Evaluation and management of Arsenic contamination in agricultural soil and water - AgriAs

Deliverable 4.1.
Collation of evaluation criteria for assessment of the risks from arsenic in agricultural soils

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Collation of evaluation criteria for assessment of the risks from arsenic in agricultural soils

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Contents

1 Introduction

This report is deliverable D4.1, from Work Package 4 “Risk assessment of the selected target sites” of the AgriAs project.

The overall goal of AgriAs is to provide the European Union with reliable data on the existing risks of As exposure through agriculture, a complete summary of existing tools available for As remediation as well as an array of tools for ecotoxicity and bioavailability assessment.

When assessing the risks to human health of a substance in the environment, estimates or measurements of the exposure of people the substance are made. In order to determine whether or not harmful health-effects are likely, the estimated or measured exposure is usually compared to toxicological reference values. Toxicological reference values indicate an exposure level below the likelihood of harmful health effects are judged to be at low level. Toxicological reference values are derived by panels of experts (for example the international panels of WHO and EFSA) from experimental and epidemiological studies of the toxic effects of substances in animals and in humans.

Health-risk assessments of contaminants in the soil usually consider the transport of the contaminant to various environmental media, for example groundwater, surface water, foodstuffs and air, and the exposure of people to contaminants in these media. Models of these transport and exposure processes are used to estimate the exposure of people to the contaminant, which is then compared with the toxicological reference values.

Simplified health risk assessments make the use of reference concentrations, or criteria for the contaminant in various environmental media. In these cases, the toxicological reference values are used as the start point for the calculation of reference concentrations using exposure models, and in some cases, transport models. Reference concentrations are often calculated by expert groups and given out by relevant authorities (for example, Food Safety Organisations). The risk assessment then takes the form of comparison of measured or estimated concentrations in environmental media with the relevant reference values. Reference values can be generic or can consider some site-specific characteristics.

A simplified overview of the use of reference values as criteria for the assessment of health risks is shown in Figure 1-1.

For the assessment of risks to the environment, ecotoxicological reference have been compiled for various media, including soils, surface waters and sediments. These reference values are derived to protect the biota in the media, and some reference values are also intended to protect predator animals higher in the food chain from contaminants which bioaccumulate in the food chain. The methods used to derive these reference values are described in the relevant chapters (6 and 7).

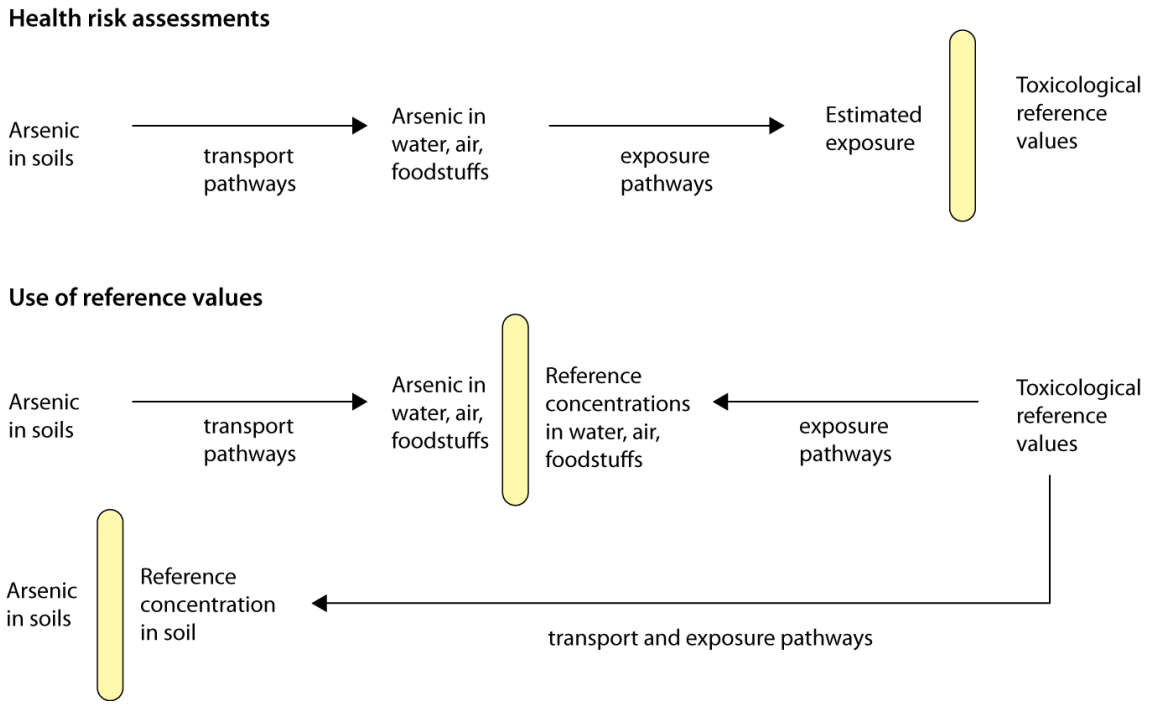

Figure 1-1 Health risk assessments for contaminants in soil, and the use of reference values or criteria for various media in simplified risk assessments. The yellow bar shows the point at which estimated values are compared with criteria (reference, guideline or limit values).

This report collates relevant criteria for use in health- and environmental risk assessments of arsenic in agricultural soils. Criteria have been compiled for:

- Toxicological reference values for the assessment of risks to health (Chapter 2)
- Criteria for drinking water (Chapter 4)
- Criteria for foodstuffs (Chapter 5)
- Criteria for animal fodder (Chapter 6)
- Criteria for soils (both for protection of health and protection of the environment) (Chapter 7)
- Criteria for surface water (Chapter 8)
- Criteria for groundwater (Chapter 9).
- Criteria for air (Chapter 10).

Chapter 3 gives a short overview of biomarkers for arsenic exposure and health effects in people.

Particular attention has been paid to criteria applicable at the two test sites adopted by AgriAs, and therefore criteria from France and Germany (and Saxony, the local authority) have been included in the compilation.

2 Toxicological reference values for assessment of risks to health

The most important arsenic compounds and species known to be present in water and food consumed by humans have been listed by NRC (1999) and by JECFA (2011). Both inorganic and organic arsenic compounds occur in food and water. Arsenic in drinking water is generally inorganic, with As(III) and As(V) in varying proportions, for example, the proportion of arsenite is generally greater in anaerobic waters. Methylated species would rarely be present in water supplies. In surface waters and soils, methylated arsenic species occur as a result of bacterial methylation. Organic arsenicals occur to greater extent in foodstuffs, for example, in fish almost all the arsenic present is in organic form.

Arsenic compounds found in food, water and biological samples that were considered by JECFA were;

Arsenate	As(V)
Arsenite	As(III)
Methylarsonic acid	Monomethylarsonic acid, methyl arsonate, MMA(V)
Dimethylarsonic acid	Dimethylarsnitie, cacodlic acid, DMA(V)
Methylarsonous acid	Monomethylarsonous acid, MMA(III)
Dimethylarsonous acid	DMA(III)
Arsenobetaine	AsB
Arsenocholine	AsC
Trimethylarsine oxide	TMAO
Tetramethylarsonium ion	TMA+
Dimethylarsionylethanol	DMAE
Trimethylarsoniopropionate	TMAP
Dimethylarsionylribosides	Oxo-arsenosugars
Dimethylmonothiarsinic acid	DMMTA(V)
Dimethyldithioarsinic acid	DMDTA(V)

Note that it is often not possible to know the valency of MMA and DMA and in biological samples, it is assumed that MMA and DMA refer to the totals of both valencies.

Elemental arsenic and inorganic arsenic species share the same metabolic pathway: arsenate → arsenite → methylarsonate → dimethylarsenite, see Figure 2-1.

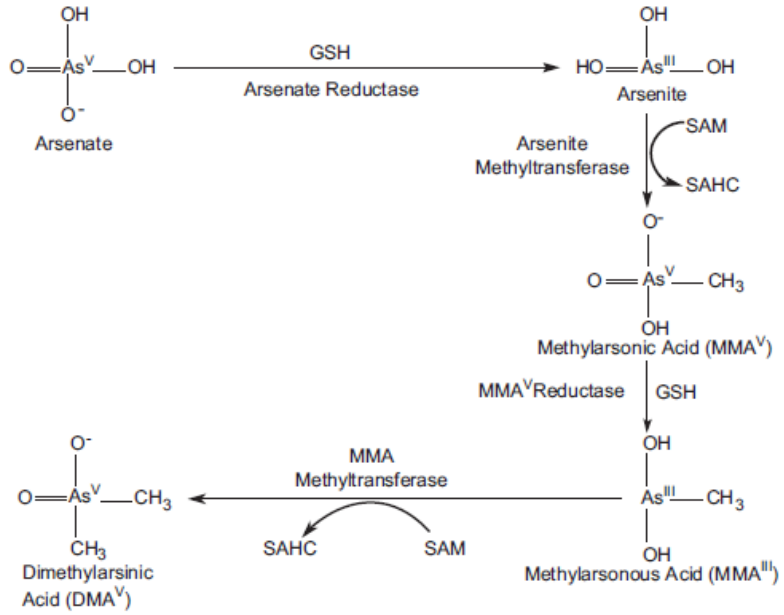

Figure 2-1 Pathway for biotransformation of arsenic (GSH, glutathione; SAHC, S-adenosylhomocysteine; SAM, S-adenosylmethionione) (From JECFA, 2011).

EFSA considered that, compared to dietary exposure, non-dietary exposure to arsenic is likely to be of minor importance for the general population in the European Union (EU).

In humans, soluble inorganic arsenic is rapidly and nearly completely absorbed after ingestion. Absorption of different organic arsenic compounds is generally greater than 70 %. After being absorbed, arsenic is widely distributed to almost all organs and readily crosses the placental barrier. Because experimental animals differ considerably from humans with regard to arsenic metabolism and other aspects of toxicokinetics, the results of toxicity studies in animals do not provide a suitable basis for risk characterisation.

