAEL* of 0.91 mg/d Safety factor of 2 for extrapolation to a NOAEL	Yang *et al.*, 1989
ATSDR 2001	MRL Minimum Risk level	5 µg/kg/d	Adults	Selenosis	NOAEL* of 0.85 mg/d Safety factor of 3	Yang *et al.*, 1989
Institute of Medecine of US National Academies 2000	UL Tolerable Upper intake Level	45 µg/d 60 µg/d 90 µg/d 150 µg/d 280 µg/d 400 µg/d 400 µg/d	0-6 months 7-12 months 1-3 years old 4-8 years old 9-13 years old 14-18 years old Adults	Selenosis	NOAEL* of 0.80 mg/d Safety factor of 2 for individual variability	Yang *et al.*, 1989 Shearer et Hadjimarkos, *1975* et Brätter et *al.*, *1991*
SCF 2000	UL Tolerable Upper intake level	60 µg/d 90 µg/d 130 µg/d 200 µg/d 250 µg/d 300 µg/d	1-3 years old 4-6 years old 7-10 years old 11-14 years old 15-17 years old adults	Selenosis	NOAEL* of 0.85 mg/d Safety factor of 3	Yang *et al.*, 1989
WHO 1996	NOAEL*	4 µg/kg b.w./d 240 µg/d	Adults	Increased level of serum alanine aminotransferase		Longnecker *et al.*, 1991
Martin 1996	Limit of safety dose	150 µg/d	Adults	Selenosis .	NOAEL* of 0.85 mg/d Safety factor of 10 for the difference in Chinese/French diet	Yang *et al.*, 1989

*NOAEL : no observed adverse effect level; LOAEL: low observed adverse effect

Certain international bodies propose safety limits by age band. The term "Tolerable Upper Intake Level" is equivalent to a daily dose of a substance which when ingested daily by an age band does not cause adverse consequences to health *(Recommended daily intake, 2001)*.

- **Scientific Committee on Food (EU):**

  According to this committee the available data do not allow a NOAEL to be established for the critical effect “stained enamel”. Despite the absence of data on the specific sensitivity of children to selenium this organisation considered it appropriate to extrapolate the Tolerable Upper Intake Level proposed for adults to children based on a reference body weight *(SCF, 2000).*

- **Institute of Medicine (USA):**
  This institute established limits of safety in children of different age bands although there was no proof that young children were more sensitive to selenium *(Institute of Medecine, 2000)*. The values were established based on the results obtained by Shearer and Hadjimarkos *(1975)* and Brätter et *al. (1991)* from comparisons between selenium content in breast milk and the absence of effect or blood selenium concentrations in infants.

Conclusion:
The French tolerable upper intake level for adults (150 μg/d) proposed by the Conseil superieur d'hygiène publique de France (Public Hygiene Higher Council in France) in 1995 is conservative. This dose was set from the study by Yang et *al.* (1989) using a safety factor of 10 (inter species) in order not to encourage excessive selenium supplementation. Based on the same study (Yang *et al., 1989)*, the Scientific Committee on Food proposed a higher tolerable upper intake level in 2000 (300 μg/d for adults).
In the adult population, the toxicological reference value proposed by the WHO, which is similar (240 μg/d for adults or 4 μg/kg b.w./d) is adopted in our study. The WHO considers that water soluble selenium salts are more toxic than the organic selenium present in foods.

The tolerable upper intake level proposed for children by the Scientific Committee on Food have been adopted in this study.

Reference values in water

For the public drinking water supply, the quality limit is set at 10 µg/L by the Code of Public Health legislation. Several recommendations and limits were found in the literature. These values are summarised in table 6.5. Details of their construction are shown in table 6.6.
In the revision of the quality directives for drinking water, the WHO does not propose any new guideline value for this substance.

Table 6.5 : Reference values proposed by different organisations

Value from directive 98/83/CE Annex IB	WHO guideline value 1994	Health Canada (1986)	US EPA (1992)
10 µg/L	10 µg/L	10 µg/L	50 µg/L

Table 6.6 : Details on the construction of reference values in water

Organisation	Dose identified	Date of study	Toxicological value	FI	Reference value	Proportion of drinking water	Body weight	Water consumption	Value obtained
WHO 1994	NOAEL	1991	0.24 mg/d	1	4 μg/kg bw/d	10%	60 kg	2 L	12 μg/L*
Health Canada 1986	US Food and Nutrition Board (1980)				0.05 to 0.2 mg/d	10 to 25%	60 kg	2 L	10 μg/L

* rounded up to 10 µg/L

7 – Comparison of daily intakes with the reference value

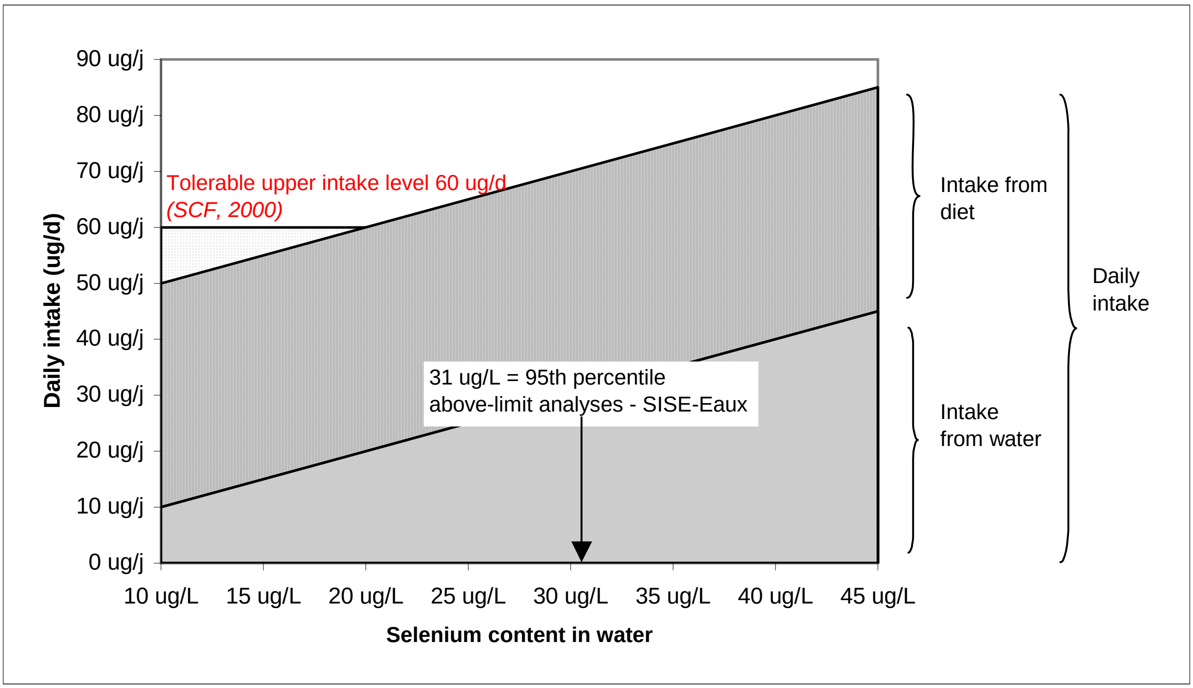
Different bodies propose specific recommendations for children, which set limits of safety for each age band. Although the studies available on the specific susceptibility in children are limited in number, an evaluation was conducted taking account of these different age bands.

Children under 4 years old

The sum of intake from solid foods and intake from drinking water with increasing concentrations of selenium is shown in graph 6.1.
The following assumptions were made :

- from the studies available in the literature, selenium intake from the diet in children under 4 years old is estimated to be less than 40 µg/d, based on the estimate by the Afssa nutritional consumption observatory *(Afssa, 2004).*
- intake from drinking water was calculated for children based on individual water consumption of 1 L/day which is equivalent to the highest water consumption.

Estimated daily intakes are compared to the tolerable upper intake level of 60 µg/d proposed by the Scientific Committee on Food for children under 4 years old.



Graph 6.1: Selenium intake from water and food for increasing concentrations in drinking water – children under 4 years old drinking 1 L of water/day.

It appears that for a selenium concentration of 20 µg/L in drinking water, total intake from water and solid food is equivalent to the tolerable upper intake level of 60 µg/d proposed by the Scientific Committee on Food for children under 4 years old.

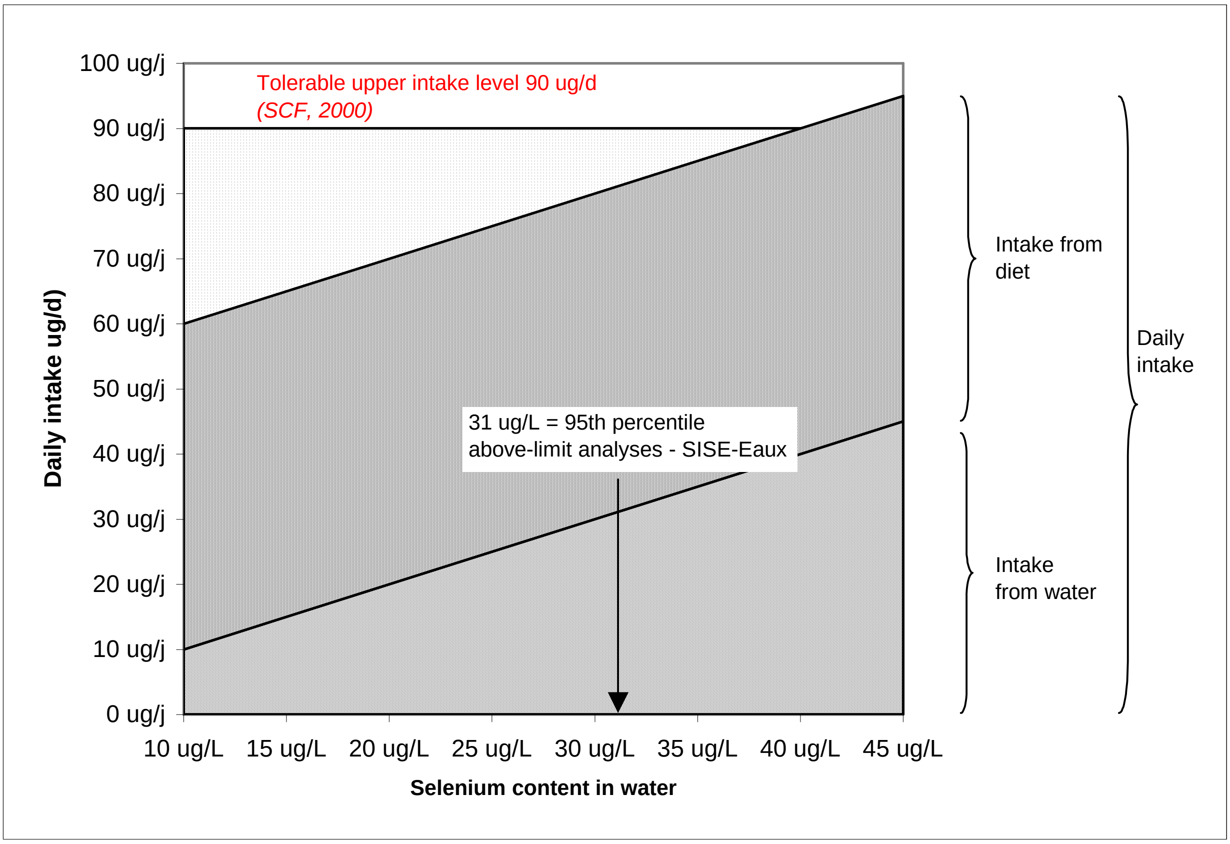
Children between 4 and 7 years old

The sum of intake from solid foods and intake from drinking water with increasing concentrations of selenium is shown in graph 6.2.
The following assumptions were made :

- from studies available in the literature selenium intake from the diet in children under 15 years old is estimated to be less than 50 µg/d, based on the French study (Leblanc *et al.*, 2003).
- intake from drinking water was calculated for children based on individual water consumption of 1 L/day which is equivalent to the highest water consumption.

Estimated daily intakes are compared to the tolerable upper intake level of 60 µg/d proposed by the Scientific Committee on Food for children between 4 and 7 years old.

It appears that for a selenium concentration of 40 µg/L in drinking water, total intake from water and solid food is equivalent to the tolerable upper intake level of 90 µg/d proposed by the Scientific Committee on Food for children between 4 and 7 years old.



Graph 6.2: Selenium intake from water and food for increasing concentrations in drinking water – children between 4 to 7 years old drinking 1 L of water/day.

