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SCIENTIFIC OPINION

Risks for public health related to the presence of chlorate in food¹

EFSA Panel on Contaminants in the Food Chain (CONTAM)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following a request from the European Commission, the risks to human health related to the presence of chlorate in food were assessed by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel). The presence of chlorate in food can arise from the use of chlorinated water for food processing and the disinfection of food-processing equipment. Inhibition of iodine uptake in humans was identified as the critical effect for chronic exposure to chlorate. A tolerable daily intake (TDI) of 3 µg chlorate/kg body weight (b.w.) was set by read-across from a TDI of 0.3 µg/kg b.w. derived for this effect for perchlorate, multiplied by a factor of 10 to account for the lower potency of chlorate. Formation of methaemoglobin was identified as the critical acute effect of chlorate. An acute reference dose (ARfD) of 36 µg chlorate/kg b.w. was derived from a no-observed-effect-level for chlorate in a controlled clinical study. Chronic exposure of adolescent and adult age classes did not exceed the TDI. However, at the 95th percentile the TDI was exceeded in all surveys in 'Infants' and 'Toddlers' and in some surveys in 'Other children'. Chronic exposures are of concern in particular in younger age groups with mild or moderate iodine deficiency. Mean and 95th percentile acute exposures were below the ARfD for all age groups indicating no concern. Based on the current practices in food industry, application of a hypothetical maximum residue limit (MRL) of 0.7 mg/kg for all foodstuffs and drinking water would only minimally reduce acute/chronic exposures and related risks. Assuming chlorate concentrations of 0.7 mg/kg for all foods and drinking water consumed in a day, acute exposures would increase by up to about 5-fold and the ARfD be exceeded at mean estimates in 'Infants' and 'Toddlers' and at 95th percentile also in 'Other children' and 'Adults'.

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KEY WORDS

chlorate, human health risk assessment, food

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SUMMARY

Following a request from the European Commission, the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) was asked to deliver a scientific opinion on the risks for public health related to the presence of chlorate in food from all sources taking into account also its presence in drinking water.

Chlorate (ClO_3^-) is a substance that is no longer approved as a pesticide according to Commission Decision No 2008/865/EC. No specific maximum residue levels (MRLs) have been established for chlorate under Regulation (EC) No 396/2005. Therefore, a default MRL of 0.01 mg/kg is applicable to all foods listed in its Annex.

Chlorate is formed as a by-product when using chlorine, chlorine dioxide or hypochlorite for the disinfection of drinking water, water for food production and surfaces coming into contact with food. Chlorination of animal-derived food is not allowed in the EU, while washing of plant-derived food with chlorine disinfected water can be permitted under national regulations. No maximum levels for chlorate in drinking water have been set in the European Union (EU) while the World Health Organisation (WHO) has established a guideline level for chlorate in drinking water of 0.7 mg/L.

In many fruit and vegetable commodities chlorate levels exceeding the default MRL of 0.01 mg/kg are found.

Based on the available information, the CONTAM Panel assumes that chlorate residues in food result mainly from the use of chlorinated water for food processing (e.g. washing) and from the disinfection of surfaces and food processing equipment coming into contact with food.

The EFSA Evidence Management Unit (DATA Unit) launched a call for data on chlorate levels in food and drinking water. After a quality assessment of the analytical data and their evaluation, 8 028 samples remained for analysis of which about 5% were drinking water samples.

The majority of the samples ($n = 4\,838$) came from Germany. The food groups represented best were 'Vegetable and vegetable products' ($n = 3\,752$), followed by 'Fruit and fruit products' ($n = 2\,607$). The highest mean concentrations were observed for 'Chilli pepper' (lower bound, LB = 164 $\mu\text{g/kg}$, upper bound, UB = 169 $\mu\text{g/kg}$), 'Aubergines' (LB = 157 $\mu\text{g/kg}$, UB = 164 $\mu\text{g/kg}$) and 'Vegetable and vegetable products, unspecified' (LB = 216 $\mu\text{g/kg}$, UB = 222 $\mu\text{g/kg}$). A total of 453 samples of 'Drinking water' were available. Mean chlorate values for 'Drinking water' were 28 $\mu\text{g/L}$ and 39 $\mu\text{g/L}$ at the LB/UB scenarios, respectively. The 99th percentile UB concentration in drinking water used to estimate acute exposure was 196 $\mu\text{g/L}$.