2.1 Health effects

Inorganic arsenic (As) is very toxic and chronic exposure can lead to a number of health effects. The inorganic forms of arsenic are more toxic than organic arsenic. Epidemiological studies have shown that arsenic is carcinogenic.

The main adverse effects reported to be associated with long term ingestion of inorganic arsenic in humans are skin lesions, cancer, developmental toxicity, neurotoxicity, cardiovascular diseases, abnormal glucose metabolism, and diabetes. These effects have mainly been studied in adults. Neurotoxicity is mainly reported with acute exposure, or at high concentrations in drinking water. Evidence of cardiovascular disease (Blackfoot disease, peripheral vascular disease, coronary heart disease, myocardial infarction and stroke) and diabetes in areas with relatively low levels of inorganic arsenic exposure is inconclusive. There is emerging evidence of negative impacts on foetal and infant development, particularly reduced birth weight and the child's cognitive development (Tyler and Allen 2014). There is a need for further evidence regarding the dose-response relationships and critical exposure times for these outcomes. It also appears that exposure in early life or as a foetus can increase the risk of developing lung or bladder cancer later in life (Steinmaus et al. 2014).

Inorganic arsenic is metabolized in the body through methylation to MMA and DMA, which are excreted in the urine. While DMA can be considered a detoxification mechanism, the proportion of MMA has been associated with an increased risk of adverse health effects (Vahter, 2009).

2.1.1 Carcinogenic effects

Epidemiological data show that chronic inorganic arsenic exposure can cause cancer of the skin, bladder, lung and kidneys.

The evaluation in IARC (2012) concluded that:

- There is sufficient evidence in humans for the carcinogenicity of mixed exposure to inorganic arsenic compounds, including arsenic trioxide, arsenite and arsenate. Inorganic arsenic compounds cause cancer of the lung, urinary bladder and skin. Also, a positive association has been observed between exposure to arsenic and inorganic arsenic compounds and cancer of the kidney,liver and prostate.
- There is limited evidence in experimental animals for the carcinogenicity of sodium arsenate, gallium arsenide, arsenic trioxide and trimetylarsine oxide.
- There is inadequate evidence in experimental animals for the carcinogenicity of monomethylarsonic acid and arsenic trisulphide.

Arsenic compounds were classified as follows:

- Arsenic and inorganic arsenic compounds are carcinogenic to humans (Group I).
- Dimethylarsinic acid and monomethylarsonic acid are possible carcinogenic to humans (Group 2B).
- Arsenobetaine and other organic arsenic compounds are not metobolised in humans and are not classifiable as to their carcinogenicity to humans (Group 3).

The working group made the overall evaluation on “arsenic and inorganic arsenic compounds” rather than on individual arsenic compounds, based on the combined results of epidemiological studies, carcinogenicity studies in experimental animals, and data on the chemical characteristics, metabolism and modes of action of carcinogenicity. Elemental arsenic and inorganic arsenic species share the same metabolic pathway: arsenate → arsenite → methylarsonate → dimethylarsenite. Thus independent of the mechanisms of the carcinogenic action and independent of which of the metabolites is the actual ultimate carcinogen, different inorganic arsenic species should be considered as carcinogenic.

Some forms of arsenic have been shown to be genotoxic. Several mechanisms have been proposed to explain the genotoxicity of arsenic. Experimental evidence indicates that the generation of reactive oxygen species (ROS) during the biotransformation of arsenic (see Figure 2-1) is the primary mechanism of genetic damage induced by arsenic. The ROS produced are able to generate DNA adducts, DNA strand breaks, cross-links and chromosomal damage. Arsenic may also inhibit DNA repair processes.

USEPA (IRIS, 2017) has classified arsenic in class A – Human carcinogen, based on sufficient evidence from human data.

2.2 Quantitative assessments

Arsenic causes both health effects where the dose-response relationship can be assumed to have a threshold (i.e. a dose below which no health effects are expected) and non-threshold health effects, where even low doses are associated with a low risk for health effects. For non-threshold effects, such as those that are exhibited by genotoxic carcinogens, an acceptable risk level often defined, and the toxicological reference value refers to the dose which is equivalent to the acceptable risk level. The acceptable risk level varies between authorities, partly depending on the type of assessment being carried out. Most usually, a lifetime risk of one extra cancer per 100 000 exposed ($1 \cdot 10^{-5}$) is used, but in some cases $1 \cdot 10^{-4}$ and $1 \cdot 10^{-6}$ are the risk levels applied.

The toxicological risk value in the case of non-threshold effects is calculated from the slope of the dose-response relationship, often called the slope factor (oral or inhalation), or cancer potency factor.

2.2.1 EFSA

EFSA (2009) assessed the risks to human health related to the presence of inorganic arsenic in food. Modelling of the dose- response data from key epidemiological studies was reported and the results of other dose-response modelling studies were reported. EFSA found that the evidence is sufficient to assume causality for skin lesions and for cancers of the urinary bladder, lung and skin. Therefore, the data for cancers of the urinary bladder, lung and skin, which are causally associated with oral exposure to inorganic arsenic, and skin lesions were considered as possibly providing an appropriate reference point.

A benchmark response of 1 % extra risk was selected because it could be within the range of the observed data. A limitation in all of the available studies is that total dietary exposure to inorganic arsenic was not measured. In most studies, the concentration of arsenic in drinking water was used as the exposure metric. Because of the uncertainties in the exposure in the key epidemiological studies, a range of values for the 95 % lower confidence limit of the benchmark dose of 1 % extra risk ($BMDL_{01}$) was identified for each endpoint. The lowest $BMDL_{0.1}$ was for lung cancer.

A range of benchmark dose lower confidence limit ($BMDL_{01}$) values between 0.3 and 8 µg/kg b.w. per day was identified for cancers of the lung, skin and bladder, as well as skin lesions.

EFSA concluded that the provisional tolerable weekly intake (PTWI) of 15 µg/kg b.w. established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) is no longer appropriate as data had shown that inorganic arsenic causes cancer of the lung and urinary bladder in addition to skin, and that a range of adverse effects had been reported at exposures lower than those reviewed by the JECFA.

2.2.2 JECFA (FAO/WHO)

Arsenic was evaluated by JECFA (Joint FAO/ WHO Expert Committee on Food Additives Committee) in 1983 and in 1988. The most recent evaluation was published by JECFA in 2011.

The review in 1983 concluded that on the basis of the data available the Committee could arrive at only an estimate of 0.002 mg/kg b.w. as a provisional maximum tolerable daily intake for ingested inorganic arsenic; no figure could be arrived at for organic arsenicals in food". This was based on the observation that health effects can be observed in association with water supplies containing an upper arsenic concentration of 1 mg/l or greater and that a

concentration of 0.1 mg/l may give rise to presumptive signs of toxicity. Assuming a daily water consumption of 1.5 litres, the Committee concluded that inorganic arsenic intakes of 1.5 mg/day were likely to result in chronic arsenic toxicity and that daily intakes of 0.15 mg may also be toxic in the long term to some individuals.

The Committee noted that the International Programme on Chemical Safety (IPCS) had estimated that an arsenic concentration of 0.2 mg/l in drinkingwater would lead to a 5% lifetime risk of skin cancer, but that skin cancer did not occur in the absence of other toxic effects due to arsenic.

In 1988, JECFA considered information relevant to assessing the significance of organoarsenicals in fish. The previous evaluation was confirmed by assigning a provisional tolerable weekly intake (PTWI) of 0.015 mg/kg body weight (bw) for inorganic arsenic, "with the clear understanding that the margin between the PTWI and intakes reported to have toxic effects in epidemiological studies was narrow" (Annex 1, reference 84). The Committee noted that the organic forms of arsenic present in seafood needed different consideration from the inorganic arsenic in water. It concluded that there had been no reports of ill-effects among populations consuming large quantities of fish that result in organoarsenic intakes of about 0.05 mg/kg bw per day, but further investigation would be desirable to assess the implications for human health of exposure to naturally occurring organoarsenic compounds in marine products.

In 2011, JECFA was asked to consider all information related to the toxicology and epidemiology, exposure assessment, including biomarker studies, analytical methodology, speciation and occurrence in food and drinking-water, in order to re-evaluate and review the PTWI for *inorganic* arsenic. The evaluation concluded that the former PTWI for inorganic arsenic is in the region of the $BMDL_{0.5}$ and therefore was no longer appropriate. The previous PTWI was withdrawn, but no new value has been given. Based partly on new data, JECFA calculated a $BMDL_{0.5}$ of 3 µg/kg body weight and day for an icreased incidience of lung cancer of 0.5 % over background. This is equivalent to 0.006 µg/kg and day for a risk for 1 extra cancer per 100 000 exposed.

2.2.3 USEPA, ATSDR

In the United States, assessments have been made by USEPA and by ATSDR.

USEPAs IRIS database (IRIS, 2017) contains the following toxicological reference values for inorganic arsenic:

Reference dose for effects other than cancer (RfD)	3 x 10^{-4} mg/kg bodyweight and day
Oral slope factor; risk for cancer	1.5 per mg/kg and day (equivalent to 0.0066 µg/kg day for a risk of 1 in 100 000).
Inhalation slope factor; risk for cancer	4.3 x10^{-3} per µg/m^3

The above values were last updated in 1991 (non-cancer effects) and 1995 (risk for cancer).

2010, EPA released a revised draft inorganic arsenic assessment, focused on cancer health effects following oral exposure to inorganic arsenic, for public comment and review by the Science Advisory Board. The oral slope factor for cancer risk was estimated to be 25.7 per mg/kg body weight and day, based on the risk for internal cancer (lung and bladder) and for women, who are the most sensitive population. This is an increase in the estimated cancer potency for inorganic arsenic, and the main difference between this estimate and earlier

estimates is differences in the dose-response models and changes in the assumptions related to the relative drinking water consumption by the USA population and other populations, as well as epidemiological data from the USA. However, the report is not yet finalized.