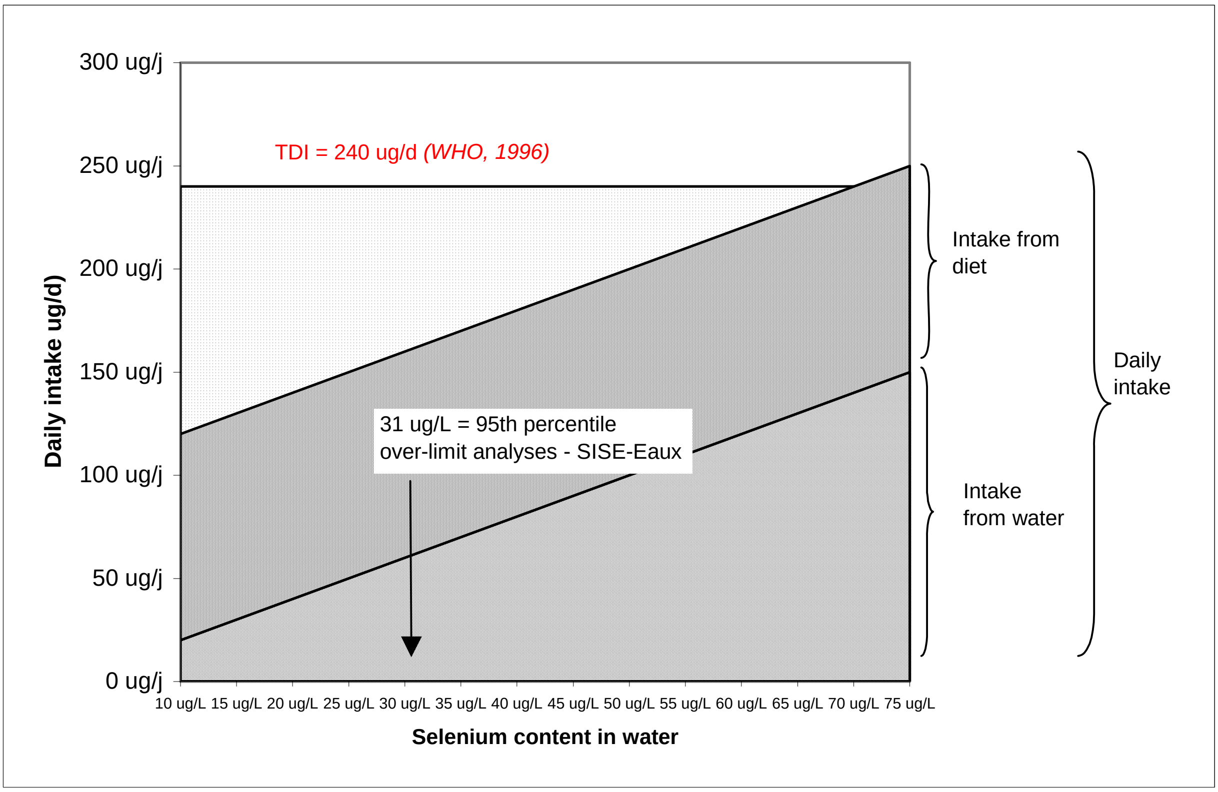
Children over 7 years old and adults

The following assumptions were made :

- from studies available in the literature selenium intake from the diet in children over 7 years old is estimated to be less than 50 µg/d and is estimated to be less than 100 µg/d for adults.
- intake from drinking water was calculated for children based on individual water consumption of 1 L/day for children over 7 years old and 2 L/day for adults which is equivalent to the highest water consumption.

For adults, the estimated daily intakes were compared to the tolerable daily intake of 240 µg/d, determined from the NOAEL proposed by the WHO and an estimated body weight of 60 kg. The sum of intake from solid foods and intake from drinking water with increasing concentrations of selenium is shown in graph 6.3.

For children over 7 years old, the limit of safety of 130 µg/d proposed by the Scientific Committee on Food was used.



Graph 6.3 : Selenium intake from water and food for increasing concentrations in drinking water –adult drinking 2 L of water/day.

It appears that for the age band from 7 to 15 years old and for adults, who drink water which has a selenium content of 40 µg/L, the total intake in water and solid food is below the tolerable upper intake level of 130 µg/d proposed by the Scientific Committee on Food for children between 7 and 15 years old and less, for adults, than the Tolerable daily intake (TDI) adopted by the WHO (these values are obtained for selenium concentrations of 80 and 70 µg/L, respectively without supplementation).

In addition, at a concentration of 40 µg/L, total intake in water and solid foods are close to the limit of safety of 150 µg/d proposed previously by the CSHPF.

8 - Opinion

After consulting the “Waters” specialist expert committee on 4th Mai and 7th September 2004, the French Food Safety Agency (Afssa) publishes the following opinion:

Considering the quality limit set at 10 micrograms per litre for selenium in annex 13-1-I-B. of the Code of Public Health legislation ;

Considering that:

- selenium may be present naturally in water sources and may also be linked to human activities on the catchment area;
- the SISE-Eaux database (Ministry responsible for health) has found that 95% of above-limit analyses that are recorded are below 35 micrograms per litre;
- selenium is a non genotoxic substance with a threshold toxic effect;
- the reference toxicological value of 4 micrograms per kilogram body weight per day proposed as the tolerable daily intake by the WHO i.e. estimated to be the most suitable in conducting this evaluation in adults;
- the tolerable upper intake levels [1] proposed by the European Union Scientific Committee on Food for children are estimated to be the most suitable when conducting this evaluation in children;
- selenium is an essential element and recommended selenium intake varies from 15 micrograms per day for infants to 80 micrograms per day for adults;
- the diet (solid food and drinking water) is the major source of exposure to selenium outside of a specific occupational context;
- results of most of the European surveys available in the literature estimate the daily selenium intake in the diet to be less than 100 micrograms in adults;
- the results of a French study estimate that daily selenium intake from the solid food:
  - o close to 40 micrograms per day for children between 0 and 2.5 years old who are high consumers (97.5th percentile),
  - o close to 50 micrograms per day for children between 3 and 15 years old who are high consumers (97.5th percentile) ;
- treatment procedures approved by the Ministry responsible for health can be used to reduce selenium content of waters;

Afssa :

1 – Reiterates that measures should be used to reduce selenium concentration to the quality limit level as soon as possible,

2 – Notes:

- that ingestion of water containing 20 micrograms of selenium per litre, exposes a child under 4 years old to a dose equivalent to the tolerable upper intake level, proposed by the SCF of 60 micrograms per day taking account of dietary intake,
- that ingestion of water containing 40 micrograms of selenium per litre, exposes:
  - ➢ children between 4 and 7 years old to a dose equivalent to the tolerable upper intake level' proposed by the SCF of 90 micrograms per day taking account of dietary intake,
  - ➢ children over 7 years old and adults to a dose below the tolerable upper intake levels proposed by the SCF or the tolerable daily intake proposed by the WHO, taking account of dietary intake,

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[1] the term tolerable upper intake level represents the daily dose of a substance which when ingested daily does not cause adverse consequences to health in the age band concerned.

- the 95th percentile of values above the quality limit recorded in the SISE-Eaux database is close to 35 micrograms per litre,

3 – States :

- that in a context of informing populations, reference must be made to the fact that taking a nutritional supplement containing selenium should be reviewed if the quality limit is exceeded,
- that no doubt is cast on the quality limit which flows from the risk assessment conducted by World Health Organisation.

File 7: Assessment of health risks related to exceeding the quality limit for vinyl chloride in water intended to for human consumption.

Vinyl chloride is highly volatile and is soluble in water (1.1 g/L at 25°C or 0.11 % by weight at 25°C, *INRS, 2000*).

1 – Origin and sources of contamination

Resource : the presence of vinyl chloride in water is principally due to industrial waste. The major sources of waste are gaseous and liquid emissions from production units for materials made of polyvinyl chloride (PVC).

Vinyl chloride may also be formed from trichloroethylene and tetrachloroethylene, which may be present in groundwater or from percolation of rain water passing through technical waste processing plant.

Water distribution networks : vinyl chloride may leach from PVC pipes and for this reason PVC in contact with water must have proof of health conformity by the modified rule dated 29 May 1997,[1].

2 – Treatment reducing vinyl chloride content in water

In accordance with article R.* 1321-48 of the Code of Public Health legislation, the use of products and treatment procedures depends on the approval from the Ministry of health. The lists of products and procedures presently approved are detailed in the circular of 28 March 2000[2].

The following treatments were identified in order to reduce vinyl chloride content although it should be assured on a case by case basis that the treatments proposed are approved.

Selective adsorption : activated carbon adsorption is delicate and difficult,
Leaching may occur after few weeks (3 to 6 weeks) of use of granular activated carbon

Doses of powdered activated carbon to be added are proportional to the amount of vinyl chloride to be removed; in some cases it may be as high as 100 mg/L.

Stripping: As vinyl chloride has a high vapour pressure, stripping allows its decrease in water. Air water ratio must however be, in many cases 10 or more. These high air flow rates may induce calcium carbonate precipitations by removing CO_2.

For high contamination levels, stripping and adsorption on granular activated carbon must be performed complementarily.

Free radical oxidation: vinyl chloride may be destroyed by advanced oxidation processes[3] :

- ozone + hydrogen peroxide,
- ozone + U.V,
- hydrogen peroxide + U.V.

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[1] Rule dated 29 May 1997 relating to materials and objects used in fixed production treatment or distribution installations for water intended to human consumption

[2] DGS/VS 4 circular no. 2000-166 dated 28 March relating to substances for treatment procedures for water destined for human consumption, NOR: *MESP0030113C*

[3] As stated in the circular above, free radical oxidation is reserved for “the treatment of volatile, chlorinated solvents in groundwater which does not contain other pollutants: pesticides etc.".

3 – Analytical methods

The rule of 17 September, 2003[1] on analytical methods for water samples and their characteristics and performances states that these should be *"controlled as a function of the specified quality criteria for the product".*

Vinyl chloride in water may be assayed by the "purge and trap" or "headspace" technique with gas phase chromatography followed by specific (electron capture) detection or by mass spectrometry. Only the "purge and trap" technique allows reaching a limit of detection of less than 20% of the quality limit for vinyl chloride in water. The limit of quantification with the "headspace" method is 5 µg/L.

4 – Exposure

4.1 Intake from air

The concentration in ambient air is usually between 0 and 24 µg/m^3 *(WHO, 1999, 2004)*, although is generally less than 3 µg/m^3. Concentrations measured close to industrial sites or technical waste processing centres may be far higher *(WHO 1999).*

According to ATSDR[2] *(Draft, 2004)*, the mean daily intake in air is between 0 and 2.1 µg/d. Air is the major route of exposure ranging from 2 to 60 µg/d and rising to 400 µg/d close to industrial installations *(WHO 2004).*

4.2 Intake from food

Vinyl chloride can be detected in foods after contact with materials containing vinyl chloride. Current regulations limit the vinyl chloride content in materials in contact with foodstuff[3].

The daily intake of vinyl chloride in the diet is estimated by ECETOC[4] to be between 0.02 and 0.025 µg *(ECETOC in WHO, 2004)*. According to Health Canada *(1992)* daily vinyl chloride intake through food and drink consumption is believed to be 0.1 µg/day. According to ATSDR *(Draft, 2004)*, average daily intake from water and food in the general population is close to 0 µg/day. Exposure to vinyl chloride *via* foodstuff packagings has been assessed by different national agencies, and United Kingdom and United States data show that mean intake estimated at the end of the 1970s and beginning of the 1980s was less than 0.0004 µg/kg b.w./d (*WHO, 1999*).

4.3 Intake from water

Vinyl chloride is a highly volatile; water soluble compound is rarely detected in surface waters although may be found in water close to sites contaminated by chlorinated hydrocarbons *(WHO, 2004)*.

A study of data available from the SISE-EAUX database (Ministry for Health, DDASS, DRASS – SISE-Eaux) shows that of the 640 analyses recorded between January 1999 and April 2004, most of the results were below the limit of detection. Only three analyses were above this limit but were still below 1 µg/L.

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[1] Rule dated 17 September 2003 relating to the analytical methods for water samples and their performance characteristics, NOR : SANP0323688A, JORF of 7 November 2003, p. 19027 to 19033

[2] Agency for toxic substances and disease registry

[3] Vinyl chloride appears on the list of substances which may be used for the manufacture of materials which come into contact with foodstuffs proposed in directive 2002/72/EC, modified. The instrument of 12 February 1984 on materials and objects containing monomer vinyl chloride (destined to come into contact with food and drink products) set the maximum residual amount of MVC at 1 mg/kg of material and states that the materials in contact with foodstuff or drink products must not leave detectable vinyl chloride in them which is detectable by the method laid down in the rule of 30 January 1984 relating to official analytical methods for the determination of MVC in materials in contact with foods. A European regulation relating to materials and objects in contact with foods is currently in draft form.