Food commodities reported as 'frozen' showed the highest levels of chlorate within each food group. However, in many samples reported as 'frozen' the chlorate levels were below the limit of quantification, indicating that chlorate levels may depend on how food is actually processed (levels of chlorine in water and rinsing).

There were indications that high levels of chlorate might be present in yoghurt and infant/follow-on formula but the data were insufficient for exposure assessment.

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) updated in 2015 was used to estimate dietary exposure to chlorate.

The CONTAM Panel concluded that a variability factor accounting for residue variation within composite samples of food commodities for acute exposure assessment of chlorate is not needed, mainly since the unit weight in frozen vegetables is small. Additionally, chlorate residues are highly soluble and an even distribution in processing water is expected.

The CONTAM Panel performed the exposure assessment of chlorate using chronic and acute exposure scenarios. Highest chronic exposures were estimated for the youngest population groups ('Infants', 'Toddlers' and 'Other children'). The mean chronic dietary exposure ranged between 0.5 µg/kg b.w. per day in 'Adolescents' (LB) and 4.1 µg/kg b.w. per day in 'Infants' (UB). At the 95th percentile, the lowest dietary exposure of 1.0 µg/kg b.w. per day (LB) was estimated for the age classes 'Elderly' and 'Very elderly'. The highest 95th percentile exposure was in 'Infants' (6.6 µg/kg b.w. per day, UB). The estimates of chronic dietary exposure to chlorate in the available dietary survey on 'Pregnant women' and the one on 'Lactating women' were similar or lower than those calculated in the general population.

Overall, in all age classes and vulnerable population groups (pregnant and lactating women) the main average contributor to the chronic dietary exposure to chlorate was 'Drinking water'. Range of contribution at the LB estimation across surveys: 'Infants' (25–58 %), 'Toddlers' (12–48 %), 'Other children' (0–38 %), 'Adolescents' (0–38 %), 'Adults' (6.2–48 %), 'Elderly' (8.1–35 %), 'Very elderly' (5.5–39 %).

Considering all available occurrence data, mean acute exposure (UB) ranged between 1.0 µg/kg b.w. per day in 'Adolescents' and 13 µg/kg b.w. per day in 'Infants'. The 95th percentile acute exposure estimates were between 2.6 µg/kg b.w. per day in 'Adolescents' and 31 µg/kg b.w. per day in 'Infants'. Acute 95th percentile exposure (UB) through the daily consumption of individual foods was highest for 'Drinking water' (32 µg/kg b.w. per day), 'Broccoli' (21 µg/kg b.w. per day), and 'Whey and whey products, excluding whey cheese' (19 µg/kg b.w. per day).

Acute and chronic estimates of exposure when excluding the occurrence data above a hypothetical MRL of 0.7 mg/kg were only slightly lower than those using all available occurrence data. This is explained by the fact that only few commodities were excluded and most of them belong to food groups with a relatively low contribution to the exposure.

It should be emphasised that the occurrence data set applies to current practice in the food industry under which the occurrence is, in general, substantially lower than 0.7 mg/kg. It cannot be predicted whether application of a MRL of 0.7 mg/kg would result in different practices leading to higher residue levels and higher exposures to chlorate.

In a hypothetical scenario, acute exposures were estimated assuming that all food items consumed have an occurrence value of 0.7 mg/kg. This led to a substantial increase of the acute exposure estimates as compared to the scenario using the reported occurrence levels.

Estimating acute exposure assuming an occurrence value of 0.7 mg/kg for individual food commodities generally results in lower acute exposure as compared to the use of the reported occurrence data. Important exceptions were the estimates of acute exposure calculated through the daily consumption of 'Drinking water' and 'Cow milk' that reached values up to 111 µg/kg and 56 µg/kg b.w. per day, respectively.