Comments and recommendations on the draft were received in 2011. The EPA is now working to develop an updated IRIS assessment of inorganic arsenic (focused on both cancer and noncancer health effects). When a draft assessment has been developed, EPA will submit it for peer review and review by the National Research Council.

ATSDR in the United States published a toxicological profile for arsenic in 2007.

A MRL for chronic exposure for inorganic arsenic of 0.0003 mg/kg body weight and day was established, based on dermal effects. This value, based on epidemiological studies was calculated from the NOAEL value and a safety factor of 3 (to account for human variability).

For organic forms of arsenic, ATSDR, (2007), established MRLs for chronic exposure of 0.01 mg/kg body weight and day for MMA (based on effects in the gastrointestinal tract in rats), For DMA a chronic MRL of 0.02 mg/kg body weight and day was based on effects on the bladder in mice for DMA. Both of the MRLs for organic forms of arsenic were calculated from the $BMDL_{10}$ using an uncertainty factor of 100.

2.2.4 France

The toxicological reference values for inorganic arsenic given by Ineris (2010) are shown below. The sources of the values chosen are also shown:

Type of value and effect	Value	Source
Chronic oral, threshold effelcts	0.45 µg/kg bodyweight and day	Forschungs- und Beratungsinstitut Gefahrstoffe GmbH (FoBiG) (See Schuhmacher-Wolz et al. 2009.
Chronic inhalation, threshold effects	1.5 x 10^{-5} mg/m^3	Californian EPA
Oral slope factor, non-threshold effects	1.5 per mg/kg body weight and day	USEPA
Inhalation, non-threshold effects.	4.3 x 10^{-3} per µg/m^3	US EPA

2.2.5 Germany

In Germany, there are no nationally established toxicological reference values, and recommendations are usually based on the European values (EFSA, 2009). However, in Saxony, the Daily tolerable resorbed dose (TRD) of 0.45 µg inorganic arsenic per kg bodyweight and day, established by FoBiG (see Schuhmacher-Wolz et al., 2009), is used in risk assessments. This value is based on epidemiological data for the occurrence of skin lesions and is based on $BMDL_{05}$ of 109.2 µg arsenic per day (body weight 55 kg), using an extrapolation factor of 5. The evaluation does not include any consideration of carcinogenic effects as skin lesions occur at lower doses than those necessary for other health effects to occur.

2.3 Dietary exposure

EFSA (2014) collated more than 100,000 occurrence data from 15 European countries on arsenic in food with approximately 98 % reported as total arsenic. Two thirds of the samples were below the limit of detection. Making a number of assumptions for the contribution of inorganic arsenic to total arsenic, the inorganic arsenic exposure from food and water across 19 European countries, using lower bound and upper bound concentrations, has been estimated to range from 0.13 to 0.56 µg/kg bodyweight (b.w.) per day for average consumers, and from 0.37 to 1.22 µg/kg b.w. per day for 95th percentile consumers.

This estimate can be compared with the estimate from JECFA (WHO, 2011) which reported mean dietary exposure to inorganic arsenic in the USA and various European and Asian countries ranged from 0.1 to 3.0 µg/kg bw per day. Drinking water was a major contributor to total inorganic arsenic dietary exposures and, depending on the concentration, can also be an important source of arsenic in food through food preparation and possible irrigation of crops. At the lower end of the exposure range, food can also be a major contributor to total inorganic arsenic exposure.

The minimum and maximum dietary exposure varied by a factor of 2 to 3 across the 19 European countries, due to on different dietary habits rather than different occurrence data. Extrapolating from the main food categories of the EFSA Concise Food Consumption Database the food subclasses of cereal grains and cereal based products, followed by food for special dietary uses, bottled water, coffee and beer, rice grains and rice based products, fish

and vegetables were identified as largely contributing to the inorganic arsenic daily exposure in the general European population.

High consumers of rice in Europe, are estimated to have a daily dietary exposure of inorganic arsenic of about 1 µg/kg b.w. per day, and high consumers of algae-based products can have dietary exposure of inorganic arsenic of about 4 µg/kg b.w. per day. The limited available evidence does not indicate a different dietary exposure for vegetarians from that of the general population, unless they consume a large amount of algae-based products.

Children under three years of age are the most exposed to inorganic arsenic. Exposure estimates reported in two different studies show an inorganic arsenic intake ranging from 0.50 to 2.66 µg/kg b.w. per day. Dietary exposure to inorganic arsenic for children under three years old, including from rice-based foods, is in general estimated to be about 2 to 3-fold that of adults. These estimates do not include milk intolerant children substituting rice-drinks for formula or cows' milk.

2.3.1 Speciation of arsenic in dietary components

Approximately 98 % of the results were reported as total arsenic, and only a few investigations differentiated between the various arsenic species. The highest total arsenic levels were measured in the following food commodities: fish and seafood, food products or supplements based on algae, especially hijiki, and cereal and cereal products, with particularly high concentrations in rice grains and rice-based products, and bran and germ. Depending on the type of food processing, temperature and time, changes in total arsenic concentration and arsenic species may occur.

As representative speciation data are scarce, EFSA was not able to assess the typical ratios between inorganic and organic arsenic in different groups of foodstuffs. Consequently, a number of assumptions had to be made about the contribution of inorganic arsenic to total arsenic in the exposure assessment. The proportion of inorganic arsenic was assumed to vary from 50 to 100 % of the total arsenic reported in food commodities other than fish and seafood, with 70 % considered as best reflecting an overall average. These estimates are confirmed by the study made by the Swedish National Food Agency, who found that in rice, inorganic arsenic was on average 67 % (between 33 and 91 %) of the total amount of arsenic. (Swedish National Food Agency 2015a).

In fish and seafood, the relative proportion of inorganic arsenic is small and tends to decrease as the total arsenic content increases, and the ratio may vary depending on the seafood type. Based on the limited data on inorganic arsenic in the present dataset and on published data, fixed values for inorganic arsenic of 0.03 mg/kg in fish and 0.1 mg/kg in seafood were considered realistic for calculating human dietary exposure.

2.4 Risk characterization

EFSA (2009) concluded that the estimated dietary exposures to inorganic arsenic for average and high level consumers in Europe are within the range of the BMDL01 values identified, and therefore there is little or no margin of exposure and the possibility of a risk to some consumers cannot be excluded. Because there is little margin of exposure, the interpretation and communication of risk assessments for arsenic may sometimes be difficult.

The National Food Agency in Sweden has used a method called the "Risk Thermometer" to help with the evaluation of risks from arsenic in food (Swedish National Food Agency 2015b). The Risk Thermometer describes risks in the case of chronic exposure to a substance.

The Risk Thermometer shows risks from a chemical element in food for an exposed group (for example, children) on a five-point scale; from no risk, insignificant risk, medium risk, significant risk and high risk. The results of the risk evaluation can be presented graphically, to aid understanding of the risk situation. An example is shown in Figure 2-2 below.

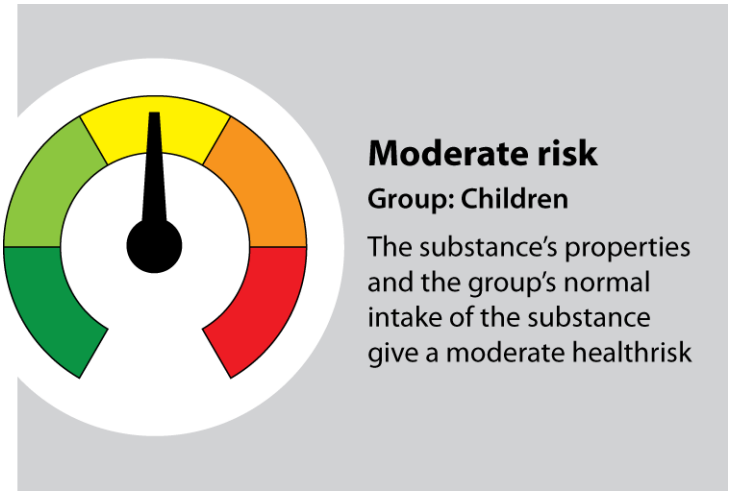

Figure 2-2 Swedish National Food Agency's classification of the risks from arsenic in food with the Risk Thermometer (redrawn from www.livsmedelsverket.se).

The Risk Thermometer is based on the same toxicological reference values for chemicals as those used in other risk assessments (se chapter 2). However, the Risk Thermometer uses the Margin of Exposure (MOE); the quote between the toxicological reference value and actual exposure to the substance. As long as the MOE is greater than 1, the exposure is lower than the reference value and the risks for health are judged to be insignificant. An MOE of 1 means that exposure is equivalent to the toxicological reference value, which describes a small increase in risk or effect, usually 10%, with respect to a certain health effect (BMD_{10}). Note that exposure to a substance can vary between different groups of the population because of difference in diet and therefore the MOE can also vary. The MOE is therefore an indirect measure of risk. If exposure is reduced, the MOE-value increases and the risk is therefore reduced.

Another difference between the risk thermometer and the more usual way of evaluation risks from chemicals in food is that the Risk Thermometer also the nature of the health effect that the toxicological reference value describes. The more usual method for evaluation risks takes into the relationship between dose a parameter which is more or less related to the occurrence of a harmful effect. For some substance, the toxicological reference value is related to indicators of the occurrence of a fairly mild health effect, whereas for other substances the toxicological value is related to the actual occurrence of a serious disease. The Risk Thermometer includes a classification system that ranks different health-parameters, where a mild effect is ranked which does not directly relate to the occurrence of a disease, is ranked lower than a parameter which directly describes the frequency of disease. The health effect classification scheme is shown in Figure 2-3.

Health effect classification scheme where the severity factor, SF = 10^x.