[4] European Centre for Ecotoxicology and Toxicology for Chemicals

However, the regulatory programme for health control defined by the Code of Public Health legislation does not require periodic analysis of this parameter (systematically)[1].

4.4 Contribution from exposure sources

The major route of exposure to vinyl chloride is by inhalation : 30-40% of the dose inhaled is absorbed. Oral intake is a minor source, but in this case absorption is close to 100%.

5 – Effects on health[2]

Genotoxicity, mutagenicity and oncogenicity

In vitro, vinyl chloride can induce different types of genotoxic effects : sister chromatids exchange in human lymphocytes, mutations in Chinese hamster ovary cells, unscheduled DNA synthesis in rat hepatocytes and cellular transformation in the BAB/c mice 3T3 cells. Mutations are also described in drosophila and in yeasts. *In vivo*, the compound causes chromosomal aberrations, sister chromatids exchange and micronucleus formation in the rat.

Genetic mutations have been observed in H-ras and p53 genes in hepatic tumours induced by vinyl chloride in the rat. *(IARC, 1987 ;IRIS US-EPA, 2000 ;)*

This compound has been shown to be oncogenic in the animal, mostly on the liver. Hepatic angiosarcomas and hepatocellular carcinomas have been described in several animal species following exposure to vinyl chloride. Other tumours can also be observed depending on species (nephroblastoma in rats, pulmonary and breast tumours in mice and pre-stomach papilloma in hamsters) (*Ferron et al., 1981; Til et al., 1983, 1991)*

Mutagenic and clastogenic properties are also demonstrated in human beings : chromosomal aberrations, sister chromatids exchange and micronucleus formation have been observed in the lymphocytes of workers exposed to high concentrations of vinyl chloride. The genomic mutations observed in animals are also present in human beings. Epidemiological studies show a strong causal relationship between the exposure to vinyl chloride and the development of hepatic angiosarcomas. These findings justify the classification of the compound in the group of “definite carcinogens to human beings” by both the International Agency for Research on Cancer (IARC) (class 1) and by the US EPA (class A).

Brain tumours and hepatocellular carcinomas have also been linked to vinyl chloride exposure in human beings. Cancers of the lung, lymphoid organs and skin appear to be less specifically related to the compound. *(IRIS US-EPA, 2000 ; IARC, 1987)*

Organisation	Proposed classification	
European Union	Category 1	Carcinogenic to human
CIRC – IARC	Group 1 (1987)	Carcinogenic to human.
US EPA	Group A (1993)	Carcinogenic to human
Health Canada	Group I	Carcinogenic to human

6 – Reference values[3]

6.1 Toxicological reference values for ingestion

Toxicological reference values (TRV) are proposed by different bodies. These values are summarised in table 7.1 and have been obtained from studies listed below.

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[1] Materials which come into contact with waters destined for human consumption are subject to a ACS (Attestation of Conformity). Vinyl chloride contents are regulated in order to limit migration of the substance into water.

[2] Acute and chronic non-carcinogenic effects are not discussed in this part although the reader is referred to the bibliography references for further information.

[3] Only the TRV for chronic exposure are summarised in this part.

Table 7.4 : Summary of TRV proposed for chronic oral exposure.

Source	TRV	Value		Study	Effect
ATSDR Draft for public comment (2004)	MRL (minimal risk level)	3 µg/ kg b.w./d		Til et *al.*, 1983, 1991	Hepatic damage
US EPA (2000)	RfD (reference dose)	3 µg/ kg b.w./d		Til et *al.*, 1983, 1991	Hepatic damage
US EPA (2000)	Oral Slope Factor *adult*	7.2.10^{-4} (µg/kg/d)$^{-1*}$	7.5.10^{-4} (µg/kg/d)$^{-1**}$	Feron et *al.*, 1981	Hepatic angiosarcoma
WHO (2004)	Guideline value	0.3 µg/L for an excess risk of 10^{-5}		Feron et *al.*, 1981	Hepatic angiosarcoma

**Multi-stage linearised model **Alternative model (EPA 1996)*

Threshold toxic effects :

- ATSDR *(Draft, 2004)* proposes a MRL of 3 µg/kg b.w./d, based on the observation of a NOAEL (No Observed Adverse Effect Level) of 170 µg/kg b.w./d which takes into account the incidence of hepatic nodules in the rat *(Til et al., 1983, 1991).* A pharmacokinetic model (PBPK) proposed by the US-EPA to determine the RfD, defines a dose equivalent for human beings of 90 µg/kg b.w./d. An uncertainty factor of 30 is applied (3 for extrapolation from animals to human beings and 10 to take account of intra-species variability).
- The US-EPA proposes an RfD based on the study by Til et *al.* (*1991*) conducted in the rat (for 149 weeks) during which vinyl chloride (PVC powder) was administered orally. The estimated NOAEL was 130 µg/kg b.w./d taking account of abnormalities of liver cells. An uncertainty factor of 30 was applied (3 for extrapolation from animals to human beings and 10 to take account of intra-species variability). Inter-species dose adjustments were made using a PBPK model (*Clewell et al., 1995*).

Non threshold Toxic effects :

- The TRV (Oral Slope Factor) proposed by the US-EPA is based on the results of a study by Feron et *al.* (*1981*) on Wistar rats, which showed mostly the development of hepatic angiosarcomas, hepatocellular carcinomas and neoplastic nodules following whole life exposure (149 weeks) to vinyl chloride. The extrapolation to low doses was performed after inter-species dose adjustment using a PBKP model, firstly with a linearised multi-stage model and secondly from an alternative model. The two calculation methods produced similar results. Taking the susceptibility of young animals into account, the US-EPA differentiates an excess risk of cancer for continuous lifetime exposure during adulthood from excess risk of cancer for continuous lifetime exposure from birth by applying a safety factor of 2. Two TRVs are therefore proposed *(IRIS, 2000)*.

- In 1994 the WHO applied a linearised multi-stage model to the results obtained in the rat by Til et *al., in order* to establish the dose in human beings which induce an additional risk of hepatic angiosarcoma. In the revision of the guidelines for drinking water quality in 2004, the WHO proposes a new guideline value based on the results of the study by Feron et *al.*, using the PBPK model to calculate the dose equivalent for human beings and linear extrapolation to low doses from the LED$_{10}$[1]. The WHO takes into account the specific susceptibility of children, considering that exposure from birth doubles the risk, leading to a guideline value of 0.3 µg/L associated with the upper-bound excess risk of liver tumours of 1x10^{-5} (*WHO, 2004*).

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[1] The LED$_{10}$ is the lower 95% confidence interval value of the estimated dose causing a 10% response in the exposed population.

6.2 Toxicological Reference values from inhalation

Table 7.5 : Summary of proposed TRV for chronic respiratory exposure.

Source	TRV	Value		Study	Effect
ATSDR (1997, 2004)	MRL minimal risk level	Insufficient data			
US EPA (2000)	RfC reference concentration	0.1 mg/m^3 (0.038 ppm)		Til et *al*., 1983, 1991	Liver damage
US EPA (2000)	Inhalation Slope Factor *adult*	4,4.10^{-6} (µg/m^3)$^{-1*}$	4,4.10^{-6} (µg/m^3)$^{-1**}$	Maltoni et *al.* 1981, 1984	Hepatocellular tumours
WHO (2000)	Guideline value for air quality	1 µg/m^3		Epidemiological studies in WHO, 2000	Hepatic angiosarcomas

**Linearised multi-stage model **Alternative model (EPA 1996)*

Toxic effects at threshold:

The US-EPA proposes an RfC based on data obtained for chronic oral exposure in the rat *(Til et al., 1991)*. The NOAEL of 130 µg/kg b.w./d was converted into a no effect value of equivalent concentration in human beings, an NOAEL (HEC) (Human Equivalent Concentration), of 2.5 mg/m^3. An uncertainty value of 30 was applied (3 for extrapolation from animals to human beings and 10 for intra-species variability) following intra-species adjustments of doses using a PBPK model (*Clewell et al., 1995*).

Toxic effects without thresholds:

- The TRV (Inhalation Slope Factor) proposed by the US-EPA is based on the results of the study by Maltoni et *al.* (1981, 1984), which estimated the incidence of hepatocellular tumours (angiosarcomas, hepatocellular carcinomas, hemangiomas and neoplastic nodules) in female rats exposed to inhalation of vinyl chloride for 52 weeks. The extrapolation to low doses was performed after inter-species dose adjustment using a PBPK model firstly from a linearised multi-stage model and secondly from an alternative model. Both calculation methods produced similar results. Taking account of the susceptibility of young animals, the US-EPA differentiates an excess risk of cancer for continuous lifetime exposure during adulthood from excess risk of cancer for continuous lifetime exposure from birth by applying a safety factor of 2. Two TRV are therefore proposed *(IRIS, 2000)*.
- In 2000 the WHO proposed associating whole life exposure to a concentration of 1 µg/m^3 to an excess risk of hepatic angiosarcomas of 1x10^{-6} from epidemiological studies conducted in occupationally exposed people (*WHO, 2000*).

6.3 Reference values for drinking water

Since January 2004, the quality limit for vinyl chloride is 0.5 µg/L.
Several recommendations and limits are found in the literature and are presented in table 7.3.

Table 7.3 : Reference values proposed by different organisations

Directive 98/83/CE Annex IB value	WHO guide value 1994	WHO guide value 2004	Health Canada (1997 revision 2001)	US EPA (revision 2002)
0.5 µg/L	5 µg/L[1]	0.3 µg/L[1]	2 µg/L	MCLG[2] = 0 µg/L MCL[3] = 2 µg/L

[1] concentration associated with an additional risk of hepatic angiosarcomas close to 10^{-5}

[2] Maximum Contaminant Level Goal

[3] Maximum Contaminant Level

7 - Evaluation of level of risk due to exceeding the quality limit

7.1 Estimation of risk from ingestion of drinking water

Based on the Oral slope factor of 7.2 x 10^{-4} (µg/kg b.w./d), proposed by the US-EPA for hepatic angiosarcomas and on the approach proposed in 2003 by the US-EPA *(US-EPA, 2003)* which take into account the susceptibility of newborn infants and children:

- the level of individual risk from consumption of drinking water with a vinyl chloride concentration of 0.5 µg/L, is believed to be approximately 4.4 x 10^{-5} for whole life exposure,
- table 7.4 shows estimates of excess individual risk from exposure to a concentration above the quality limit over a period of 1 to 9 years followed by exposure to a concentration at/equal to the quality limit for the remainder of the subject's life.

Table 7.4: Estimation of excess individual risk from drinking water depending on the level and time for which the quality limit for vinyl chloride is exceeded[1]

Concentration	Time				
	1 year	*2 years*	*3 years*	*6 years*	*9 years*
0.75 µg/L	4.7×10^{-5}	5.1×10^{-5}	5.2×10^{-5}	5.4×10^{-5}	5.7×10^{-5}
1 µg/L	5.1×10^{-5}	5.9×10^{-5}	6.0×10^{-5}	6.5×10^{-5}	7×10^{-5}
1.5 µg/L	5.9×10^{-5}	7.4×10^{-5}	7.7×10^{-5}	8.7×10^{-5}	9.6×10^{-5}
2 µg/L	6.7×10^{-5}	9×10^{-5}	9.4×10^{-5}	1.1×10^{-4}	1.2×10^{-4}

7.2 Estimation of level of risk from inhalation from showering

Because of the volatile nature of vinyl chloride, some exposure to the compound may come from showering. The oral slope factor from inhalation proposed by the US-EPA is 4.4 x 10^{-6} $(\mu g/m^3)^{-1}$ for entire life exposure *(IRIS, 2000).*

Details of the estimate of risk level from vinyl chloride inhalation when showering are shown in the annex.

At a vinyl chloride concentration of 0.5 µg/L and a daily shower time of 10 minutes, the whole life excess risk of cancer due to inhalation would be in the range of 1×10^{-6}. This is an upper estimate based on the assumption that all of the vinyl chloride initially present in the water is volatilised during the shower and that the shower cubicle air is not renewed.

In adults, therefore, and based on conservative hypotheses, the excess risk of cancer from inhalation of vinyl chloride from showering is less than 10% of the excess risk of cancer from drinking water.

The risk from skin contact with vinyl chloride in water is considered to be minor compared to the risk by inhalation when showering. The calculation assumes that all of the vinyl chloride passes into the shower cubicle air.