Following oral exposure, chlorate is rapidly absorbed, widely distributed throughout the body, metabolised to chloride and eliminated via the urine in rats. Chlorate is of very low acute toxicity in rats, ($LD_{50} \geq 3\,861$ mg/kg b.w.). The thyroid gland and the haematological system are the primary targets of chlorate toxicity in repeat oral dose studies with laboratory animals. Decreases in erythrocytes, haemoglobin and haematocrit were observed in mice, rats, dogs and monkeys. Next to altered thyroid hormone levels (decreases in triiodothyronine and thyroxine, increases in thyroid-stimulating hormone), histopathological changes in the thyroid gland (follicular cell hypertrophy, increase in colloid depression and in follicular cell hyperplasia) were observed in rats after repeated exposure. Chronic exposure to sodium chlorate induces also bone marrow hyperplasia, and haematopoietic cell proliferation in spleen of rodents. There is equivocal evidence of carcinogenic activity of sodium chlorate in mice based on marginally increased incidences of pancreatic islet cell adenoma and carcinoma in female mice and some evidence in rats based on increased incidences of

thyroid gland neoplasms. Chlorate is unlikely to pose a genotoxic hazard. Overall, the CONTAM Panel concluded that the thyroid tumours observed are induced via a non-genotoxic mode of action and are not relevant for humans. Chlorate has not been shown to have reproductive or developmental effects in rats and rabbits.

No long term studies on chlorate in humans or adequate epidemiological studies were identified. Like perchlorate, chlorate is a competitive inhibitor of iodine uptake in the thyroid. Chronic adaptive changes compensating sustained inhibition of thyroid iodine uptake could lead to long term effects such as the development of toxic multinodular goitre, in particular in populations with mild to moderate iodine deficiency. Fetuses, neonates, individuals with low iodine intake or genetically predisposed to develop hypothyroidism, are potentially more susceptible to these effects. The CONTAM Panel considered the inhibition of thyroid iodine uptake as the critical effect for the chronic hazard characterisation. Humans are less sensitive than rats towards the effects of agents that disrupt thyroid hormone homeostasis. However, there are no *in vivo* human studies on the inhibition of iodine uptake by chlorate. Therefore the CONTAM Panel derived a tolerable daily intake (TDI) of 3 µg/kg b.w. per day for chlorate by reading across from the TDI of 0.3 µg/kg b.w. per day established for perchlorate for this effect based on human data and by multiplying by a factor of 10 for the difference in potency between the two substances in rats.

Chlorate is of high acute toxicity in humans as lethality is reported from oral doses of approximately 50 mg chlorate/kg b.w. and toxicity from doses of 11–23 mg chlorate/kg b.w. onwards. The critical acute effect in humans identified in cases of poisoning is induction of methaemoglobinaemia, followed by lysis of red blood cells that can lead eventually to renal failure. The CONTAM Panel considers that the no observed effect level (NOEL) of 36 µg chlorate/kg b.w. per day from a controlled clinical study can be the basis for the establishment of an ARfD. The CONTAM Panel concludes that the differences between the NOEL in the controlled clinical study and the effect levels in poisoning cases are sufficiently large that no uncertainty factor is required for more vulnerable individuals (e.g. glucose-6-phosphate dehydrogenase deficient individuals or hereditary methaemoglobinaemia) and established an ARfD of 36 µg chlorate/kg b.w.

As for perchlorate, the CONTAM Panel noted that a single acute exposure to chlorate at levels found in food and water is unlikely to cause adverse effects in thyroid function, including in the more vulnerable groups of the population.

The mean and 95th percentile chronic exposure estimates for surveys from adolescent and adult age classes did not exceed the TDI of 3 µg/kg b.w. per day. In the younger populations ('Infants' and 'Toddlers'), the TDI was exceeded at the 95th percentile in all surveys and in some surveys for the UB mean exposure estimates. At the 95th percentile at median LB, the TDI was also exceeded in the group 'Other children'. Thus, chronic dietary exposure to chlorate is of potential concern in particular at high exposure in the younger age groups of the population with mild to moderate iodine deficiency. Fetuses, neonates, and individuals with low iodine intake or genetically predisposed to develop hypothyroidism are likely to be more sensitive to the effects of exposure to chlorate.

Mean and 95th percentile acute exposure estimates for all age groups are below the ARfD of 36 µg/kg b.w. and do not indicate a concern.