Category 1			Category 2			Category 3		
1a $x = 0$ (mild)	**1b** $x = 0.5$	**1c** $x = 1$ (moderate)	**2a** $x = 0.5$	**2b** $x = 1$ (moderate)	**2c** $x = 1.5$	**3a** $x = 1$ (moderate)	**3b** $x = 1.5$	**3c** $x = 2$ (severe)
Early clinical signs of toxicity **1a)**: For example, ruffled hair or changed activity in experimental studies, or irritation (e.g., redness, salivation) of epithelial or mucosal surface in contact with chemical. **Markers of toxicity** Changes in biological parameters considered or suspected to be early precursors of adverse response or disease. **1a)**: Change in biological or bio-chemical parameter unspecifically related to Category 2 or 3 effects (e.g., hematology, red blood cells, hematocrit, plasma protein). **1b)**: Change in precursor for Category 2 effects. **1c)**: Change in precursor for Category 3 effects.			**Hepatotoxicity or nephrotoxicity** Effects on the liver or kidney. **2a)**: Change in liver/kidney enzyme/marker levels. Change in relative liver/kidney weight. **2b)**: Change in liver/kidney pathology/function. **2c)**: Manifest liver/kidney disease. Increase of cell necrosis. Severe organ dysfunction. **Neurotoxicity** Effects on the nervous system. **2a)**: Change in (mild) neurochemical or neurophysiological markers. **2b)**: Change in central or peripheral neuropathology. Change in brain weight. **2c)**: Change in behavioral or neurological/neurophysiological endpoints. Manifest disease. **Pulmonary or cardiovascular toxicity** Effects on either the lung or lung function or the heart or heart function. **2a)**: Change in clinical chemistry parameters/markers. **2b)**: Change in function (e.g., change in blood pressure, ECG rhythm). Hypertrophy or hyperplasia. **2c)**: Manifest disease, severe organ dysfunction. **Immunotoxicity** Effects on the immune system. **2a)**: Change in immune cell parameters/markers (e.g., antibody or cytokine/chemokine levels, lymphocyte numbers). **2b)**: Functional effects on the immune system (e.g., reduced antibody production, decreased NK cell activity). Sensitization. **2c)**: Reduced host resistance in experimental infection and tumor models. Allergic reactions.			**Developmental toxicity** Effects on the developing organism that may result from exposure prior to conception, during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include; death of the developing organism, structural abnormality, altered growth, and functional deficiency (EPA 1991). **3a)**: Change in offspring or-gan/body weight or size, and litter data. **3b)**: Functional deficiencies; alterations/delays in the physiological and/or biochemical competence of an organ or organ system. Mild structural variation. **3c)**: Increase in offspring malformations (teratogenicity; moderate/severe structural variation). Severe functional deficiencies. Death of developing organism. **Reproductive toxicity** Effects on the reproductive capacity of the parent generation. **3a)**: Change in biochemical markers (e.g., hormones, enzymes). Change in reproductive organ weights. **3b)**: Pathological changes in reproductive organs. Functional effects of changes in estrus cycle. Change in sperm counts, motility, or morphology. Change in duration of pregnancy. **3c)**: Decreased fertility or number of fetuses.		

Figure 2-3 The health effect classification scheme in the Swedish Food Agency's Risk Thermometer methodology (taken from Swedish Food Agency, 2015a).

According to the Risk Thermometer methodology, the toxicological reference value is adjusted downwards according to the classification of the health-parameter, by a factor of 1 to 100. The resulting reference value is called the "severity adjusted reference point" or SARP. The quote between the SARP and the actual exposure is called the severity adjusted margin of exposure, or SAMOE. The relationship between the SAMOE and risk class is shown below in

Table 2-1 Relationship between the risk thermometer and traditional risk assessment metrics (from Swedish Food Agency, 2015a).

SAMOE	Risk class	Concern level	Risk
<0.01	5	High	>5 in 1000
0.01-0.1	4	moderate to high	5 in 1000 to 5 in 10 000
0.1-1	3	low to moderate	5 in 10 000 to 5 in 100 000
1-10	2	none to low	5 in 100 000 to 5 in 1 000 000
>10	1	none	<5 in 1 000 000

The methodology also includes an assessment of the uncertainties associated with the SAMOE.

For arsenic, the Swedish National Food Agency's assessment with the Risk Thermometer was based on JECFA's toxicological risk values (Swedish National Food Agency, 2015c). This was partly because newer data were taken into account than in the EFSA assessment (JECFA did take EFSAs assessment into account). The JECFA assessment was also preferred because the main reference point ($BMDL_{0.5}$) of 3.0 µg per kilo body weight per day refers to cancer (lung cancer) specifically, while EFSA range of reference points also includes skin lesions, which were judged to be less serious health effects than cancer. The $BMDL_{0.5}$ was adjusted to the equivalent of BMD_{10}.

The severity factor was assumed to be a factor of 100, as the critical effect in the case of arsenic is cancer.

Various exposure scenarios were considered, and the results of the assessment are shown in Figure 2-4 .

This type of method may offer a way of presenting the results of risk assessments for arsenic from a contaminant source, where traditional methods are made difficult because of the large contribution from background exposure to the total exposure.

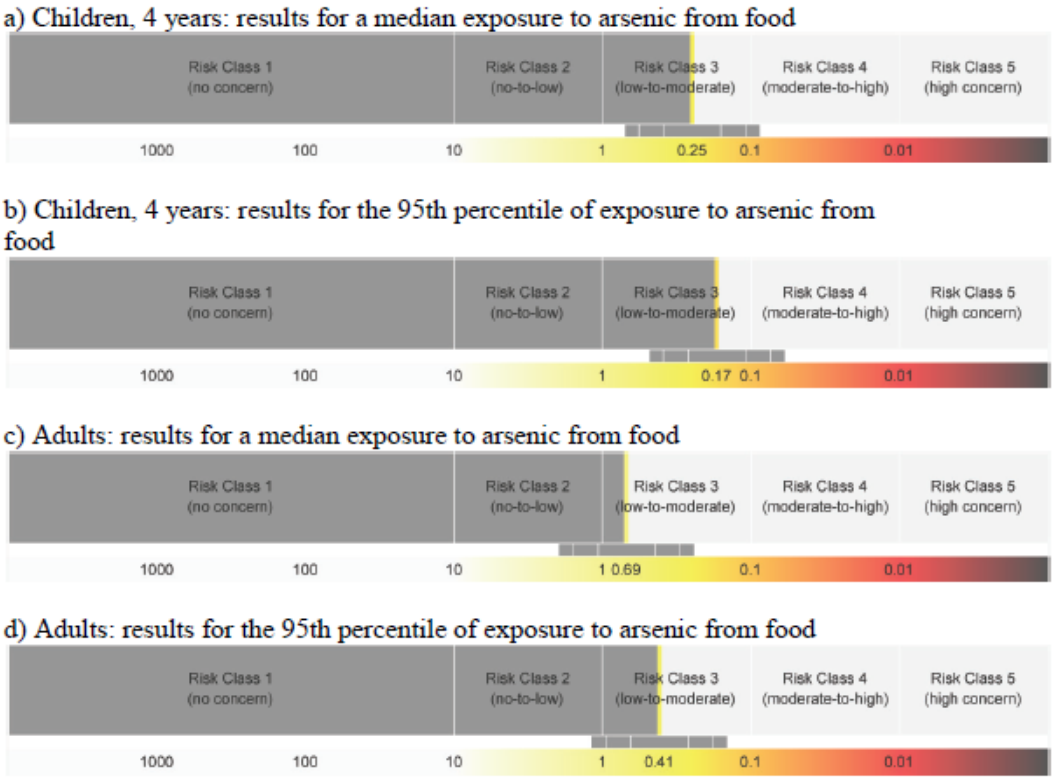

Figure 2-4 Results of the risk thermometer for arsenic and 4 year-old children and adults who consume rice. The wide grey bars show the size of the SAMOE value. The thin grey bars show the uncertainty interval: The ends of the intervals describe the 5th and 95th confidence limit and lines show the 10th and 90th and the 25th and 75th confidence limits (taken from Swedish Food Agency, 2015c).

3 Biomarkers of arsenic exposure in humans

In the assessment of health risks from exposure to arsenic, biomarkers are used. Biomarkers in human health studies are typically divided into three groups; biomarkers of exposure, effect and susceptibility (Silins and Högberg, 2011).

Exposure assessment is complex when exposure may occur via multiple pathways, routes and media. Human biomonitoring gives a snapshot of internal or absorbed dose and is often the most reliable exposure assessment methodology as it integrates exposure from all routes. As an alternative to the estimation of arsenic exposure from concentrations in environmental media using exposure models, biological monitoring may be used to provide data on the absorbed dose for each individual studied. For arsenic, a number of different biomarkers have been used as measures of the internal exposure. Some are used as indicators of acute exposure, some as indicators of chronic exposure. Biomarkers of exposure, preferable specific to arsenic, can involve measurements of the parent compound, metabolites of DNA- or protein adducts and reflect internal doses, biologically effective doses or target doses. The most usual biomarkers of exposure are discussed in sections 3.1.1- 3.1.4, below. The review of Marchiset-Ferlay et al. (2012) gives many examples of studies of the relationship between exposure to arsenic in drinking water and the concentrations in different biological samples.

Biomarkers of effects can be changes on a cellular level, such as altered expression of metabolic enzymes, but can also include markers for early pathological changes in disease development, such as mutations and lesions. Sometimes biomarkers of exposure and effect can overlap, e.g. DNA adducts can be biomarkers of exposure, but also imply an effect. Biomarkers of susceptibility indicate the ability of an individual to respond to specific exposures.

In many investigations, the correlation between biomarkers of exposure and biomarkers of effects are studied. A brief section is included below about the biomarkers of the effects of exposure to arsenic. Biomarkers of susceptibility are also briefly mentioned in the sections below.