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[1] These figures represent an upper range taking account of the possible susceptibility of newborn and children

8 - Opinion

After consulting the “Waters” specialist expert committee on 7 December 2004, Afssa publishes the following opinion :

Considering the quality limit in annex 13-1 I. B. of the Code of Public Health legislation of 0.5 micrograms of vinyl chloride per litre;

Considering in particular:

- that vinyl chloride is a substance which does not have a toxic effect threshold;
- that the International Agency for Research on Cancer (IARC) has classified vinyl chloride into group 1 based on sufficient evidence about carcinogenicity, with an increased risk of hepatic angiosarcomas;
- that the whole life excess risk of cancer due to drinking water containing a vinyl chloride concentration equal to the quality limit of 0.5 micrograms per litre is in the range of 4.4×10^{-5}, based on the excess unit risk for oral intake proposed by the US-EPA and taking into account the specific susceptibility of children;
- that in the context of the third version of the guidelines for drinking water quality the World Health Organization considers that drinking water with a vinyl chloride content of 0.3 micrograms per litre carries an excess risk of hepatic angiosarcomas of 1×10^{-5};
- that using conservative hypotheses, in adults, the excess cancer from inhalation and skin contact with vinyl chloride during showering is relatively insignificant compared to the risk from ingestion (< 10%);
- *that the treatments approved by the Minister responsible for health can significantly reduce vinyl chloride content in water and that these can be rapidly implemented,*

The French Food Safety Agency :

Reiterates that the means required to bring vinyl chloride concentration to the lowest level must be implemented as soon as possible

Considers it is the responsibility of the health authorities to examine situations when the limit is exceeded for short periods of time according to the level of risk. An upper estimate taking account of specific susceptibility of children is shown in the table below:

Concentration	Time				
	1 year	*2 years*	*3 years*	*6 years*	*9 years*
0.75 µg/L	4.7×10^{-5}	5.1×10^{-5}	5.2×10^{-5}	5.4×10^{-5}	5.7×10^{-5}
1 µg/L	5.1×10^{-5}	5.9×10^{-5}	6.0×10^{-5}	6.5×10^{-5}	7×10^{-5}
1.5 µg/L	5.9×10^{-5}	7.4×10^{-5}	7.7×10^{-5}	8.7×10^{-5}	9.6×10^{-5}
2 µg/L	6.7×10^{-5}	9×10^{-5}	9.4×10^{-5}	1.1×10^{-4}	1.2×10^{-4}

Annex – File 7 : Risk assessment associated with inhalation from showering

In order to assess the risk associated with inhalation of vinyl chloride when showering we must first assess the level of exposure by estimating the concentration reached in air during a shower and the daily exposure frequency.

A - Estimation of mean concentration inhaled per day:

The mean inhaled concentration per day may be expressed as the following equation:

$$C°_{\text{mean inhaled}} = [C°_{\text{shower inhaled}} \times t_{\text{shower}}] \times F$$

Where:

- $C°_{\text{shower inhaled}}$: the mean concentration of vinyl chloride in the inhaled air during the shower;
- t_{shower}: exposure time fraction to the concentration $C°_{\text{shower inhaled}}$ during a day, equal to the time exposed to the concentration divided by the length of the day.
- F : exposure frequency, equal to the number of days of exposure as a proportion of the total number of days in a year.

<u>Estimate of concentration of vinyl chloride in the shower cabin :</u> $C°_{\text{shower inhaled}}$

As a first approach we can examine the situation in which all of the vinyl chloride initially present in the water passes into the air and the shower cubicle air is not renewed.

The mean concentration in air is estimated from the mean value between the concentration at the start of the shower, (i.e. 0 µg/L) and the concentration at the end of the shower which is equal to $(C°_{\text{water}} * Q_{\text{water}}) / V$)

The mean concentration in air is therefore estimated by:

$C°_{\text{shower inhaled}} = [(C°_{\text{water}} * Q_{\text{water}}) / V)] / 2$

Where

$C°_{\text{water}}$: concentration of the pollutant in the water,

Note : as a first approach the concentration used is the quality limit in water;

Q_{water} : quantity of water used in the shower,

Note: based on the US-EPA recommendations in the "Exposure Factor Handbook" (*US-EPA, 1997*), the median amount of water (based on 11 studies) used when taking a shower or bath is close to 65 L[1] ;

V : the volume of shower cubicle which is estimated to be 2 m^3.

<u>Estimate of the exposure time fraction :</u> t_{shower}

Based on the US-EPA recommendations in the "Exposure Factor Handbook" (*US-EPA, 1997*), the length of the shower is estimated to be 10 minutes.

The exposure time fraction is therefore :

$t_{\text{shower}} = 10 / (24 \times 60) = 0.00694$

<u>Estimation of exposure frequency : F</u>

The frequency is estimated to be 1 shower per day, 365 days per year.

B – Estimate of excess risk of cancer:

The whole life risk due to exposure to a carcinogenic substance by inhalation is expressed as an excess individual risk, calculated as follows :

$EIR = C°_{\text{mean inhaled}} \times EUR$

Where:

For vinyl chloride, EUR (excess unit risk) by inhalation proposed by US-EPA is 4.4×10^{-6} $(\mu g/m^3)^{-1}$ for whole life exposure *(IRIS, 2000).*

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[1] In the European Environmental Agency document (EEA, 2001), the estimated water consumption for body hygiene purposes is less than 57 L/person/day for 4 European countries.

C – Comparison of the estimate of excess risk of cancer from inhalation from showering with the estimate of excess risk of cancer from drinking water.

For a vinyl concentration of 0.5 µg/L, and a daily shower time of 10 minutes, the whole life excess risk of cancer due to inhalation would be less than 10^{-6}. The excess cancer risk associated with inhalation of vinyl chloride when taking a shower represents less than 10% of the excess risk of cancer associated with drinking water.

This is an upper estimate which assumes that all of the vinyl chloride present initially in the water is volatilised during the shower and that the air in the shower cubicle is not renewed.

File 8: Assessment of health risk related to exceeding the quality limit for aluminium in water for human consumption

1 – Origin and sources of contamination

Resource

Aluminium is mainly of geological origin (mainly natural alteration of rocks and run-off from soils) and may be found in water in three forms: insoluble, colloidal and soluble, corresponding mainly to silico-aluminates, hydroxides, soluble free forms and mineral or organic complexes (measured indirectly in water by turbidity).

Drinking water production
Aluminium salts (mainly aluminium sulphate and pre-polymerised aluminium salts) are used in water treatment processes as chemical reagents in the coagulation stage.

2 – Treatment reducing aluminium content in water

According to the article R.* 1321-48 of the French Code of Public Health Legislation, the use of products and procedures depends on the Minister of health. The lists of products and procedures currently approved are detailed in the circular of 28th March 2000[1].The following treatments *were identified in order to* reduce aluminium content although one must ensure that the treatments proposed are approved on a case by case basis:

Clarification steps:

- coagulation – flocculation – separation – filtration,
- Biological filtration or slow sand filtration.

The turbidity of the filtered water must be ≤ 0.5 NFU.

Aluminium trihydroxides are amphoteric, i.e. the pH of the water during decantation or flotation is a parameter which determines the equilibrium between the ionised forms (cationic or anionic) and the hydroxide. Outside the pH range of 6.0 to 7.2 the ionised fractions result in exceeding the quality limit of 200 µg/L and this exceeding increases as divergence from this pH range increases.

Under its micro-floc[2] form, aluminium can also cross filters. The optimisation of the coagulation and the addition of coagulation adjuvant (cationic and anionic poly-electrolytes) contribute to the reduction of this micro-floc.

Thus leaks of aluminium into water treated with a salt of this metal may arise from a default in treatment plant design or, more frequently from poor treatment conditions. In general, the level of aluminium in filtered water is always higher during the maturation phase of the filter (the first 20 minutes following reset).

3 - Analytical methods

The rule of 17 September 2003[3] concerning analytical methods for water samples and their performance characteristics specifies that, in the case of total aluminium, the accuracy reproducibility and detection limit must not exceed 10 % of the reference value (i.e. 20 µg/L) and that the quantification limit must not be greater than 30 µg/L.
It is further specified that the analysis must be carried out on a non-filtered sample acidified to pH ≤ 2.

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[1] DGS/VS 4 circular no. 2000-166 dated 28 March relating to substances for treatment procedures for water destined for human consumption, NOR: *MESP0030113C*

[2] Interaction of fine particles with each other and/or larger elements to constitute larger particles.

[3] Ministerial order dated 17 September 2003 concerning the methods of analysis of water samples and their performance characteristics, NOR : SANP0323688A, JORF dated 7 November 2003, p. 19027 to 19033

Several normalised methods are proposed for measuring the level of total aluminium in water:

- NF EN ISO 12020:2000 – Water Quality – Measurement of Aluminium – Atomic Absorption Spectrometry Method (SAAF and SAAET).
- ISO 10566:1994 - Water Quality – Measurement of Aluminium – Pyrocatechol violet spectrometry method.
- NF EN ISO 11885:1998 – Water Quality – Measurement of 33 elements by inductively coupled plasma/atomic emission spectroscopy (ICP-AES).
- PR NF EN ISO 15586:2001 (In preparation) - Water Quality – Measurement of trace elements by graphite furnace atomic absorption spectrometry.
- FD T90-119 (Fascicle) - Water Quality – Measurement of mineral elements (Al, Sb, Ag, As, Ti, V, etc.) (AAS).
- ISO 17294-2:2003 – Water Quality - Application of Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) – Measurement of 62 elements.

Analytical uncertainty

The uncertainty of measurements may be estimated from inter-laboratory studies by determining the coefficient of variation (CVR%).

Table 8.: Variation in uncertainty for different ranges of concentration of aluminium in water from the CVR% estimated by the French Association of Environmental Analysis Laboratories (AGLAE[1]), based on inter-laboratory studies, all analytical methods included – Source: AGLAE, 2003

Concentration in water(µg/L)	50	100	150	200
CVR %	17.2%	15.5%	14.9%	14.7%
Estimation of the uncertainty* (µg/L)	± 17	± 31	± 45	± 59

**95 % Confidence interval for a quality-controlled measurement carried out by any given laboratory*

4 - Exposure

4.1 Public Water System

4.1.1 Pre-2004 data from the French Health-Environment Information System (SISE-Eaux[2]) database

The regulatory programme for health control defined in the Code of Public Health legislation requires, for plants producing more than 100 m^3/d, from 1 analysis every two years to 20 analyses per year, depending on water origin (surface water orgroundwater) and size of the water supply. For plants producing less than 100 m^3/d no control/analysis are required. Samples should be taken at either resource or distribution point

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[1] Association Générale des Laboratoires d'Analyses de l'Environnement

[2] Système d'Information en Santé-Environnement

Table 8.2 :Percentage of volumes of water distributed, according to levels of total aluminium and origins of production 1999 – 2001

Source: SISE-EAUX /Directorate General for Health (DGS)/ Regional Directorate for Health and Social Affairs (DRASS)/Departmental Directorate for Health and Social Affairs (DDASS)[1] – AFSSA

Total aluminium mg/L	Mean values				Maximum values			
	Groundwater		Surface Water		Groundwater		Surface water	
≤ 0.2		99.3 %		99.2 %		97.5 %		85.3 %
> 0.2 and ≤ 0.5	0.51 %	0.7 %	0.73 %	0.8 %	2.02 %	2.5 %	10.65 %	14.7 %
> 0.5 and ≤ 1	0.02 %		0.02 %		0.26 %		2.46 %	
> 1	0.14 %		0.02 %		0.22 %		1.56 %	

The study covers 25 % of water production plants (7 018 plants) which represent 85% of water distributed (78 % of underground supplies and 95 % of surface supplies). For approximately 99% of the volume produced the mean concentration complies with the value of 0.2 mg/L.

Furthermore, analysis of available data for a 4-year period (January 1999 to December 2002) shows that the 95th percentile of results from 2730 analyses[2] exceeding the quality reference level is 2.41 mg/L (the 50th percentile is 0.32 mg/L).

4.1.2 Data from a survey carried out in 2001

The French ministry of health performed a survey in order to assess the concentration of aluminium in water.