For chronic exposures based on the current occurrence data, removing foods containing more than 0.7 mg/kg chlorate from the exposure assessment would have a minimal impact on the exposure and consequently on the risk characterisation based on current occurrence data.

Likewise, for acute exposure based on the current occurrence data, removing foods and drinking water containing more than 0.7 mg/kg chlorate from the exposure assessment would also have a minimal impact on the exposure. Mean and 95th percentile acute dietary exposures would all remain below the ARfD. The occurrence data used for assessment applies to current practice in the food industry and it

cannot be predicted whether application of an MRL of 0.7 mg/kg would result in different practices leading to higher residue levels and higher exposures to chlorate.

When assuming an occurrence value of 0.7 mg/kg for all foods covered by Annex I of Regulation 396/2005 and drinking water, acute exposures would increase by up to approximately five-fold, and the ARfD would be exceeded at mean exposure in 'Infants' and at 95th percentile exposures also in 'Toddlers', 'Other children', and 'Adults'. The CONTAM Panel considered that such exceedances of the ARfD resulting from this scenario are unlikely, because it is highly implausible that all foods consumed on a single day would have chlorate concentrations in the range of 0.7 mg/kg. A potential exception would be drinking water, which by itself contributes to a large extent to the intake of chlorate.

When considering food commodities one by one, mean acute chlorate exposure did not exceed the ARfD from any food item, with the exception of drinking water. The scenario indicated that if the chlorate concentration in drinking water would be 0.7 mg/kg, the exposure to chlorate could be similar to the ARfD at mean water consumption and up to 3-fold the ARfD at high (95th percentile) water consumption. .

The CONTAM Panel identified a need for human data on inhibition of iodine uptake by chlorate and relative potency compared to perchlorate and information on levels of chlorate in humans and association with possible effects. The CONTAM Panel recommended that more information about the impact of food processing (e.g. blanching) on chlorate residues in food be collected. More occurrence data are needed for foods for which there are currently no data (e.g. animal derived foods, tea, coffee, beer). More data are also needed on chlorate in foods where there are currently indications of high chlorate levels such as infant/follow-on formula and yoghurt. Any efforts to reduce chlorate residues in food should take into account whether these would have an impact on microbiological food safety. There is also a need for a better understanding of the contribution of various dietary factors and contaminants to the overall thyroid iodine uptake inhibition.

TABLE OF CONTENTS

Abstract	1
Summary	2
1. Introduction	8
Background and Terms of reference as provided by the requestor	8
1.1. Interpretation of the Terms of reference	10
1.2. Additional information	10
1.2.1. Previous assessments	10
1.2.2. Chemistry	12
1.2.3. Analytical methods	12
1.2.4. Legislation	13
2. Data and methodologies	14
2.1. Data	14
2.1.1. Occurrence data	14
2.1.1.1. Data collection on food including drinking water	15
2.1.1.2. Analytical methods used	16
2.1.1.3. Food consumption data	17
2.1.2. Toxicokinetic and toxicological data	17
2.2. Methodologies	17
2.2.1. Collection and appraisal of previous occurrence results	17
2.2.2. Exposure assessment	18
2.2.3. Hazard assessment	19
2.2.3.1. Strategy for literature search	19
2.2.3.2. Appraisal of studies	19
2.2.4. Methodology applied for risk assessment	19
3. Assessment	20
3.1. Occurrence data	20
3.1.1. Previously reported occurrence results	20
3.1.1.1. Fruit and vegetables	20
3.1.1.2. Food of animal origin	20
3.1.1.3. Food supplements and flavour enhancing ingredients	21
3.1.1.4. Drinking water	21
3.1.2. Food processing	21
3.1.3. Current occurrence results	22
3.2. Exposure assessment	24
3.2.1. Previously reported exposure assessments	24
3.2.2. Non-dietary exposure	25
3.2.3. Current exposure assessment	25
3.2.3.1. Chronic dietary exposure to chlorate	25
3.2.3.2. Consideration of the use of a variability factor for acute exposure assessment	27
3.2.3.3. Acute dietary exposure	28
3.2.3.4. Acute dietary exposure assuming an occurrence value of 0.7 mg/kg in all food commodities (scenario B.3)	31
3.2.4. Potential contribution to dietary exposure to chlorate of infant/follow-on formula and yoghurt	33
3.3. Hazard identification and characterisation	34
3.3.1. Toxicokinetics	34
3.3.1.1. Laboratory animals	34
3.3.1.2. Humans	35
3.3.2. Toxicity in experimental animals	35
3.3.2.1. Acute toxicity	35
3.3.2.2. Short term toxicity	36
3.3.2.3. Long term toxicity and carcinogenicity	40
3.3.2.4. Genotoxicity	42