3.1.1 Arsenic in urine

The concentration of total arsenic in urine has often been used as an indicator of recent exposure, because urine is the main route of excretion of most arsenic species. The half-life of inorganic arsenic in humans is about 4 days (se NRC, 1999, Hughes, 2006, Kippler et al. 2016). Background levels of urinary arsenic range from 5- 50 µg/l (Hughes, 2006). However, the total arsenic concentration in urine provides no information about the form of arsenic absorbed. Some foods, especially fish and shellfish, have high concentrations of arsenic mainly in the form of arsenobetaine, which is not metabolized in the body but is rapidly excreted in the urine. These foods give a rapid increase of total arsenic in the urine, which disturbs the correlation between urinary total arsenic concentration and exposure to total inorganic arsenic.

Correlations have been observed between the concentration of arsenic in urine and in water, soil, and air. For inorganic arsenic in drinking water, correlations are generally very clear. For inorganic arsenic in soil, the relationship to urinary arsenic is less straightforward, being influenced by arsenic geochemistry and bioavailablity. For air, both linear and non-linear relationships have been observed.

The concentration of the metabolites of inorganic arsenic in urine (monomethylarsonic acid, MMA and dimethylarsonic acid, DMA) give a better measurement of the intake of inorganic

arsenic. Exposure to MMA or DMA will influence the estimate, but such exposure is low in most countries and situations. Only the consumption of some shellfish and seaweed may give rise to consumption of significant amounts of DMA. Population averages of arsenic metabolites in the urine correlate with the average concentrations of arsenic in drinking water. However, the relationship between the metabolite concentration in water and in urine varies from population to population, depending on the amount of water consumed and the amount of water used for cooking.

Because of the variations in the proportions of different arsenic metabolites in urine, the concentration of the sum of the metabolites is a better indicator of exposure than is the concentration of inorganic arsenic or DMA in urine. A number of studies (reported in NRC, 1999) have reported that on average, background concentrations of inorganic arsenic and its metabolites (inorganic arsenic + MMA + DMA) in urine are generally below 10 µg/l. The proportion of arsenic occurring in metabolites in the urine compared with in the inorganic arsenic has been used as an indicator of the efficiency of the metabolism of inorganic arsenic (for example, Gardon et. al, 2016, Skröder Löverborn et al, 2016), and thus as a biomarker of the susceptibility to the toxic effects of arsenic. This efficiency varies between populations, and is influenced by a number of factors, including nutritional status.

One point to consider when planning and interpreting studies of urinary arsenic concentrations is the period of time over which urine is collected. Ideally, 24-hour samples should be assessed, but because of practical difficulties, spot samples or first-morning samples may be analysed. The dilution of the urine should also be considered. To compensate for the dilution, the concentration of arsenic can be related to the concentration of creatinine or to the specific gravity.

3.1.2 Arsenic in blood

Most of the absorbed inorganic and organic arsenic has a short half-life in blood (NRC, 1999), and therefore analysis of arsenic in blood is best suited for recent, high-dose exposures (Hughes, 2006). However, if exposure is continuous and steady, such as exposure through drinking water, the blood arsenic might reach a steady state and then reflect the degree of exposure. Background arsenic blood levels range from 0.5 – 2 µg/l (NRC, 1999). An example of studies using blood as a biomarker of exposure is Abhinav et al. (2016). Generally, total arsenic concentrations are reported in blood; speciation of arsenic has been reported in only a few studies. As with studies of arsenic in urine, the consumption foodstuffs with high concentrations of organic arsenic, such as seafood, may interfere with studies of inorganic arsenic intake.

Compared with urine, blood arsenic concentrations are a much less sensitive biomarker of exposure to arsenic via drinking water.

3.1.3 Arsenic in hair and nails.

Arsenic concentrations are normally higher in hair and nails than in other parts of the body, because of the binding of trivalent inorganic arsenic to the keratin in these tissues. Arsenobetaine, the major organic arsenic compound in seafood, and other forms of organic arsenic such as arsenocholine and arsenosugars, are not accumulated in hair, and therefore, arsenic in hair reflects exposure to inorganic arsenic only. Incorporation of DMA in skin and hair has also been reported to be low (NRC, 1999).

Background concentrations of arsenic in hair are reported to be <1µg/g and in nails from <1.5 – 7.7 µg/g (studies reviewed in Hughes, 2006).

The concentration of hair at the hair root is in equilibrium with the blood. Therefore, varying arsenic exposure over time is reflected in variation of the arsenic concentration along the length of the hair.

The main disadvantage of using hair and nails as indicators of exposure to arsenic is external contamination via air, water and detergents, making it difficult to distinguish between arsenic incorporated into the hair from the blood and arsenic bound externally eg. when washing with water containing arsenic. Therefore, hair and nails are good biomarkers for exposure but not of absorbed dose. However, this problem is less important in newborns, and nails have been used as a biomarker for this group.

On a group basis, the correlation between the concentration of arsenic in drinking water and the concentration in hair is good (see studies reviewed in Hughes, 2006). Toenails were also reported to be suitable biomarkers of exposure at sites with elevated environmental As, such as former mining sites (Button et al., 2008).

3.1.4 Other media

Placental arsenic concentrations have been studied in order to assess their potential as biomarkers of both maternal and infant exposures (Punshon et al., 2016). Placenta arsenic concentrations were related to arsenic concentrations in maternal urine, maternal and infant toenails and household drinking water. Thus, the data suggest that placenta arsenic concentrations reflect both maternal and infant exposures.

Sampling of exfoliated buccal cells and urothelial cells has also been used for biomonitoring with the detection of micronuclei in these media functioning as a biomarker for exposure, see for example, Bandyopdhyay et al, (2016) and Marchiset- Ferlay et al. (2012).

3.1.5 Biomarkers of the effects of arsenic exposure

The epidemiologically associated human diseases resulting from arsenic exposure include a variety of cancers (e.g. lung, urinary, bladder, liver, kidney, pancreas, skin) and cardiovascular disease. Major biological effects that may link arsenic to the diseases include the generation of reactive oxygen species (ROS) leading to oxidative stress and DNA damage, induction of epigenetic DNA modification, induction of genomic instability, inflammation and effects on the immune system (Rao et al., 2017). Biomarkers of all of these types of effects have been considered as biomarkers of the effects of arsenic. Evaluations have included;

- Histopathological evaluation of tissues of interest. An example is the use of several assays related to the capability of wound repair to study the effects of arsenic on the cardio-vascular system (Krohn, et al, 2016).
- DNA damage evaluation. Base oxidation is one of the most frequent forms of DNA-damage and the end products of oxidative DNA-damage are often used as biomarkers (Silins and Högberg, 2011). These include 8-oxodG and 8-OHdG (Chou et al, 2014) and Xu et al, 2008). DNA-methylation is also a form of DNA-damage and a biomarker of this type of damage is N^7-MeG (N^7-methylguanine), which was also used in the study of Chou et al. DNA-methylation of specific, cancer related genes has also been studied by Engström et al., (2016).
- ROS-related biomarkers and antioxidant enzymes (for example glutathione-S-transferase (GST), superoxide dismutase (SOD), catalase (CAT)

- Anti-oxidative activity, which decreases with arsenic exposure in tissues of interest
- Lipid oxidation as a marker of ROS exposure
- Markers for tissue damage such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and bilirubin
- Biomarkers for genotoxic effects, such as chromosome aberrations, sister chromatid exchange, micronuclei and aneuploidy are markers of early effects related to cancer.
- Tissue-specific cellular assay such as sperm motility
- Behavioural evaluation.

Some of these biomarkers have been used mainly in animal studies, though there are many studies where biomarkers of effect have been used in human health risk assessment (se Marchiset-Ferlay et al. 2012).

Combinations of biomarkers have been used in health risk assessment. Rapid health risk assessment of contaminated water releases to a river were carried out by Ng et al. (2016) using the following tests; Cytotoxicity (MTS assay), oxidative stress response (Nrf2 induction in Antioxidant Response Element-reporter cells), and genotoxicity (micronucleus test).

In a review of biomarkers for oxidative stress and damage from arsenic exposure in humans, Vizcaya-Ruiz et al (2009) found the most used biomarkers of oxidative stress and damage to be the urinary excretion of 8-OHdG (a guanine oxidation product), the comet assay in lymphocytes, and DNA-repair mechanism markers.

Metabolomics, involving multivariate analysis of metabolites in blood and urine has also been used to find biomarkers for arsenic (Stybo M et al. 2016). Zhang et al., (2014) have studied the use of urinary metabolomics and identified five potential biomarkers related to arsenic exposure (i.e., testosterone, guanine, hippurate, acetyl-N-formyl-5-methoxykynurenamine, and serine) from 61 candidate metabolites. These biomarkers suggest that endocrine disruption and oxidative stress were best associated with urinary arsenic levels.

Biomarkers of arsenic methylation efficiency have also used to study susceptibility to arsenic. Methyl transfer is mainly accomplished by the arsenic (3+)-methyltransferase (AS3MT). Polymorphisms in the AS3MT-genes accounts for differences in the efficiency of arsenic methylation. Harari et al (2016).

4 Criteria for drinking water

In Europe, the concentration limit of 10 µg/l for arsenic in drinking water is given by EU directive 98/83/EC, on the quality of water intended for human consumption.

WHOs drinking water guidelines also give the value of 10 µg/l for arsenic. This guideline was based on the JECFA PTWI of 15 µg/kg body weight, assuming an allocation of 20% to drinking-water, which was withdrawn (JECFA 2011). Nevertheless, the WHO retained the drinking water guideline on the basis of "treatment performance and analytical achievability" (WHO, 2017) with the proviso that every effort should be made to keep concentrations as low as reasonably possible. With respect to treatment performance, the WHO assume that removal of arsenic to concentrations below 10 µg/l is difficult in many circumstances, particularly from small supplies. In view of these practical difficulties the guideline value of 10 µg/l is retained as a goal and designated as provisional.