The distribution of the population according to maximum levels of aluminium recorded is shown in Table 8.3. The survey covers 630 plants using an aluminium-based treatment for which data are available. These plants supply a total population of 15 920 950 individuals throughout France

Tableau 8.3: Distribution of population supplied by treatment plants using an aluminium-based treatment in relation to the maximum aluminium levels recorded

Level of aluminium	≤ 0.2 (RQ)	between 0.2 and 0.5 mg/L	between 0.5 and 1 mg/L	between 1 and 2 mg/L	between 2 and 3 mg/L	> 3 mg/L	Total
Number of treatment plants	412 (65%)	133 (20.6%)	57 (8.8%)	18 (2.8%)	3 (0.5%)	7 (1.1%)	*630*
Population potentially affected	12 055 231 (75.7%)	3 060 558 (19.22%)	478 175 (3%)	291 752 (1.83%)	6 725 (0.04%)	28 509 (0.18%)	*15 920 950*

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[1] DGS, Directeur Général de la Santé; DRASS, Direction Régionale des Affaires Sanitaires et Sociales; DDASS, Direction Départementale des Affaires Sanitaires et Sociales

[2] Analyses carried out on samples taken from either production or distribution.

Thus, 3 865 719 individuals (nearly 25% of the population affected) are potentially exposed to levels of aluminium in water above the quality reference level and 5 % (approximately 805 000 individuals) are exposed to levels of aluminium in water which may exceed 0.5 mg/L.

These data are the maximum-recorded values from each plant : periods where the maximum permitted levels are exceeded may be of short duration.

More complete data are available in part 6 of the report (Afssa – Afssaps – Invs, 2003).

4.2 Aluminium in food

The presence of aluminium in food or in drinking water results from several sources, food additives, or migration from the container into the contents (packaging or cooking utensils).

Table 8.4 presents estimated aluminium exposure to food drawn from scientific literature data.

Table 8.4: Summary of food-related aluminium exposure from different countries

Country	Type of study	Estimated intakes			Reference
		population	*Mean intake of aluminium (mg/d)*	*Maximum intake or higher percentile (mg/d)*	
France	Total diet study (including water)	Adults (> 15 years)	1.62	3.21 (97.5th percentile)	Leblanc *et al.*, 2004
		Children (3 to 14 years)	1.26	2.53 (97.5th percentile)	
France	Consumption × contamination	Adults (> 15 years)	2.8 8	5.57 (97.5th percentile)	(Afssa – Afssaps – Invs, 2003) from r Biego *et al.*, 1998
		Children (3 to 14 years)	1.8	4.07 (97.5th percentile)	
France	Duplicated meal – mass catering*		2.03	5.96 (97.5th percentile)	Noël and Guerin, 2003
France	Duplicated meal		2.8	5.7 (97.5th percentile)	Biego *et al.,* 1998
UK	Total diet study	(adults)	3.4	5.7 (97.5th percentile)	1997 UK Total Diet Study - Ysart *et al.*, 2000
UK	Total diet study	(general population) (adults)	11 12	29 (upper limit)	1994 UK Total Diet Study Ysart *et al.*, 1999
Italy	Total diet study		2.5 – 6.3		Gramiccioni *et al.*, 1996
USA	Total diet study		14.3		Iyengar *et al.*, 1987

* Assuming that food prepared by caterers has inevitably been in contact with aluminium (utensils, containers etc.)

Estimation of intake due to migration from packaging and utensils.

Migration depends on the quality of the material, the presence of a coating, the length of contact and the nature of the food. Analysis of bibliographical data allows estimating of the quantity of aluminium deriving from packaging. These intakes are summarised in table 8.5.

Table 8.5: Estimation of food-related intakes of aluminium for adult, including from packaging, (foodstuffs and drinks other than non-bottled water)– Source: Afssa – Afssaps – Invs, 2003

Source	Minimum	Maximum
Food intake, France (mg/d) (Leblanc *et al.*, 2004)	1.62	3.21
Intake from packaging and utensils (mg/d)*	4	12
Intake from drinks supplied in aluminium containers (mg/d)**	0.01	1.04
Total (mg/d)	5.63	16.25

* postulate: daily consumption of 1 kg of food packaged in aluminium or cooked with aluminium utensils

** postulate: daily consumption of 1 L of drinks in aluminium containers

It can however be assumed that the current estimation of exposure resulting from packaging is a considerably over-estimated since 'Duplicated meal' type studies such as those of Noël and Guérin (2002) which give an estimation of global exposure to aluminium (aluminium present in food and arising from containers and utensils) show that intake is of the order of 3 mg/d on average and close to 6 mg/d for high consumers. (Afssa – Afssaps – Invs, 2003)

4.3 Sources of exposure

In humans, the principal recognised route of exposure, apart from work-related exposure, is ingestion of food, which constitutes 95% of daily intake. In the case of an aluminium-based therapy using gastric plasters, this source of exposure becomes predominant in relation to food intake. Inhalation remains a minor route of exposure, except in work situations where workshop dust may contain high levels of aluminium.

The quantity of aluminium provided or attributable to the public water supply represents less than 10% of all intakes and the quantity provided by the air less than a 1% (estimation of airborne contribution at 0.02 mg/d in an urban environment).

However, daily aluminium intake via food remains lower than quantities used during a treatment with antacids (500 to 5000 mg/d). Moreover, a proportion of the exposure may be due to the use of cosmetic products, particularly antiperspirants (100 mg/d) (Afssa – Afssaps – Invs, 2003).

Conclusion: Global Exposure of the Population

In view of these results, daily food-related aluminium intake (food, utensils and packaging) can be estimated at close to 6 mg/d for high consumers adults without any particular working context and not taking into account any intake linked to medical treatment with aluminium-based antacids.

5 – Health effects linked to aluminium

Almost all the effects observed in humans are linked to chronic exposure. The first signs of toxicity linked to a chronic exposure to aluminium have appeared in the workplace and in patients suffering from renal failure and undergoing dialysis. Subsequently, investigations have been undertaken which covered the population in general and focused principally on the neurological risk.

Some effects, observed in people suffering work-related exposure and dialysed patients, are currently accepted as being linked to a chronic exposure to aluminium (encephalopathy, psychomotor disorders, osteomalacia and hypochromic anaemia). In other cases, and given the current state of knowledge, it appears that for certain, initially suspected, effects (Alzheimer’s disease being an example), a causal relationship cannot reasonably be accepted. *(Afssa – Afssaps – Invs, 2003)*

Further data on the toxicity of aluminium are available in the report “Assessment of health risk linked to the exposure of the french population to aluminium – water, food and health products – November 2003”[1].

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[1] "Évaluation des risques sanitaires liés à l'exposition de la population française à l'aluminium - Eaux, aliments, produits de santé - novembre 2003" *Afssa – Afssaps – Invs*

6 – Reference Values

6.1 Toxicological Reference Values

Table 8.6: Summary of studies used to establish TRVs for aluminium following oral ingestion

Source	Reference Value	Value	Study	Species	Critical Effect
WHO (1994)	PTWI Provisionally tolerable weekly intake	7 mg/ kg b.w./week		Dog	No effect
EPA (1991)	RfD reference dose	0.4 μg/kg b.w./d	Hackenburg et al.	Rat	No effect
ATSDR (1999)	MRL chronic maximum risk level	Not defined[1]	-	-	-
OEHHA	Public Health Goal (Reference value for water quality)	0.6 mg/L	Golub et al., 1993	Mouse	Altered cytokine production (rates)
			Greger and Braier, 1983 ; Bishop et al., 1997 in OEHHA, 2001	Adult Human Premature Infants	No effect Neurological effects

[1] The ATSDR did not wish to draw a chronic TRV from studies which had been used to determine sub-chronic TRV *(ATSDR, 1999).*

<u>WHO (World Health Organization)</u>:

In 1989 the WHO defined a Provisionally Tolerable Weekly Intake (PTWI) of 7 mg/kg body weight *(WHO, 1989)*, based on a study using dogs (aluminium and sodium hydrogen phosphate in food represent a dose equivalent to 110 mg/kg b.w.). In its monograph N° 194, published in 1997, the IPCS[1]-WHO indicates that evidence for a relationship between exposure to aluminium and health effects is insufficient to justify a revision of previous guideline values for the exposure of individuals in good health and not exposed in the workplace. This PTWI value corresponds to a tolerable intake of 420 mg per week for an adult of 60 kg. Which is equivalent to a tolerable daily intake (TDI) of 1 mg/kg of body weight or 60 mg/d for an adult.

<u>US-EPA - Environmental protection agency (1988)</u> : A chronic feeding study of aluminum phosphide was conducted by Hackenburg *et al.,* 1972. Male and female rats exposed over 2 years. A single experimental dose was used. No significant effect was observed and the dose administered during this study (0.043 mg/kg b.w./d of aluminium phosphide) was retained as a NOAEL. The use of an uncertainty factor of 100 led the US-EPA to establish an RfD of 0.4 μg/kg b.w./d.

The inter-agency working group on aluminium considers that *"numerous questions concerning the study selected reduce the relevance of this toxicological reference value:*

- *It was carried out using only a single administered dose. It is therefore not possible to state that a dose-effect relationship exists.*
- *This single dose is taken to be a NOAEL whereas no other data support this interpretation.*
- *The chemical form of aluminium used appears to be unrelated to those normally encountered in the environment.*
- *No information on bioavailability is presented, preventing any comparison or understanding of its importance.*
- *No kinetic data on animal exposure is available.*
- *No written report on the evaluation carried out within the American agency is available."*

<u>ATSDR - Agency for Toxic Substances and Disease Registry</u> : Golub *et al.* (1989) exposed adult mice over 6 weeks to aluminium lactate mixed with their food. The observed effect was a 20% decrease in spontaneous motor activity in the exposed group compared to the control group. A No Observable Effect Dose was determined at 62 mg/kg b.w./d and the use of an uncertainty factor of 30 led the ATSDR to establish an MRL of 2 mg/kg b.w./d.

The ATSDR did not wish to derive a chronic TRV from studies which had been used to determine a sub-chronic TRV *(ATSDR, 1999).*

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[1] IPCS: International Programme on Chemical Safety

OEHHA - Office of Environmental Health Hazard Assessment (2001) :

The studies selected by OEHHA to determine the reference value for drinking water are described in the Afssa-Afssaps-Invs document *(2003)*. The following weak points have been identified by the working group :

- *"The criteria for selection of the three studies serving as support for the final calculation are not detailed.*
- *The effects described in each of these studies are different, raising questions over the reason behind the concentration calculations and the final choice.*
- *The hypotheses underlying the numerical values assigned to certain variables, such as the relative contribution of the source or intestinal absorption, are not always clear.*

Finally, this lack of precision gives a mitigated impression, given that the 3 calculated concentrations are very close to each other. The mean of the three values is retained without any justification. There is an absence of complete transparency."

6.2 Reference Values for Drinking Water

The quality reference level for tap water is set at 200 µg/L by the Code of Public Health. This quality reference corresponds to an indicator of effective treatment.

This position reflects the recommendations of the World Health Organization set out in 1994, 1998 and 2004 in its directives on drinking water: the WHO specifies that, taking into account *"Owing to the uncertainty surrounding the human data and the limitations of the animal data as a model for humans, a health-based guideline value for aluminium cannot be derived at this time*". In 2004, taking into account, on the one hand the beneficial effects of the use of aluminium as a coagulant in water treatment, and on the other hand, considering the potential health concerns, the WHO derived a practical level based on the optimisation of the coagulation process in drinking-water plant using aluminium-based coagulant, to minimize aluminium levels in finished water *(WHO, 2004)*.

Several recommendations and reference values for water can be found in the literature and are presented in table 8.7.

Table 8.7: Reference values proposed by different organizations

Value from Directive 98/83/EC Annex IB	WHO (1994)	WHO (2004)	OEHHA (2001)	Health Canada (1998) *Operational Guidance Value*	US EPA (1988)
0.2 mg/L	0.1 or 0.2 mg/L depending on the size of the plant	0.1 or 0.2 mg/L depending on the size of the plant	0.6 mg/L[1]	0.1 or 0.2 mg/L depending on the type of plant[2]	0.05 to 0.2 mg/L[3]

[1] The OEHHA proposes a Public Health Goal (PHG) of 0.6 mg/L . The agency relies on different studies to justify this value. The reasoning used to establish this value is described in the Afssa- Afssaps-Invs document.