3.3.2.5. Developmental and reproductive toxicity	46
3.3.3. Observations in humans.....	48
3.3.3.1. Acute effects	48
3.3.3.2. Controlled clinical trials.....	48
3.3.3.3. Epidemiological studies	49
3.3.3.4. Biomarkers.....	49
3.3.4. Mode of action.....	49
3.4. Consideration of critical effects, dose response assessment and derivation of health-based guidance values	51
3.4.1. Derivation of a chronic health-based guidance value.....	52
3.4.2. Derivation of an acute reference dose	53
3.5. Risk characterisation.....	54
3.5.1. Risk characterisation based on current occurrence data	54
3.5.1.1. Chronic.....	54
3.5.1.2. Acute.....	55
3.5.2. Risk characterization based on a hypothetical MRL of 0.7 mg/kg.....	55
3.5.2.1 Chronic.....	55
3.5.2.2. Acute	55
3.5.3. Risk characterization assuming an occurrence value of 0.7 mg/kg in all commodities ...	55
3.6. Uncertainty analysis.....	56
3.6.1. Assessment objectives	56
3.6.2. Exposure scenario/Exposure model.....	56
3.6.3. Other uncertainties.....	56
3.6.4. Summary of uncertainties	57
4. Conclusions	57
5. Recommendations	62
Documentation provided to EFSA	63
References	65
Appendices	73
Appendix A. EFSA guidance documents applied for the assessment.....	73
Appendix B. Comparative evaluation of the potency of chlorate and perchlorate to induce thyroid gland follicular cell hypertrophy in rats	74
Appendix C. Dietary surveys used for the estimation of chronic and acute dietary exposure to chlorate	78
Appendix D. Chlorate occurrence values in different food commodities.....	80
Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate	82
Appendix F. Exposure estimates for chlorate obtained in different dietary surveys.....	88
Appendix G. Range of acute exposure estimates for individual food commodities assuming an occurrence value of 0.7 mg/kg	90
Glossary.....	99
Abbreviations	101

1. Introduction

Background and Terms of reference as provided by the requestor

BACKGROUND

Chlorate

Chlorate is a substance that is no longer approved as a pesticide according to Commission Decision No 2008/865/EC.⁴ Since no specific MRL was fixed under Reg. (EC) No 396/2005,⁵ the default MRL of 0.01 mg/kg is applicable to all food products included in Annex I to that Regulation.

In many fruit and vegetable commodities chlorate levels exceeding the default MRL have been found. It is unlikely that these residues result from the illegal use of chlorate as a pesticide. Chlorate is formed as a by-product when using chlorine, chlorine dioxide or hypochlorite for the disinfection of drinking water or water for food production. Especially in food production lines where the washing water is recycled and chlorine disinfection is used to keep the microbial quality of the water at an acceptable level, chlorate residues have a tendency to concentrate, resulting in residues in food. However, also in products that have only been treated with drinking water, the chlorate levels exceed the legal limit of 0.01 mg/kg. For drinking water a guideline level of 0.7 mg/L⁶ chlorate in drinking water has been established by the World Health Organisation (WHO) based on a TDI of 0.03 mg/kg b.w. per day (WHO, 2005⁷). Chlorate levels of up to the level of 0.7 mg/L can be found depending on the extent of chlorination, which varies amongst Member States. Furthermore, chlorate residues can also arise from their uptake by plants resulting from:

- the use of chlorine-disinfected irrigation water;
- the use of potassium nitrate and monopotassium phosphate fertilisers which contain certain amounts of chlorate;
- the chlorate present in the soil or groundwater.

Findings in the European Union

In a survey performed by the CVUA (Chemisches und Veterinäruntersuchungsamt) Stuttgart, 600 samples of products of plant origin were analysed. In 19.8 % of them, residue levels were found between 0.01 and 0.92 mg/kg.