In the USA, the USEPA have also set a drinking water standard for arsenic of 10 µg/l (USEPA, 2001), and in Canada, Health Canada have also adopted 10 µg/l in their drinking water guidelines (Health Canada, 2017a).

In France and in Germany the EU directive has been implemented and therefore the limiting concentration is 10 µg/l. In France, the directive has been implemented by Décret nº 2001-1220 and in Germany by the Trinkwasserverordnung (drinking water directive) (TrinkwV 2001 as amended by the Ordinance (Änderungsverordnung) dated 18.11.2015).

In 2015 the Association of Dutch drinking water companies (Vewin) concluded that a guideline value of arsenic (1.0 µg/l) is both achievable and appropriate in the Netherlands. This conclusion followed the WHO-guideline to keep the concentrations of arsenic in drinking water as low as reasonably possible. The decision was based on a conservative estimation of human health effects of arsenic exposure via drinking water as well as on arsenic-removal cost/health benefit analysis.

5 Criteria for foodstuffs

In Europe, the Commission Regulation (EU) 2015/1006 of 25 June 2015 amending Regulation (EC) No 1881/2006 as regards maximum levels of inorganic arsenic in foodstuffs gives the concentration limits for rice and rice products shown in Table 5-1:

Table 5-1 Concentration limits for arsenic in rice products (EU 2015/1006)

Rice product	Arsenic (mg/kg wet weight)
Non-parboiled milled rice (polished or white rice)	0.20
Parboiled rice and husked rice	0.25
Rice waffles, rice wafers, rice crackers and rice cakes	0.30
Rice destined for the production of food for infants and young children.	0.10

Rice is not produced at the AgriAs test sites, and therefore these criteria are not directly applicable the risk assessment to be carried out. However, the criteria are examples of criteria for foodstuffs, and the method for derivation of the criteria may be applied to other foodstuffs.

The concentration limits were set with regard to the EFSA study (EFSA, 2009) in which consumers of large amounts of rice were found to be the most highly exposed group. The limit rice products intended for young children takes into account that childrens' exposure to arsenic is greater than that of adults. The concentration limits refer to the total of As(III) and As(V).

In the USA, the FDA (2016) have also proposing an action level for inorganic arsenic in infant rice cereals of 100 µg/kg (0.1 mg/kg), intended to reduce the possible risks of neurodevelopmental and other health effects. The FDA (2013) have also proposed action levels for inorganic arsenic in apple and pear juice of 10 (µg/kg) for single-strength (ready to drink) apple juice. FDA considers the action level for inorganic arsenic in apple juice to be protective of public health, particularly with regard to the high consumption of apple juice by children. The FDA is also proposing to apply this action level to pear juice (FDA, 2012).

In Canada, part 2 of Health Canadas List of Contaminants and other Adulterating Substances in Foods (Health Canada, 2017b) includes the concentration limits shown in Table 5-2. The list forms part of Canadas food and drug regulations.

Table 5-2 Concentration limits for arsenic in some foodstuffs (Health Canada, 2017b)

Foodstuff	Arsenic, mg/kg (wet weight)
Fish protein	3.5
Edible bone meal	1
Fruit juice, fruit nectar, beverages when ready to serve, water in sealed containers other than mineral water or springwater.	0.1

In Australia and New Zealand, a list of maximum levels of contaminants and natural toxicants, which is part of the Australia New Zealand Food Standards Code, includes the concentration limits (ANZ, 2017) shown in Table 5-3:

Table 5-3 Concentration limits for arsenic in some foodstuffs (ANZ, 2017)

Form of arsenic	Foodstuff	Arsenic (mg/kg wet weight)
Arsenic, total	Cereal grains and milled cereal products	1
	Salt	0.5
Arsenic, inorganic	Crustacea	2
	Fish	2
	Molluscs	1
	Seaweed	1

6 Criteria for animal fodder

In Europe, contaminant limits for animal feed are given in Commission regulation (EU) 2015/186 of 6 February 2015. The values given are shown in Table 6-1:

Table 6-1 Contaminant limits for animal feed – arsenic. EU 2015/186

Undesirable substance	Products intended for animal feed	Maximum content in mg/kg (ppm) relative to a feed with a moisture content of 12 %
'1. Arsenic (1)	Feed materials with the exception of:	2
	– meal made from grass, from dried lucerne and from dried clover, and dried sugar beet pulp and dried molasses sugar beet pulp;	4
	– palm kernel expeller;	4 (2)
	– phosphates, calcareous marine algae;	10
	– calcium carbonate; calcium and magnesium carbonate (10); calcareous marine shells;	15
	– magnesium oxide; magnesium carbonate;	20
	– fish, other aquatic animals and products derived thereof;	25 (2)
	– seaweed meal and feed materials derived from seaweed.	40 (2)
	Iron particles used as tracer.	50
	Feed additives belonging to the functional group of compounds of trace elements with the exception of:	30
	– cupric sulphate pentahydrate; cupric carbonate; di copper chloride trihydroxide; ferrous carbonate;	50
	– zinc oxide; manganous oxide; cupric oxide.	100
	Complementary feed with the exception of:	4
	– mineral feed;	12
	– complementary feed for pet animals containing fish, other aquatic animals and products derived thereof and/or seaweed meal and feed materials derived from seaweed;	10 (2)
	– long-term supply formulations of feed for particular nutritional purposes with a concentration of trace elements higher than 100 times the established maximum content in complete feed;	30
	Complete feed with the exception of:	2
	– complete feed for fish and fur animals;	10 (2)
	– complete feed for pet animals containing fish, other aquatic animals and products derived thereof and/or seaweed meal and feed materials derived from seaweed.	10 (2)'

Generally, the limit value is 2 mg/kg in feed with a moisture content of 12 %, with a number of exceptions for complementary feed or feed for certain groups of animals. The most notable exception is the limit of 4 mg/kg in dried meal from grass, lucerne, clover and dried pulp of sugar beets.

The Canadian Food Inspection Agency issues regulatory guidance concerning metal contaminants in animal feed (CFIA, 2017). For arsenic, an action level of 8.2 ppm (mg/kg) is given for metal contaminants in total livestock diets on an "as fed" basis, including feeds and forages. Water content at analysis is presumably also on an “as fed” basis.

7 Criteria for soils

7.1 Criteria for contaminated land

In many countries, criteria for contaminated land consider health effects, effects on the soil environment and effects in recipient waters. However, for arsenic, it is usually the value for protection of health which is the lowest value, and therefore which is the determining value for overall integrated guideline values. Guideline values for soils are shown in Table 7-1.

For some of the organisations listed below, it has only been possible to obtain an integrated value. In this case, the value is presented in the section on protection of human health, below.

7.1.1 Protection of human health

Many countries have developed guideline or limiting values for concentrations of arsenic in soils, and it is not possible to review all the values in this report. In the following section, the guideline values from selected organisations are reviewed to show the different types of value which have been developed. The guideline values applicable at the two test sites are discussed at the end of the section.

Types of value

Different types of guideline value are given by different organisations for the protection of human health.

Many organisations give only one type of value, where arsenic concentrations below the guideline value are not considered to give any risks to human health. These organisations may however, give guideline values for different types of land use.

Other organisations give two values; a trigger value and an action value. Concentrations under the trigger value are not assumed to give any risks to human health. Concentrations over the trigger value are indicative of potential risks, and further investigations of the site are necessary. Concentrations over the action value are indicative of serious risks to health, and therefore action is required to reduce risks, e.g. remediation. The Netherlands and Germany (see below) have two types of guideline value.

Exposure pathways considered.

The exposure pathways considered in the models used to derive guideline values are shown in Table 7-2. The models consider direct exposure to soils by oral intake, inhalation of dusts and dermal uptake. They also consider exposure due to the consumption of vegetables grown on the contaminated area and consumption of drinking water that is contaminated by leaching from the contaminated area. Generally, exposure due to consumption of fish or of dairy products, eggs and meat, is not considered. Please note that many countries also consider inhalation of vapours, but this exposure pathway is not considered relevant for arsenic in the models studied.

Table 7-1 Numerical Guideline values for soil

	Land use/type of value	**mg As/kg dry weight**	**Comment**
Swedish EPA, Sweden	Sensitive land use	10	Value protection of health is adjusted upwards so as not to be lower than background concentrations in soils
	Less sensitive land use	25	Based on protection of health
CCME, Canada	Residential	12	Based on protection of health
	Agricultural	12	
	Commercial	12	
	Industrial	12	
RIVM, Netherlands	Residential	27	
	Play areas	27	
	Residential with vegetable garden	27	
	Agricultural	20	
	Nature areas	20	
	Green areas with nature value	27	
	Other green, buildings, infrastructure and industry	76	
USEPA	Soil Screening, ingestion	0.4	
	Soil Screening – inhalation of particles	750	
	Soil Screening – migration to groundwater, dilution factor 20	29	
	Soil Screening – migration to groundwater, dilution factor 1	1	
UK EA, “trigger” values	Residential	32	Health risk based
	Commercial land use	43	Health risk based
	Allotments	640	Health risk based

Table 7-2 Exposure pathways considered in derivation of guideline values.

	Direct oral exposure	Skin contact	Inhalation of dust	Ingestion of drinking water	Ingestion of vegetables grown on the site	Ingestion of animal products from livestock on site or fed fodder produced on site.	Ingestion of fish from recipient water bodies
Swedish EPA, Sweden	X	X	X	X	X		
BBodSchV, Germany	X	X	X	X	X		
CCME, Canada	X	X	X	X	X		
RIVM, Netherlands	X	X	X	X	X		
USEPA SSLs	X		X	X			
UK Environment agency	X	X	X		X		

In the USEPAs soil screening guidance for Superfund sites, generic soil screening levels are given for different exposure pathways and transport pathways. Direct oral exposure, inhalation of dust and ingestion of drinking water are considered to be the most important pathways, though at some sites, the importance of other pathways may need to be considered on a site specific basis.

Land use

In many countries, criteria for contaminated soils are dependent on the land use assumed.