[2] *For plants using aluminum-based coagulants, operational guidance values of less than 0.1 mg/L (100 µg/L) total aluminum for conventional treatment plants and less than 0.2 mg/L (200 µg/L) total aluminum for other types of treatment systems (e.g., direct or in-line filtration plants, lime softening plants) are recommended. These values are based on a 12-month running average of monthly samples.*

[3] Secondary Maximum Contaminant Level

6.3 Conclusion

The Inter-Agency Working Group (*Afssa – Afssaps – Invs, 2003) specifies that:*
"The analysis of values obtained from animal studies, following exposure to aluminium via the oral route, shows a large range of NOAELs and LOAELs for a single aluminium salt and a single animal species. It should also be noted that in the majority of cases there is little or no difference between the NOAELs and the LOAELs. It is therefore difficult to draw conclusions about the accuracy of these values, sometimes fixed by agencies. In the absence of toxicokinetic data in these studies, it is impossible judge the real animals exposure, a situation which may explain the wide range of values obtained. It should also be emphasised that the variable bioavailability of the different forms of aluminium (cf. kinetics and metabolism of aluminium) constitutes a complicating factor for the use of these values. These observations reinforce the reserves arisen by the Expert Groups on the difficulty in determining values which are relevant and in using them to establish one or more TRVs.
*(Certain) international agencies have, however, proposed TRVs for aluminium. These include the 'Reference Dose' (RfD) of the US EPA, the 'minimal risk level' of the ATSDR, the 'TDI' of the WHO and the '*Public Health Goal' (PHG)*, proposed by the State of California. The RfD does not seem to be based on solid scientific evidence. For the other TRVs, (it is noted that) the studies used to support their determination do not establish dose-response relationships. The approach of the* Office of Environmental Health Hazard Assessment (OEHHA)*of the State of California is interesting because it proposes directly operational TRVs in relation to the potential exposure of a general population. The justifications of the hypotheses and choices are, however, not always backed up."*

7 – Significance of the Quality reference level being exceeded

This quality reference (200 micrograms of aluminium per litre of water) is an indicator of plant operational, particularly concerning the coagulation, flocculation, decantation and filtration stages / clarification process.

Aluminium in water at a concentration above 200 µg/L generally reflects a lack of optimisation of the coagulation, flocculation, decantation and filtration stages *(Discroll and Letterman, 1995; Bérubé, 2004)*. Aluminium can then be present in water in the form of "micro floc" or in dissolved form.
- The presence of "micro floc" of aluminium results from a poor filtration stage, giving rise to a potential microbiological risk. The filter has therefore not functioned in its role as a barrier to microorganisms and organic matter, the presence of which favours the formation of by-products of disinfection,
- High residual concentrations of aluminum in some water may result in the deposition of gelatinous aluminum-containing substances in the distribution system, *(Santé Canada, 1998)*, which may favour the possible proliferation of potentially pathogenic microorganisms.

Thus, the presence of aluminium at concentrations above the quality reference level for water may result in the presence of pathogenic microorganisms in the water.

8 - Opinion

After consulting the Specialised Expert Committee on Water on 4 January 2004, the French Food Safety Agency (AFSSA) publishes the following Opinion:

Considering the quality reference level set at 200 micrograms per litre of total aluminium in annex 13-1-II-A of the Code of Public Health legislation;

Considering:

- That aluminium salts may be used as chemical reagents in the coagulation stage.
- That the World Health Organization specifies that, taking into account *"Owing to the uncertainty surrounding the human data and the limitations of the animal data as a model for humans, a health-based guideline value for aluminium cannot be derived at this time"* ".
- That the quality reference level for aluminium constitutes an indicator of a good working state of treatment plants, particularly the coagulation, flocculation, decantation and filtration stages.
- Aluminium in water at a concentration above the quality reference level of 200 micrograms per litre generally reflects a failure or a lack of optimisation of these treatment stages which could lead to:
    - An insufficient retention of microorganisms,
    - An insufficient retention of organic matter, the presence of which favours the formation of disinfection by-products .
    - A precipitation and deposition of aluminium hydroxide in the distribution system, potentially favouring the proliferation of microorganisms.
- That a strict control of the water treatment process allows the limitation of residual levels of aluminium, added during the coagulation stage, by coagulant and flocculation adjuvant dose optimisation and by the control of the pH of the water during the coagulation stage.

The French Food Safety Agency:

Considers that treatment plants using aluminium salts should be designed and operated in a way which permanently guarantees conformity to the 200 microgram per litre quality reference.

File 9: Assessment of health risks due to exceeding the quality reference level for sulphates in water intended to human consumption

Quality reference level : 250 mg/L

1 – Origin and sources of contamination

Water sources:

Sulphates occur naturally in various minerals. Calcium sulphate is the form which is most widely found in water sources. The highest concentrations in groundwaters are usually of natural origin.
Sulphates can also originate from human activities and be present in water from industrial waste and atmospheric deposits.

Water treatment stages:

Aluminium sulphate (alum) is used as a chemical reagent in the coagulation stage. Sulphuric acid may be used as a chemical reagent in the acidification stage.

2 – Treatment to reduce sulphate content in waters

In accordance with article R.* 1321-48 of the Code of Public Health legislation, the use of treatment products and processes is subject to approval from the Ministry responsible for health. The list of products and processes approved is shown in the circular of 28 March 2000[1].

The following treatments can reduce sulphate content in water although it should be assured on a case by case basis that the treatments proposed are approved.

Sulphates can be removed by anion **exchange resins**.

The **membrane demineralisation method** methods which can be used are :
- Electrodialysis ;
- reverse osmosis ;
- nanofiltration ;

The last of these methods is now the most widely used provided that the membranes have a cut off of 300 to 400 Daltons.

3 – Analytical methods

The decision dated 17 September 2003[2] on analytical methods for water samples and their performance characteristics states that in the case of sulphates inaccuracy must not exceed 10%, imprecision must not exceed 10%, the limit of detection must be less than 4% of the quality reference level (250 mg/L) and the limit of quantification must not be more than 10 mg/L.

Norm-based methods to measure sulphate ions in water are as follows:
- NF EN ISO 10304-1 June 1995: Assay of dissolved fluoride, chloride, nitrite, orthophosphate, bromide, nitrate and sulphate dissolved ions by liquid phase ion chromatography - Part 1 : method applicable to water with low contamination levels ;
- NF T 90-009: Sulphates are precipitated in the form of barium sulphate and are quantified by gravimetry;
- NF T 90-040: Sulphates are precipitated in the form of barium sulphate and stabilised. The suspension is measured by nephelometry.

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[1] Circular DGS/VS 4 no 2000-166 of 28 March on products and processes for treatment of waters intended for human consumption, NOR: *MESP0030113C*

[2] Rule dated 17 September 2003 on analytical methods for water samples and their performance characteristics, NOR : SANP0323688A, JORF dated 7 November 2003, p. 19027 to 19033

Analytical uncertainty

The maximum concentration tested in inter-laboratory studies is 140 mg/L : the coefficient of variation (CV%) at this concentration is 4.5 % and the 95% confidence interval is ± 12.6 mg/L. The upper limit for the analytical results is therefore close to 150 mg/L (*AGLAE, 2003*)

4 - Exposure

4.1 Intake from drinking water

The regulatory programme for health control defined in the Code of Public Health legislation requires analyses of sulphates at source (from once every 5 years to 12 times per year) and at the distribution point (from once to more than 144 times per year).

A study of data available from the SISE-EAUX database (Source: Ministry responsible for health– DDASS – SISE-Eaux) for a period of 4 years (January 1999 to December 2002) shows that :

- analyses[1] are available for 59 % of the UDI (i.e. 15768 water distribution units (WDU) serving 53,200,000 person,
- at least one over-limit result[3] was found in 1.8 % of the water distribution units (WDU) serving a maximum of 1,460,000 people,
- The 95th percentile of 1365 analyses[3] of more than 250 mg/L (Quality reference level) was close to 810 mg/L (the 50th percentile was close to 325 mg/L).

Some mineral waters contain sulphates greatly in excess of 250 mg/L.

4.2 Intake from food

The WHO has no information about sulphate content of foodstuff products although states that sulphates are used as additives in the food industry *(Codex alimentarius commission in WHO, 2004)*. A single study conducted in the United States of America estimated mean sulphate intake from food to be 453 mg/day based on food consumption data and the listed uses of sulphates as food additives *(WHO, 2004).*

4.3 Intake form air

According to mean sulphate concentrations measured in air in North America (Canada, United States), the mean daily intake from the atmosphere is between 0.02 and 0.63 mg *(Health Canada 1994, WHO 2004)*. Exposure from this route is considered to be negligible.

4.4 Contribution from exposure sources

The average amounts of sulphates ingested from drinking water, food and air are estimated to be 500 mg/day by the WHO *(2004).* The major source is solid foods. However, in regions in which drinking water sulphate concentration is close to the quality reference level, water makes up 50% of intake.

Conclusion: overall population exposure

Daily exposure to sulphate from the diet cannot be estimated precisely. Based on the single published value in the international literature of 500 mg/day, the total intake would rise to 1000 mg/day when the concentration in water is close to the quality reference level (250 mg/L)

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[1] Analyses conducted on samples taken either in production or in distribution.

5 – Effects on health

Sulphates are one of the least toxic anions. Laxative effect has been seen in people drinking water which contains more than 600 mg/L sulphates (*Chien et al., 1968*), although human beings can adapt to higher concentrations over time (*US-EPA, 1985*). This effect is mostly described when sulphates are associated with magnesium.

The study conducted by US-EPA (*1999a*) shows that it is unlikely that exposure to water concentrations of less than 600 mg/L would cause diarrhoea. Similar conclusions were obtained from the studies of Heizer et *al.*, 1997 and Chien et *al.*, 1968.A study conducted on a vulnerable population (infants) did not establish a link between diarrhoea in infants and consumption of water containing sulphates (median = 264 mg/L, maximum = 2787 mg/L) ; this result was explained by inadequate numbers of children exposed. (*US-EPA, 1999a*). A study conducted in the United States *(Esteban et al., 1997)* demonstrated a laxative effect in most people who drank water with a sulphate concentration of more than 1000 mg/L *(US EPA, 1999b).*

The literature review on the subject by *Backer et al. (2000)* confirms that it is difficult to establish a health based value[1].

In the new version of its recommendations, the WHO states that existing data do not allow to conclude that sulphate content in water causes adverse effects *(WHO, 2004)*. A few studies suggest laxative effect at concentrations of 1000 to 1200 mg/L, although no increase in the incidence of diarrhoea, dehydration or weight loss.

In addition, in its opinion of 2 December 2003 on setting quality criteria for natural mineral waters and bottled spring waters allowing consumption without risk to health for infants and young children, Afssa states that *"Sulphates intake in water should not be greater than in breast milk which is used as the reference value (…). Mean sulphate content in breast milk is 140 mg/L and may range from 250 to 360 mg/L. in cow's milk (…). Under these conditions the Specialist Expert Committee proposes adopting the maximum level of 140 mg/L of the sulphates in bottled water used to prepare substitute breast milk".*

6 – References values

The quality reference level for tap water is set at 250 mg/L by the Code of Public Health.

Several recommendations and guide values are found in the literature (table 9.1).

As sulphate is one of the least toxic anions, no health-based guideline value is proposed by the WHO.

Because of the gastrointestinal effects arising from ingestion of drinking water containing high sulphate concentrations, the WHO recommends that health authorities should be informed if sulphate concentration in water exceeds 500 mg/L. It states that the presence of sulphates in drinking water may confer a taste on the water. The lowest taste threshold concentration is 250 mg/L for sodium sulphate (*WHO 2004a*).

Table 9.1: Reference values proposed by different bodies

Value in directive 98/83/CE Annex IB	WHO 2004	Health Canada 1994	US EPA
250 mg/L	250 mg/L*	500 mg/L	SMCL** = 250 mg/L

** Concentration below the taste threshold*

*** Secondary Maximum Contaminant Level*

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[1] The therapeutic dose of magnesium sulphate for laxative activity in adults is between 10 and 15 grams, i.e. 8 to 12 grams of sulphate (Pharmacopoeia). Very considerable inter-individual sensitivity however is seen.

7 – Impact from exceeding the quality reference level for sulphates in water

The main reasons for limiting sulphate concentrations in water are taste and corrosion.