Both food business operators and the German authorities have been further investigating the occurrence of these residues and the reasons for their unexpected presence. The continued monitoring indicated that the levels of chlorate residues in fruits and vegetables can go up to 5 mg/kg.

As a toxicological reference value for chronic risk assessment, JECFA established an ADI of 0.01 mg/kg b.w. per day in 2007.⁸ As JECFA considered it unnecessary to establish an ARfD and as

⁴ 2008/865/EC: Commission Decision of 10 November 2008 concerning the non-inclusion of chlorate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance. OJ L 307, 18.11.2008, p. 7–8.

⁵ Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residues levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EC. OJ L 70, 16.3.2005, p. 1–16.

⁶ Guidelines for drinking-water quality, fourth edition. World Health Organization, 2011. Available at: http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/

⁷ Background document for the development of WHO Guidelines for Drinking-water Quality WHO/SDE/WSH/05.08/86.

⁸ Evaluation of certain food additives and contaminants. Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series 947. Available at: http://whqlibdoc.who.int/publications/2007/9789241209472_eng.pdf

no EFSA opinion is available so far, some Member States are currently using the value of 0.01 mg/kg b.w. per day also for the ARfD, as a conservative approach.

In 2014, so far 7 findings resulted in a RASFF (Rapid Alert System for Food and Feed) notification. The risk assessment was performed by making use of the Pesticide Residue Intake Model (PRIMO) for acute effects applying a variability factor for fruits and vegetables with a high unit weight and using the value of 0.01 mg/kg b.w. per day as an ADI and ARfD.

The European Commission would like to request from EFSA a scientific opinion on the risk for public health as the consequence of the presence of chlorate in food, taking also into account its presence in drinking water, with a view to taking permanent risk management measures.

The opinion should address the possible acute and chronic health effects, including risks for specific vulnerable population groups, and address the question whether an Acute Reference Dose (ARfD) is needed. It should also address the question whether the use of a variability factor would be appropriate.

The scientific opinion should be available by 30 April 2015.

In order to enable EFSA to carry out such risk assessment, Member States with the active involvement of food business operators were requested to monitor the presence of chlorate in food as well as drinking water and to submit those data to EFSA and the Commission before 31 December 2014. Monitoring guidelines, defining the data to be submitted and their format, have been circulated among Member States and food business operators.

TERMS OF REFERENCE

In accordance with Art. 29 (1) (a) of Regulation (EC) No 178/2002, the Commission asks EFSA for a scientific opinion on the risks to human health related to the presence of chlorate in food from all sources, taking also into account its presence in drinking water.

The scientific opinion as regards the presence of chlorate in food from all sources, taking also into account its presence in drinking water, should, inter alia, comprise the following:

- a) the evaluation of the toxicity of chlorate for humans, considering all relevant adverse chronic and – if applicable – acute health effects, including the need to establish any health based guidance values such as an Acute Reference Dose (ARfD), Acceptable Daily Intake (ADI), etc.;
- b) the estimation of the dietary exposure (chronic and acute dietary exposure, if applicable) of the EU population to chlorate, considering the consumption patterns of specific (vulnerable) groups of the population (i.e. high consumers of certain fruits and vegetables, (young) children, pregnant women,...). The assessment of dietary exposure should include the assessment of the need for a specific variability factor;
- c) the assessment of the chronic and acute (if applicable) human health risks as the consequence of the presence of chlorate in food, taking into account its presence in drinking water, with particular attention to specific (vulnerable) groups of the population (i.e. high consumers of certain fruits and vegetables, (young) children, pregnant women, iodine deficient people), based on the above points a) and b);
- d) based on the above points a), b) and c) an evaluation of the safety of a hypothetical maximum residue level of 0.7 mg/kg⁹ for chlorate in foods covered by Annex I to Regulation (EC) No 396/2005.

⁹ In analogy with the WHO guideline level for drinking water of 0.7 mg/L.

1.1. Interpretation of the Terms of reference

The CONTAM Panel concluded that the terms of reference provided by the European Commission were clear.

1.2. Additional information

1.2.1. Previous assessments

The most recent risk assessments for chlorate are described below.