Sweden, (Swedish Environmental Protection Agency, 2009) guideline values are given for sensitive and non-sensitive land uses, where sensitive land use means there are no restrictions concerning the use of the area (e.g. housing, schools, playgrounds, agriculture) and where less sensitive land use means that exposure to the soil is limited because of the type of land use, (e.g. industrial areas, roads, parking spaces).

In Canada, (CCME, 1999a) values are given for four types of land use; Residential, Agricultural, Commercial and Industrial.

In the Netherlands (RIVM, 2007), values are given for a number of different land uses.

In the UK (UK Environment Agency, 2009), guideline values are given for residential and commercial land use and for allotments (vegetable gardens).

Not all countries specifically consider agricultural land use (se criteria for agricultural soils, below).

Consideration of background values

Because arsenic is naturally occurring, all soils have some background concentration of arsenic, even when the soil is not affected by anthropogenic activities.

Germany

In the German regulations there are different levels of values set (BBodSchV) to judge the arsenic concentration in soil. The lowest level is set as a precautionary value meaning to maintain all functional aspects of any soil use. This was not done for As in 1999 when BBodSchV was set into force but there is a recent initiative for an amendment to this act (2017) were it was done. The precautionary value is dependent on soil type: sandy soils: 10 mg/kg, loamy or silty soils as well as clay soils: 20 mg/kg. Below these values soil could pose no risk and could be used for any purpose.

Risk based values were given as trigger (Prüfwerte) or action values (Maßnahmenwerte). The first one means that there could be a risk if exposure may reach a certain but quite unlikely level and therefore an assessment has to be done. If concentration is above the action value, in general there is measures have to be taken to remove or reduce risks (e.g. by remediation). For arsenic there are only trigger values set by regulation and they are based on specific land use scenarios containing standard exposure presumptions. The values are based on the assumption that bioavailability on oral ingestion is 100 %. Oral uptake of arsenic contaminated soil was judged to be the main relevant exposure pathway compared to inhalation or direct skin contact. It is possible to make a site specific adaptation of the risk assessment by analysing the site specific bioavailability to man using DIN 19738, which describes a lab scale stomach-colon-model validated by an animal test.

An overview for the values is shown in Table 7-3:

Table 7-3 Guideline values for arsenic in soil, German regulations.

Land use	**As [mg/kg]**	**path**
Arable land	200	Soil-Plant
Arable land with temporarily reducing conditions	50	Soil-Plant
Influencing plant's growth	0.4 *	Soil-Plant
Green areas	50	Soil-Plant
Playground	25	Soil-Human
Residential area	50	Soil-Human
Parks and leisure facilities	125	Soil-Human
Industrial, commercial/ business area	140	Soil-Human

*Ammonium nitrate extraction; all other values obtained with Aqua regia

In the closest surroundings of people (e.g. playgrounds and residential areas) guideline values for arsenic are much lower compared to arable land. The values for arable land and green areas are focused on the effect of arsenic on the development of plants. Due to the fact that mobility and bioavailability of arsenic is much higher under reducing conditions, the value has to be set much lower for that case.

Due to the fact that mobility and bioavailability of arsenic is much higher under reducing conditions, lower trigger values are set lower for these conditions. For arable land the trigger value is set to 50 instead of 200, if reducing conditions occur. There were several large studies done on the soil-to-plant pathway to support these values. The studies ensured that agricultural produce complies with food and fodder regulation values.

7.1.2 Protection of the environment

A number of organisations have derived guideline values for arsenic in soil based on compilations of literature data on the ecotoxicology of arsenic.

The scope of the underlying database and the method which has been used to derive guideline values by a number of organisations is summarized in Table 7-4. In the third column, the method for derivation, a number of different methods may be given. In this case, the method for the numerical guideline value given comes first.

In this section, full details about the methods used by the different organisations to derive guideline values have not been given. Reference is made to the original reports for more information.

Table 7-4 Summary of the database for environmental risk based guideline values for arsenic in soil

Referece and type of guideline value	Value (mg/kg dry weight)	Method used for derivation	Data used
RIVM MPA (Maximum permissible addition) (RIVM 2001; data compilation 1997)	0.9	The MPA is the lowest NOEC divided by a safety factor of 50 (according to EU/TGD for 3 NOEC values). The 5-percentile of the species sensitivity distribution for microorganisms/processes = 25 mg/kg d.w.	Single species: 3 NOEC-values (observations from 2 groups) Microorganisms: 20 NOEC-values (34 observations of four processes)
RIVM SRA (Serios Risk Addition) & SRC (Serious Risk Concentration) (RIVM, 2001; data compilation 1997)	56 & 85	The geometric mean of chronic data for soil dwelling species. Background concentration = 29 mg/kg d.w. (van den Hoop, 1995) The median value of the species sensitivity distribution for microbial processes, HC50 = 160 mg/kg d.w.	Single species: 3 NOEC-values (4 observations from 2 groups) Microorganisms: 20 NOEC-values (34 observations of four processes)
CCME agricultural/residential (CCME, 1999; data compilation 1997)	17	Species sensitivity distribution with data for soil species. 25-percentile (threshold effects concentration) from the distribution of NOEC and EC_{low} data. Information insufficient to derive a value for microbial processes. Value to protect wildlife on intake of soil and food = 378 mg/kg d.w., based on threshold effect dose of 4 mg/kg body weight/dag, which is the lowest LOAEL, divided by a safety factor of 2 to account for the data being from an acute study.	Soil species: 46 data Microorganisms: 0 Mammals and birds:1 LOEC-value and five LD50-values (or similar) from acute studies. Three data for birds and three for mammals.
CCME industrial (CCME, 1999; data compilation 1997)	26	25-percentile of the distribution of effect data (LC50 and EC50). Information insufficient to derive a value for microbial processes.	Soil species: 27 data Microorganisms: 0
EPA EcoSSL (soil screening level) for plants (USEPA, 2005)	18	Geometric mean of MATC-values (Maximum acceptable toxicant concentration . the geometric mean of the NOAEC- and LOAEC-values.)	3 MATC-values; 22, 69 and 4 mg/kg d.w.
EPA EcoSSL (soil screening level) for invertebrates (USEPA, 2005)	-	USEPA judge the database to be insufficient for the derivation of an EcoSSL for invertebrates	
EPA EcoSSL (soil screening level) for birds (USEPA, 2005)	43	The value is for insect eating birds. TRV-value (Toxicity reference value) = 2.25 mg/kg body weight/d, based on the lowest NOAEL for reproduction, growth and survival. The value is the concentration in soil which is equivalent to the TRV, taking into account the uptake into food, and the consumption of food and of soil. Values for other birds: herbivorous birds, 67 mg/kg d.w. carnivorous birds, 1100 mg/kg d.w.	6 LOAEL-values 8 NOAEL-values 2 NOAEL and LOAEL-values

Referece and type of guideline value	Value (mg/kg dry weight)	Method used for derivation	Data used
EPA EcoSSL(soil screening level) for mammals (EPA, 2005)	46	The value is for insect eating mammals. TRV-value (Toxicity reference value) = 1.04 mg/kg body weight/d, based on the lowest NOAEL for reproduction, growth and survival. The value is the concentration in soil which is equivalent to the TRV, taking into account the uptake into food, and the consumption of food and of soil. Values for other mammals: both herbivorous and carnivorous mammals, 170 mg/kg d.w.	138 NOAEL and LOAEL values
ORNL earthworm (USDoE 1997a)	60	Lowest LOEC, rounded downwards.	Only 1 LOEC, 1 study
ORNL soil processes (USDoE, 1997a)	100	Lowest LOEC, rounded downwards.	LOEC-values from 2 studies
ORNL plants (USDoE, 1997b)	10	10-percentile of LOEC values, rounded downwards.	16 LOEC-values
RIVM MPA (maximum permissible addition) (RIVM, 2015)	0.0012	Based on the species sensitivity distribution of data for soil processes. Note that a safety factor of 5 was applied to the concentration equivalent to protection of 95 % of species. This value is lower than the value for protection of 95 % species from the distribution of data from single species. (0.22 mg/kg d.w).	17 chronic data (NOEC/EC10) for processes and 14 chronic data for single species (insects, macrophytes and worms)
RIVM SRA (serious risk addition) (RIVM, 2015)	0.26	Baserat on the species sensitivity distributionen. Geometric mean of all the chronic data for soil processes. The value is much lower than the geometric mean of data for single species (8.67 mg/kg d.w)	17 chronic data (NOEC/EC10) for processes and 14 chronic data for single species (insects, macrophytes and worms)

In Sweden, two guideline values have been derived for two land uses; sensitive land use, where ecological functions in the soil should not restrict the land use, and less sensitive land use, where some restriction of land use is acceptable. The values are based on the data compilations shown in Table 7-4and are 20 mg/kg d.w. for sensitive land use and 40 mg/kg d.w. for less sensitive land use (Naturvårdsverket, 2016).

France

For the terrestrial compartment Ineris derived a $PNEC_{soil}$ of 1.8 mg kg d.w, which is equal to 1.6 mg/kg soil wet weight. The value is derived from the lowest observed value for *Gossypium hirsutum* (upland cotton) and a safety factor of 10. The databas consisted of 7 NOEC data; two for plants, one for an earthworm and four for microbial processes. Note that this PNEC value is a $PNEC_{additional}$, and is for the added arsenic to the background concentration.