- The average taste threshold for sulphate salts is 350 mg/L for sodium sulphate *[range 250 to 500 mg/L]* 525 mg/L for calcium sulphate *[range 250 to 900 mg/L]* and 525 mg/L for magnesium sulphate *[range 400 to 600 mg/L]* (*Health Canada, 1994*).
- The presence of sulphate salts in water promotes corrosion of metallic piping through an electrolytic effect. Sulphates can induce the proliferation of sulphate reducing bacteria in areas where water stagnation within the distribution network may occur. This phenomenon could produce hydrogen sulphide and give water an unpleasant taste and smell, accelerate corrosion (biological corrosion) and adversely affect disinfection of water in distribution networks. (*Health Canada, 1994*)

8 – Opinion

After consulting the “Waters” Specialist Expert Committee on 5 April and 3 May 2005, the French Food Safety Agency (Afssa) published the following opinion :

Considering the quality reference level of 250 milligrams per litre for sulphate ions in annex 13-1-II-A of the Code of Public Health legislation ;

Considering the Afssa opinion dated 2 December 2003 on setting quality criteria for natural mineral waters and bottled spring waters allowing consumption without health risk to infants and young children ;

Considering that sulphates may occur naturally in water sources or may be added during the coagulation stage (aluminium sulphate) or acidification stage (sulphuric acid) ;

Considering that the World Health Organization has not established a health based guideline value ;

Considering that the World Health Organization recommends that health authorities be informed if sulphate content in water exceeds 500 mg/L because of the gastro-intestinal effect which may arise from ingesting drinking water containing a high concentration of sulphates ;

Considering that studies suggest a laxative effect beyond 1000 mg/L ;

Considering that the limits of taste detection range from 250 to 900 mg/L depending on the cations associated with the sulphates and that the average threshold is 525 milligrams per litre for calcium sulphate (the salt most frequently seen in water) ;

Considering that the presence of sulphates in water either directly or indirectly promotes corrosion of metallic pipework ;

Considering that for distribution water, health control data conducted during the years 1999 to 2002, show that :

- 50% of the values which exceed the quality reference level are less than 325 milligrams per litre,
- 5% of the values which exceed the quality reference level are greater than 810 milligrams per litre ;

Considering that the treatment procedure approved by the Minister responsible for health can be used to reduce sulphate content in water,

Afssa:

Reiterates that the means required to bring concentrations to the quality reference level must be implemented as rapidly as possible,

Considers:

1. that in light of current available data, it is not possible to define a health based threshold,
2. that the sulphate concentration of 500 mg/L may be used to define the taste threshold,
3. that for infants, because of possible laxative effects, water containing a sulphate concentration above the quality reference level is not recommended for drinking or preparing foods,

if the quality reference level is exceeded, monitoring for metallic contamination due to corrosion effects should be increased at the consumer’s tap.

File 10: assessment of health risks related to exceeding the quality reference for chlorides in waters intended for human consumption

Quality reference: 250 mg/L

1 – Origin and sources of contamination

From water sources: Chlorides originate firstly from rain water where they are present as a result of evaporation from oceans and from certain industrial waste. They are concentrated by evaporation-transpiration before becoming infiltrated in the ground. In some areas chloride sources are linked to salt bearing formations and ingress of sea water in coastal shores may also contribute to increased chloride content. Sources from human activities include fertilizers (KCl), some industrial activities and content-reducing lixiviats (separators) in waste dumps.
From water treatment stages:

Ferric chloride and preneutralised aluminium chloride can be used as chemical reagent in the coagulation stage. Hydrochloric acid may be used as a chemical reagent in the acidification stage. Chloride derivatives are used to disinfect water.

2 – Treatment reducing chloride content in water

In accordance with the French drinking water regulation, the use of treatment products is subject to approval from the Minister responsible for health.

The following treatments can reduce chloride content in water, although confirmation is required on an individual case basis that the proposed treatments are approved.

The **membrane demineralisation** methods which may be used are:

- electrodialysis;
- reverse osmosis.

3 – Analytical methods

The decree of 17 September 2003[1] on analytical methods for water samples and their characteristics and performances states that in the case of chlorides inaccuracy must not exceed 10% and imprecision must not exceed 10 %, the limit of detection must be less than 4% of the reference value (250 mg/L) and the limit of quantification must not be greater than 10 mg/L

The methods listed in norms to assay chloride ions in water are as follows :

- NF EN ISO 15682 : 2001: Assay by photometric or potentiometric detection flow analysis;
- NF EN ISO 10304-1 June 1995 : Assay of dissolved fluoride, chloride, nitrate, orthophosphate, bromide, nitrate by liquid phase ion chromatography. Part 1 method applicable for low level contaminated water.
- NF ISO 9297 : 1989 (invalidation intended in 2005) Assay of chlorides – Silver nitrate titration with chromate indicator (Mohr method) ;

Analytical imprecision

Analytical imprecision can be estimated from inter-laboratory tests by calculating the coefficient of variation of reproducibility (CVR%) (AGLAE 2003)

The maximum concentration tested in the inter-laboratory studies was 40 mg/L ; the inter-laboratory CV at this value was 4% and the 95% confidence interval was ± 3.2 mg/L. The upper level of the analyses is therefore in the region of 45 mg/L. (*AGLAE, 2003*)

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[1] Rule dated 17 September 2003 relating to analytical methods for water samples and their performance characteristics, NOR : SANP0323688A, JORF dated 7 November 2003, p. 19027 to 19033

4 - Exposure:

4.1 Intake from drinking water

The regulatory programme for health control defined by the Code of Public Health legislation requires chloride analyses at the source point (from once every 5 years to 12 times per year) and at the distribution point (from once to more than 144 times per year).

A study of data available from the SISE-EAUX database (Source: Ministry responsible for health– DDASS – SISE-Eaux) over a period of 4 years (from January 1999 to December 2002) shows that:

- analyses[1] are available for more than 60% of the UDI* (i.e. 16167 UDI serving 52 760 000 people),
- at least one over-limit result[3] was found in 0.5% of these water distribution units serving a maximum of 447,200 people,
- The 95th percentile of the 198 analyses[3] over 250 mg/L was close to 460 mg/L (the 50th percentile was close to 310 mg/L).

4.2 Intake from food

The natural chloride concentration in foodstuff products generally does not exceed 0.36 mg/g of food *(OMS, 2004)*. Some foods however are major carriers of salt (NaCl) (e.g. processed meat contains between 10 and 70 mg/g *(AFSSA, 2002)* or between 6 and 42 mg/g expressed as chlorides). Two food consumption surveys *(Inca and SU.VI.MAX. in AFSSA, 2002)* have estimated salt consumption in the French population to be between 5 and 12 g/day (mean values, with extremes of up to 16 g/day for the highest salt consumers).

4.3 Intake from air

Exposure to chlorides in air is considered to be negligible *(Health Canada, 1987)*.

4.4 Contribution from exposure sources

The average amounts of chloride provided in drinking water are generally negligible compared to intake in food. Drinking water accounts for 0.33-8% of total intake.

Conclusion: Overall exposure of the population

In view of the results of French food surveys, the daily salt intake from the diet can be estimated to be between 5 and 12 g/day for adults. When expressed as chlorides this is between 3 and 7.2 g/day. The major source of chloride exposure to humans is addition of salt to foods : this is a greater source than from drinking water.

5 – Effects on health

5.1 Essential requirements

The chloride ion is the major extracellular ion of the body[2]. An adult body contains between 82 and 105 g of chloride (*Health Canada, 1987 ; WHO, 2004*). Chlorides are almost entirely absorbed in healthy people and are excreted mostly in urine and secondarily in sweat. Little chloride is lost in faeces. In view of these losses the recommended intake is 9 mg/kg body weight (i.e. approximately 0.6 g Cl^-/day) (*Health Canada, 1987 ; WHO, 2004*).

5.2 Subchronic and Chronic toxicity

No signs of toxicity have been seen in humans except when disorders of regulation of water and electrolyte balance are present, particularly in people suffering from certain renal diseases. The long term effect of a chloride rich diet is poorly understood. Hypertension associated with sodium chloride consumption appears to be due to the sodium ion rather than to the chloride ion *(Afssa, 2003)*.

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[1] Analyses performed on samples taken either in production or in distribution.

[2] Chloride is a highly mobile ion which passes easily through cell membranes and contributes towards water and electrolyte balance. 88% of chlorides in humans are in the extracellular compartment and contribute to maintenance of cell osmolarity.

* UDI – Water Distribution Units

In its opinion of 2 December 2003 on setting quality criteria for natural mineral waters and sources of bottled water allowing consumption without risk to health for infants and young children, Afssa states that *"in the absence of renal disease, chloride does not have a major impact in infants : it is not therefore proposed to set a stricter value than the quality reference contained in the regulations for waters intended for human consumption (i.e. 250 mg/L, as no guide value is set by the WHO).*

6 – Reference values

The quality reference for tap water is set at 250 mg/L by the Code of Public Health.

Several recommendations and guide values are found in the literature (table 10.1). The World Health Organisation does not propose any guideline value based on health criteria but states however that the presence of chlorides in drinking water may confer on it a significant taste. The taste threshold depends on the cation associated with chloride and is, in the region of 200 to 300 mg/L for sodium, potassium and calcium chlorides *(WHO, 2004a*).

Table 10.1: Reference values proposed by different organisation

Value in directive 98/83/CE Annex IB	WHO 2004	Health Canada (1987 revision)	US EPA
250 mg/L	250 mg/L*	250 mg/L	SMCL** = 250 mg/L

* Concentration below the taste threshold

** Secondary Maximum Contaminant Level

7 - Impact of exceeding the quality reference for chlorides in water

The major reasons for limiting the concentration of chloride ion in water are taste and corrosion.

- The taste threshold for sodium, potassium and calcium chlorides in drinking water varies between 210 and 310 mg/L (*Health Canada, 1987*).
- The presence of chloride salt in water promotes corrosion of metallic piping through an electrolytic effect *(WHO, 2004)*.

8 - Opinion

After consulting the “Waters” specialist expert committee on 5th April and 3 May 2005, the French Food Safety Agency (Afssa) publishes the following opinion:

Considering the quality reference set at 250 milligrams per litre for chloride ions in annexe 13-1-II-A of the Code of Public Health legislation ;

Considering the opinion of Afssa dated 2 December 2003 on the quality criteria for bottled natural mineral waters and bottled spring waters allowing consumption by infants and young children without risk to health ;

Considering that chlorides may be present naturally in water sources or may be added during the coagulation (ferric chlorides), acidification (hydrochloric acid) or disinfection (chlorinated compounds) stage ;

Considering that the cation mostly associated with chlorides is sodium ;

Considering that the World Health Organisation has not set a health-based guideline value ;

Considering that the taste threshold varies between 200 to 300 mg/L depending on the cations associated with the chlorides ;

Considering that the presence of chlorides in water promotes corrosion of metallic piping;

Considering that the health monitoring data for public water supplies conducted during the years 1999 to 2002, show that :

- 50% of the values which exceed the quality reference are less than 310 milligrams per litre,
- 5% of the values which exceed the quality reference are greater than 460 milligrams per litre ;

And considering that the treatment processes approved by the Minister responsible for health may be used to reduce water chloride content ;

Afssa :

Reiterates that measures should be used to reduce chloride concentration to the quality reference level,

Considers

- that in view of currently available information it is not possible to define a minimum health-based threshold,
- the daily intake of chloride from drinking-water is still minor compared to intake from solid food, even when the quality reference is exceeded (5% of values which exceed the quality reference are over 460 milligrams per litre),
- that if the quality reference is exceeded, monitoring of metallic contamination at the consumer’s tap should be increased and that sodium content should be checked,
- that people who need to follow a low sodium diet should be informed if the quality reference is exceeded.

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ANNEX I: Possible consequences of an interruption of the water supply

Interruption of the water supply as a solution to limit exposure of the population may present a number of disadvantages, briefly outlined below. Technically, interruption of the water supply is achieved by stopping supply to the system at the catchment exit or the plant or reservoir:

1. This interruption does not necessarily mean that potentially contaminated water will be immediately placed beyond the reach of the population. In fact, the water remains available in various parts of the system and in water tanks until they are completely emptied. Thus exposure of the population still remains possible if the alert messages are not issued in time.
2. Furthermore, once draining of the system has been completed, the lack of availability of water for certain uses (lavatory flushing, cooling of certain devices) can be a source of risks.
3. Use of substitution water is no simple matter and can be accompanied by health risks related notably to its quality and distribution methods.
4. Interrupting and draining a water supply system can also lead to inefficient mobilisation of reserves destined for firefighting purposes.
5. Additionally, refilling a supply system with water after draining includes increased risks of contamination, particularly microbiological. While the system is being emptied, it acts as a drain for surroundinggroundwater , which may be contaminated. System biofilms which have become detached on drying can be mobilised on refilling of the system with water and lead to downstream clogging with a further interruption in supply. Finally, draining a network increases the risk of water refluxes from domestic networks, with the associated water quality problems.

The health consequences related to interruption of a water supply can therefore be greater than the initial risk. Thus, when supply water exceeds the quality limits and/or references, the main options for handling the supply water which can be used, depending on the cases, must be assessed:

- Interruption of the supply, potentially with purging of installations to eliminate contaminated water as quickly as possible,
- Rinsing of installations by maintaining the water supply and purging of systems to eliminate contaminated water as quickly as possible without draining the system with, if necessary, restriction or prohibition of water use,
- Confinement of the water in a section of the system.
- Continuation of distribution of water under the usual conditions with, if necessary, use restrictions,

When the quality limits and/or references are exceeded, it is necessary to assess the most appropriate measure for limiting exposure of the population to the substance identified. The potential consequences of the management measure identified must be taken into consideration.