In the context of its drinking water guidelines, the World Health Organization (WHO, 2005) identified a no-observed-adverse-effect level (NOAEL) of 30 mg/kg body weight (b.w.) per day expressed as chlorate, from a 90-day study of sodium chlorate in rats, in which thyroid gland colloid depletion was reported at the next higher dose of 100 mg/kg b.w. per day (McCauley et al., 1995). Application of an uncertainty factor of 1 000 to this NOAEL (10 each for inter- and intraspecies variation and 10 for the short duration of the study) resulted in a tolerable daily intake (TDI) of 30 µg/kg b.w. per day. WHO noted that this TDI was supported by the results of human volunteer studies, in which repeated administration of chlorate at 36 µg/kg b.w. per day did not result in any adverse effects (including blood and urine analysis, electrocardiograms and physical examination, e.g. blood pressure, respiration rate, pulse and temperature) (Lubbers et al., 1981). Assuming that drinking water contributes 80 % of the total exposure and a typical consumption of 2 litres (L) of water per day by a 60 kg person, the WHO proposed a provisional guideline value of 0.7 mg/L. This guideline value was designated as provisional 'because use of chlorine dioxide as a disinfectant may result in the chlorate guideline value being exceeded, and difficulties in meeting the guideline value must never be a reason for compromising adequate disinfection'. It was noted that a long-term study was in progress that should provide more information on the effects of chronic exposure to chlorate.¹⁰

The EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC Panel) evaluated the toxicological risks to public health from possible reaction products of acidified sodium chlorite (ASC) applied on poultry carcasses as an antimicrobial agent. Chlorite and chlorate were identified as the main residues, and the AFC Panel concluded that there was no safety concern but did not specifically refer to a health-based guidance value for chlorate (EFSA, 2006a).

The US Environmental Protection Agency (US EPA) has published a Reregistration Eligibility Decision (RED) for inorganic chlorates (US EPA, 2006). A 95 % lower confidence limit for the benchmark dose response of 10 % extra effect (BMDL₁₀) for chlorate of 0.9 mg/kg per day was calculated for increased thyroid gland follicular cell hypertrophy and follicular cell mineralisation in the National Toxicology Program (NTP) carcinogenicity study of sodium chlorate in rats (NTP, 2005). The US EPA applied an uncertainty factor of 30 (three for interspecies and 10 for intraspecies differences) and established a chronic reference dose (RfD) of 0.03 mg/kg b.w. per day. The selection of the interspecies uncertainty factor of three, rather than the default factor of 10, was due to the quantitative dynamic differences between rats and humans with respect to thyroid function. The US EPA noted that the half-life of thyroid hormone thyroxine (T4) in rats is approximately 12 hours, whereas it is five to 9 days in humans. The shorter half-life in rats is likely related to a high-affinity binding globulin for T4 that is present in humans, but absent in rodents. In the absence of a functional thyroid gland, a rat requires approximately 10-times more T4 than an adult human for full reconstitution. Constitutive thyroid stimulating hormone (TSH) levels are nearly 25-times higher in rats than in humans, reflecting the increased activity of the thyroid-pituitary axis in rats. An Acute Reference Dose (ARfD) was not established because effects attributable to a single dose were not seen in the available data.

¹⁰ It is assumed that this reference was to the NTP (2005) study on the toxicity and carcinogenicity of sodium chlorate.

Health Canada (2008) set a TDI of 30 µg/kg b.w. for chlorate, with the same justification as WHO (2005).

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) evaluated the safety of chlorate residues in the context of its review of ASC as an antimicrobial agent used primarily as a spray or dipping solution for poultry, meats, vegetables, fruits and seafood, and in poultry chilling water (FAO/WHO, 2008). Like the AFC Panel, JECFA focussed its AFC safety evaluation on the residues, chlorite and chlorate. For chlorate, JECFA concluded that the most sensitive effects were changes to the thyroid gland of male rats, noting that rats are highly sensitive to the effects of agents that disrupt thyroid hormone homeostasis. A BMDL₁₀ of 1.1 mg/kg b.w. per day was calculated for non-neoplastic effects on the thyroid of male rats in the carcinogenicity study of sodium chlorate conducted by the National Toxicology Program (NTP, 2005). JECFA considered that humans are likely to be less sensitive than rats to these effects and that a safety factor for interspecies variation was not required. However, in addition to the safety factor of 10 to allow for intraspecies variability, an additional factor of 10 was required to allow for the deficiencies in the database, particularly with respect to investigation of possible neurodevelopmental effects. JECFA therefore established an acceptable daily intake (ADI) of 0–0.01 mg/kg b.w. for chlorate. JECFA noted that the estimated dietary exposure of 0.6 µg/kg b.w. per day, representing high consumers including children, was less than 10 % of the ADI and compatible with the exposure allocated to other sources within the WHO drinking-water guidelines for chlorate (FAO/WHO, 2008).