7.2 Criteria for agricultural soils

In the GEMAS survey (Reimann et al., 2014), a compilation was made of soil guideline values for agricultural and grazing land in different European countries. The values compiled are shown in table 7.5:

Table 7.5 Criteria for arsenic (mg/kg d.w.) in agricultural soils and grazing land from European countries. (Compiled in Reimann et al. 2014)

	Agricultural soil	Grazing land
Austria	20	30
Belgium (Brussels) guidelines	35	35
Belgium (Brussels) intervention values	58	58
Bosnia Herzegovina	20	20
Czech Republic	30	30
Denmark	20	20
Germany	200	50
Hungary	15	15
Lithuania	10	10
Montenegro	20	20
Poland	20	20
Serbia	25	
Slovenia	20	20

Some of these criteria are based on phytotoxic effects on plants (effect on the yield). Other criteria are based on the uptake of arsenic into plants, for example, the criteria from Germany for arable land (based on compliance with regulations on foods) and for grazing land (based on compliance with regulations on animal fodder). Criteria in the table from other countries may be based on the health effects that may result from the consumption of agricultural products from the contaminated area.

7.3 Criteria for other purposes

Application of sewage sludge

The EU directive giving criteria for protection of the soil when sewage sludge is to be applied (86/278/EEC) does not contain any criteria for arsenic.

Soil improvers/growing media

Arsenic has not been included in the latest version of the criteria proposed for Ecolabelling of soil improvers and growing media (JRC, 2015). In a previous version (JRC, 2014), 10 mg/kg was suggested for arsenic in growing media, which was the value suggested in a EU decision (COM 2006 and 2007) but this value has now been removed from the proposals. There are also no criteria for arsenic in the ongoing criteria revision for the EU fertilizer regulation.

Allotments/vegetable gardens

In the UK, guideline values are given for soil on allotments of 43 mg/kg dw.

8 Criteria for surface water

8.1 Water Framework Directive

Arsenic is not one of the 45 substances priority substances identified by the EU water framework directive 2000/60/EC, in Decision 2455/2001/EC (33 substances) and Directive 2013/39/EU (a further 12 substances). Therefore, no Environmental Quality Standards (EQS) are defined for arsenic (Directive 2013/39/EU). EQS are limits on the concentration of substances in water (or biota), i.e. thresholds which must not be exceeded if good chemical status is to be met.

However, the competent authorities of European Member States may issue complementary standards for the assessment of the status of surface waters. In Sweden, the Swedish Agency for Marine and Water Management (HaV) have issued complementary standards for arsenic (HaV, 2013). The annual average value is 0.5 µg dissolved arsenic/l and the maximum allowable concentration is 7.9 µg dissolved arsenic/l (dissolved arsenic; after filtration through a 0.45 µm filter). These values are intended to take background concentrations into account.

8.2 Protection of the aquatic environment

A number of organisations have derived guideline values for arsenic in freshwater for the protection of the aquatic environment. A summary of some of these guidelines is given in table 8-1:

Table 8-1 Guideline values for protection of the freshwater environment

Organisation /Reference	Guideline	Derivation of the Guideline value
CCME, (CCME, 2001)	5 µg/l	The lowest chronic toxicity value (a 14-d EC_{50} for the algae *Scenedesmus obliquus*) divided by a safety factor of 10. Chronic data were compiled for 11 species (plants, invertebrates and vertebrates)
USEPA (USEPA, 1984) Freshwater CCC (criterion continuous concentration)	150 µg/l	This value refers to dissolved arsenic. The value was derived in 1984 and is currently being reviewed. The value is based on chronic data for three freshwater species, *Daphnia* and two fish.
USEPA (USEPA, 1984) Freshwater CMC (criterion maximum concentration)	340 µg/l	This refers to dissolved arsenic. The value was derived in 1984 and is currently being reviewed. The value is the mean value of acute toxicity data for 16 freshwater species.
RIVM – Maximum permissible addition (RIVM, 2001)	24 µg/l	HC5 value (protection of 95 % species) from a species sensitivity distribution of pooled freshwater and marine data (no significant difference between freshwater and marine). 15 NOECs from 6 taxonomic groups were available for freshwater, 2 NOECs for a macrophytic algae and a crustacean for marine water.
RIVM – Serious risk concentration (RIVM, 2001)	890 µg/l	HC50 (protection of 50 % species) from a species sensitivity distribution of pooled freshwater and marine data. (see over for data availability).

According to CCME, the most sensitive fish seem to be equally as sensitive as invertebrates (copepods and daphnids). However, some aquatic plants are about an order of magnitude more sensitive.

8.2.1 France

Ineris (2010) derive a PNEC (or HC5) from a species sensitivity distribution for freshwater organisms. 14 chronic NOEC-data were used in the distribution; including data for algae, crustaceans, fish and protozoa, though no insects are included. Because of the lack of insect data, an extrapolation factor of 5 was applied to the HC5 value of 22.3 µg/l to give a $PNEC_{fw}$ of 4.4 µg/l for freshwater. This PNEC value is the $PNEC_{additional, fw}$, which is the PNEC for additional arsenic over background concentrations.

8.2.2 Germany

In Germany, there are no limit values of guidelines for surface water. However, the Environmental Quality Standard in surface water bodies is based on concentration in sediment (<63 µm) and is set to 40 µg/kg by the German Oberflächenwasserverordnung (OGewV, 16.06.2016). For the water itself there is no regulation in force but there is a proposal to set it to 2-3 µg/l.

8.3 Water for agricultural purposes

8.3.1 Irrigation

CCME (1999) have set an interim water quality guideline for total arsenic of 100 µg/l in irrigation water. This value is intended to protect agricultural crop species and is based on toxicity data for 25 crop species. The most sensitive plant was the green bean (Phaseolus vulgaris) and a maximum acceptable soil concentration, 0.37 mg/kg, was calculated as the geometric mean of the NOEC and LOEC for this species divided by an uncertainty factor of 10. This value was multiplied by the soil bulk density and soil bulk volume to a d depth of 25 cm and an area of 1 ha to calculate the allowable mass of arsenic (1.2 kg). This value was then divided by the irrigation rate (1.2×10^7 l/ha), giving a guideline value of 100 µg/l.

This guideline value is the same as FAOs guideline value (FAO, 1985). A Recommended Maximum Concentration of 0.1 mg/l was suggested to prevent toxicity to plants at an irrigation rate of 10 000 m^3/ha.

Other organisations, for example in South Africa (Department of Water Affairs and Forestry, 1996) the same guideline value is adopted.

8.3.2 Watering of livestock

CCME (1999) have set a water quality guideline for total arsenic for the protection of livestock of 25 µg/l.

Estimates of toxicity of livestock to arsenic were based on a compilation of data for 13 mammalian and 9 bird species. The ADI for livestock was calculated as the geometric mean of the NOEL and LOEL for the most sensitive species, beagle dogs, divided by a safety factor of 10. A water concentration was then calculated by multiplying the ADI by the lowest body weight to water intake ratio for all the animals studied, white leghorn chickens. This water concentration was then multiplied by an apportionment factor of 0.2, to allow for intake of

arsenic from sources other than drinking water. The resulting interim water quality guideline was 71 µg/l. However, the (then applicable) drinking water guideline was lower, 25 µg/l, and was adopted instead by CCME.

This guideline value is lower than FAOs guideline value (FAO, 1985). A Recommended Maximum Concentration of 0.2 mg/l was suggested by FAO.

9 Criteria for groundwater

The water framework directive (2000/60/EC) does not contain criteria for the assessment of groundwater status. The directive´s basic assumption is that groundwater should broadly be that it should not be polluted at all. For this reason, setting chemical quality standards may not be the best approach to ensure protection, as it gives the impression of an allowed level of pollution to which Member States can fill up. A very few such standards have been established at European level for particular issues (nitrates, pesticides and biocides), and these must always be adhered to. But for general protection, different, precautionary approach is taken which comprises a prohibition on direct discharges to groundwater, and (to cover indirect discharges) a requirement to monitor groundwater bodies so as to detect changes in chemical composition, and to reverse any anthropogenically induced upward pollution trend. Member states should consider establishing threshold values for certain substances in groundwater, and arsenic is included in the list of substances to be considered.

Criteria for the protection of groundwater are most based on drinking water guideline values, with the assumption that groundwater is a drinking water resource.

One example is Sweden, where the Swedish Geological Survey (SGU, 2013) has given criteria for the classification of groundwater status for a number of metals, including arsenic. Groundwater is classified in five classes according to the degree of effect of human activities or local geological features; from class 1 (no effect, background concentrations) to class 5 (very large effect). The lower boundary to class 5 is the drinking water guideline (10 µg/l). The classification is shown below:

Class 1:	<1 µg/l
Class 2:	1 - 2 µg/l
Class 3:	2 - 5 µg/l
Class 4:	5 - 10 µg/l
Class 5:	>10 µg/l

9.1.1 Germany

In Germany there is a limit value set in BBodSchV of 10 µg/l regarding water just entering the saturated zone which usually is the beginning of the groundwater body. This regulation is intended for the classification of soil: If the infiltrating water has concentrations over 10 µg/l, the soil from which this water is coming is regarded as contaminated. In the case of higher natural background concentrations, the responsible authorities may calculate an adapted limit value.

For groundwater itself there is a specific regulation named Grundwasserverordnung (GrwV as amended by the Ordinace (Änderungsverordung) dated 04.05.2017). A threshold value is set to 10 µg/l as well. But there is a specific regulation in this Ordinance which enables adjustment of the value according to the geochemical background. This is done in Saxony for several groundwater bodies up to a level of 12 µg/l.

9.1.2 France

The quality standard for arsenic in groundwater has been set to 10 µg/l, and is based on the drinking water standard in the EU directive 98/83/CE.

10 Criteria for air

EU directive 2004/107/EC established a target value for arsenic in ambient air of 6 ng/m^3. The concentration refers to the PM_{10} fraction in air.

In addition, upper and lower assessment thresholds were given of 3.6-2.4 ng/m^3 respectively. When annual average concentrations over the upper threshold are observed, measurements and modelling studies should be used to find out whether arsenic exceeds the target value. When concentrations over the lower threshold are observed, modelling studies alone may be used to check that the arsenic concentration is below the threshold value.

The target value established in the EU directive is at the same level as the reference level estimated by WHO (2000) to correspond to a lifetime risk of lungcancer of 1 in 100 000; 6.6 ng/m^3.

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