Annex II: origin of substances present in water

	Most likely origins of substances in water				
	Source		Production		Distribution
List of parameters	Natural origin	Anthropic origin	Physicochemical treatments	Disinfection	Public or domestic system
Parameters subject to a **quality limit**					
Acrylamide			×		×
Antimony	×				×
Arsenic	×				
Barium	×				
Benzene		×			
Benzo[a]pyrene		×			
Boron	×	×			
Bromates				×	
Cadmium		×			×
Chromium	×				
Vinyl chloride					×
Copper					×
Cyanides		×			
1,2-dichloroethane		×			
Epichlorohydrin			×		
Fluorides	×				
HAP		×			×
Mercury	×				
Microcystin-LR	(×)				
Nickel		×			×
Nitrates NO_3^-		×			
Nitrites NO_2^-		×			×
Pesticides		×			
Lead					×
Selenium	×				
Trichloroethylene		×			
Tetrachloroethylene		×			
THMs				×	
Turbidity	×		×		×
Parameters subject to a **quality reference**					
Ammonium	×	×			
Aluminium			×		
Chlorites				×	
Chlorides	×				
Iron	×				×
Manganese	×				
Sodium	×				
Sulphates	×	×			
Radioactivity	×	×			

ANNEX III: Concept of analytical uncertainty

Standard NF X 07-001[1] defines the measurement uncertainty as a “Parameter associated with the result of a measurement, which characterises the spread of values which could reasonably be allotted to the characteristic being measured [2]”.

In simpler terms, this corresponds to the confidence interval concept in statistics, with the hypothesis of a normal distribution of the parameter.

Major studies have been conducted relative to control of measurement uncertainties in the context of accreditation of laboratories and compliance with standard NF EN ISO/CEI 17025[3] (May 2000). In particular, standard XP T 90-220[4] (August. 03) describes the various approaches used to take into account measurement uncertainties in the field of water analysis:

- **An intra-laboratory approach**
    - Based on the application of Internal Quality Control (IQC)**:** in this case, the intra-laboratory uncertainty is estimated by reproducibility of measurements (generally analysed on control cards) on certified reference materials or, in the absence of these, on synthetic samples.
    - Based on a specific experiment plan: this more restrictive approach assumes that real samples which are stable over time are available.
    - Based on a statistical approach (Cf. NF ENV 13005[5] August 99): this involves modelling of the analytical process and assessment of the various sources of uncertainty. It is the only approach enabling determination of the relative contribution of the various influencing factors.
- **An inter-laboratory approach**
    - Based on analysis of Inter-Laboratory Tests (ILT), this approach takes into account all the influencing factors (laboratory effect, method effect, operator effect, etc.) and leads to a conservative uncertainty (NF ISO 5725-2[6], Dec. 94).

Using inter-laboratory tests destined for external quality control, it is possible to obtain an estimation of the analytical uncertainty, expressed using the reproducibility coefficient of variation (CVR%).

Data are currently available, notably from the AGLAE association (Association Générale des Laboratoires d'Analyses de l'Environnement) which has prepared a summary (covering almost 10 years of tests). *(AGLAE, 2003)*

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[1] NF X 07-001 (December 1994) Basic standards – International vocabulary of basic and general terms in metrology

[2] The characteristic being measured is a physical, chemical or biological entity.

[3] NF EN ISO/CEI 17025 (May 2000) General recommendations relative to the competence of calibration and testing laboratories

[4] XP T 90-220 (August 2003) Water quality – Protocol for elimination of measurement uncertainty associated with an analytical result for physicochemical methods

[5] NF ENV 13005 (August 1999) Guidelines for the expression of measurement uncertainty

[6] NF ISO 5725-2 (December 1994) Application of statistics - Accuracy (trueness and precision) of measurement methods and results – Part 2: basic method for the determination of repeatability and reproducibility of a standard measurement method

ANNEX IV: Classification or carcinogenic substances

Classification criteria for carcinogenic substances by IARC
http://www.iarc.fr

1	Carcinogenic to humans: sufficient evidence
2A	Probably carcinogenic to humans: limited evidence in humans and sufficient evidence in animals
2B	Possibly carcinogenic to humans: limited evidence in humans or sufficient evidence in animals
3	Not classifiable
4	Probably not carcinogenic to humans

Classification criteria for carcinogenic substances by the European Union

1	Carcinogenic to man
2	Substances which should be regarded as if they are carcinogenic to man
3	Substances which cause concern for man owing to possible carcinogenic effects

- First category:

Substances known to be carcinogenic to man. Introduction of these substances into category 1 is based on epidemiological evidence establishing a causal relationship between human exposure to these substances and the development of a cancer.

- Second category:

Substances which should be regarded as if they are carcinogenic to man. There is a strong presumption that human exposure to these substances may result in the development of cancer. This presumption is generally on the basis of:

- appropriate long-term animal studies,
- other relevant information: metabolic studies, biochemical studies, structural relationships with other carcinogenic substances, or data from epidemiological studies.

- Third category:

Substances which cause concern for man owing to possible carcinogenic effects. These can be divided into two sub-categories:

- substances which are well investigated but for which the evidence of a carcinogenic effect is insufficient for classification in category 2.
- substances which are insufficiently investigated. The available data are inadequate, but they raise concern for man. This classification is provisional; further experiments are necessary before a final decision can be made.

Classification criteria for carcinogenic substances by the US EPA

http://www.epa.gov/ncea/cancer.htm

A	Carcinogenic to humans
B1	Probably carcinogenic to humans: limited evidence
B2	Probably carcinogenic to humans: evidence in animals only
C	Possibly carcinogenic to humans
D	Not classifiable
E	Evidence of non-carcinogenicity for humans

Classification criteria for carcinogenic substances by Health Canada

http://www.hc-sc.gc.ca/hecs-sesc/dse/

I	Carcinogenic to humans
II	Probably carcinogenic to humans
III	Possibly carcinogenic to humans
IV	Unlikely to be carcinogenic to humans
V	Probably not carcinogenic to humans
VI	Unclassifiable: the data available do not enable assessment

ANNEX V: Reference values in water

The table below presents the reference values proposed by various bodies for substances subject to quality limits or references in the French Public Health Code.

- The guideline values proposed by the European Union in annexes I-B and I-C of directive 98/83/EC of 3 November 1998 on the quality of water destined for human consumption.
- The guideline values proposed by the World Health Organisation in the drinking water quality directives *(WHO, 1994 and WHO, 1996)*, as well as the guideline values that could be proposed in the context of reassessment of these WHO recommendations begun at the start of 2003 *(WHO, 2003)*.
- The maximum acceptable concentrations (MAC) proposed by "Health Canada" *(Health Canada, 2003)*
- The "Maximal Concentration Levels" (MCL) proposed by the US-EPA. *(US-EPA, 2002)*

	Reference values				
List of parameters	Guideline value directive 98/83/EC	*Guideline value WHO1994*	Guideline value WHO 2004	Health Canada MAC	US EPA MCL/ MCLG
Acrylamide	0.1 µg/l	*0.5 µg/l*	0.5 µg/l		0
Aluminium	0.2 mg/l	*0.1 or 0.2 mg/L depending on size of installation*	0.1 or 0.2 mg/L depending on size of installation		0.05 to 0.2 mg/l
Antimony	5 µg/l	*5 µg/l (provisional, LOD)*	20 µg/l	6 µg/l	6 µg/l
Arsenic	10 µg/l	*10 µg/l*	10 µg/l (Assay limit)		10 µg/L
Barium	no value	*0.7 mg/l*	0.7 mg/l	1 mg/L	2 mg/L
Benzene	1 µg/l	*10 µg/l*	10 µg/l	5 µg/L	5 µg/l
Benzo[a]pyrene	0.01 µg/l	*0.7 µg/l*	0.7 µg/l	0.01 µg/l	0.2 µg/l
Boron	1 mg/l	*0.3 mg/l (1994)* *0.5 mg/l (1998)*	0.5 mg/l	5 mg/L provisional	
Bromates	10 µg/l (2009) 25 µg/l (2003 to 2009)	*25 µg/l (1994)*	10 µg/l	10 µg/L	10 µg/L
Cadmium	5 µg/l	*3 µg/l*	3 µg/l	5 µg/l	5 µg/l
Chlorides	250 mg/l	*250 mg/l*	Health based value > C° in DW	250 mg/l aesthetic	
Chlorites	no value	*0.2 mg/l* *"sanitary value" (1994)*	0,7 mg/l	_	0,8 mg/l (1 mg/l)
Chromium (total)	50 µg/l	*50 µg/l*	50 µg/l (Provisional)	50 µg/l	100 µg/l
Vinyl chloride	0.5 µg/l	*5 µg/l*	0.3 µg/l	2 µg/L	2 µg/l
Copper	2 mg/l	*2 mg/l*	2 mg/l	1 mg/l	1.3 mg/l
Cyanides	50 µg/l	*70 µg/l*	70 µg/l	200 µg/l	200 µg/l
1,2-dichloroéthane	3 µg/l	*30 µg/l*	4 µg/l	5 µg/l	5 µg/l
Epichlorohydrin	0.1 µg/l	*0.4 µg/l Provisional*	0.4 µg/l Provisional	/	0 (restriction on materials in contact with water)
Iron	200 µg/l	*0.3 mg/l* *acceptability criterion*	Health based value > C° in DW	0.3 mg/l aesthetic	0.3 mg/l
Fluorides	1.5 mg/l	*1.5 mg/l*	1.5 mg/l	1.5 mg/l	2 mg/l
Benzo[b]fluoranthene	0.1 µg/l for the sum of concentrations of the 4 substances (HAP)				
Benzo[k]fluoranthene					
Benzo(ghi)perylene					
Indenol(1,2,3-cd)pyrene					
Manganese	50 µg/l	*0.1 mg/l* *acceptability criterion*	0.05 mg/l acceptability 0.4 mg/L health	0.05 mg/l aesthetic	
Mercury	1 µg/l	*1 µg/l*	1 µg/l	1 µg/l	2 µg/l

	Reference values				
List of parameters	Guideline value directive 98/83/EC	*Guideline value WHO1994*	Guideline value WHO 2004	Health Canada MAC	US EPA MCL/ MCLG
Microcystin-LR	no value	*1 µg/l*	1 µg/l Provisional	1.5 µg/l	
Nickel	20 µg/l	*20 µg/l*	70 µg/l	_	_
Nitrates NO3$^-$	50 mg/l (C nitrite/VG nitrite) + (C nitrate/VG nitrate) < 1	*50 mg/l*	50 mg/l	45 mg/l	10 mg/l (N)MCL
Nitrites NO2$^-$	0.5 mg/l 0.1 mg/l at start of treatment installations (C nitrite/VG nitrite) + (C nitrate/VG nitrate) < 1	*3 mg/l* *3 mg/l acute guideline value* *0.2 mg/l chronic guideline value* *(C nitrite/VG nitrite) +* *(C nitrate/VG nitrate) < 1*	3 mg/l guideline value – acute exposure 0.2 mg/l guideline value – chronic exposure	3.2 mg/l	1 mg/l (N)MCL
Lead	10 µg/l from 2013 25 µg/l from 2003 to 2013	*10 µg/l*	10 µg/l	10 µg/l	15 µg/l
Selenium	10 µg/l	*10 µg/l*	10 µg/l	10 µg/l	50 µg/l
Tetrachloroethene	10 µg/l for the sum of the 2 parameters	*40 µg/l*	40 µg/l	30 µg/L	5 µg/L
Trichloroethene		*70 µg/l*	20 µg/l Provisional	50 µg/L	5 µg/L
Bromoform	100 µg/l (2003 to 2009) 150 µg/L (2009) sum of concentrations for the 4 specified compounds	*100 µg/l*	100 µg/l	100 µg/l	80 µg/l
Chloroform		*200 µg/l*	300 µg/l	100µg/l	80µg/l
Dibromochloromethane		*100 µg/l*	100 µg/l	100µg/l	80µg/l
Bromodichloromethane		*60 µg/l*	60 µg/l		80 µg/l
Turbidity	Acceptable for consumers and no abnormal changes	*5 NTU*	no value (recommended < 1 NTU)	1 NTU	
Ammonium	0.50 mg/l	*1.5 mg/L olfactory detection threshold* *35 mg/L gustatory detection threshold acceptability criterion (1994)*	-	_	_
Sodium	200 mg/l	*200 mg/l acceptability criterion (1994)*	Health based value > C° in DW	200 mg/l aesthetic	
Sulphates	250 mg/l	*250 mg/l acceptability criterion (1994)*	Health based value > C° in DW	500 mg/l aesthetic	250 mg/l taste threshold