The European Chemicals Agency (ECHA) has provided risk assessments for sodium and potassium chlorate (ECHA, 2015a, b). For sodium chlorate a derived no effect level (DNEL)¹¹ of 0.036 mg/kg b.w. per day was identified for oral exposure of the general population, based on the finding of thyroid gland follicular cell hypertrophy in the NTP carcinogenicity study (NTP, 2005), incorporating an assessment factor of 100 (ECHA, 2015a). For potassium chlorate a DNEL of 0.06 mg/kg b.w. per day was identified for oral exposure to the general population, apparently by read-across from sodium chlorate (ECHA, 2015b).

A Draft Assessment Report (DAR) was prepared for sodium chlorate by the rapporteur Member State France in the context of the review programme referred to in Article 8(2) of Council Directive 91/414/EEC¹² (EU DAR, 2008). The DAR noted that two main targets of sodium chlorate have been identified in animal studies: the thyroid gland and red blood cells (RBCs). Based on acute toxicity, the DAR concluded that humans are obviously more susceptible to toxicity of sodium chlorate than laboratory animals. No ADI or ARfD was proposed because sodium chlorate was not used in cropping areas. An Acceptable Operator Exposure level (AOEL) of 0.35 mg/kg b.w. per day was proposed, based on the lowest relevant NOAEL of 70 mg/kg b.w. per day in male and female rats treated by gavage in a reproduction toxicity study. A safety factor of 200 was used allowing for a potential higher sensitivity of glucose-6-phosphate-deficient individuals.

The German Federal Institute for Risk Assessment (BfR) recommended using the ADI of 0.01 mg/kg body weight derived by JECFA as the basis for both chronic and acute risk assessments of chlorate residues in food (BfR, 2013). The BfR noted that there was a need for an acute risk assessment for chlorate due to the high acute oral toxicity of chlorate to humans, resulting from the harmful effects on erythrocytes (methaemoglobin formation, haemolysis). In addition, the possibility of a one-time intake of chlorate triggering adverse effects on thyroid function could not be ruled out. This applied particularly to more sensitive subpopulations such as persons with thyroid function disorders or iodine deficiency, as well as to newborn infants and children. Pregnant women exhibiting manifest or subclinical thyroid function disorders were considered to constitute a particularly critical group since thyroid hormones play a key role in early childhood development, especially in brain development.

¹¹ REACH legislation defines the Derived No-Effect Level (DNEL), as the level of exposure above which humans should not be exposed.

¹² Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, 1–32.

The ADI was used for the acute risk assessment since there were no toxicology data adequate for deriving an ARfD for chlorate.

The assessment of the chronic risk indicated that the health of European consumer groups is not adversely affected by the reported chlorate residues in foods. In the absence of data available on the possible origin of the reported chlorate residues, the BfR estimated short-term intake in accordance with its recommendations for perchlorate,¹³ using the EFSA Pesticide Residue Intake Model (PRIMo). On the basis of this worst case approach, the BfR estimation of short-term intake for certain product groups led to an exceedance of the ADI proposed for the acute risk assessment of chlorate. The BfR noted that refinement of both the toxicological assessment and the residue assessment would be possible with a better database (BfR, 2013).

1.2.2. Chemistry

Chlorate (ClO_3^-) is an anion that can form salts, e.g. with sodium. Since all the Cl-O bonds are the same length and the chlorine atom is hypervalent, chlorate it is often thought of as a hybrid of multiple resonance structures (Figure 1). Chlorate anions have trigonal pyramidal structures.

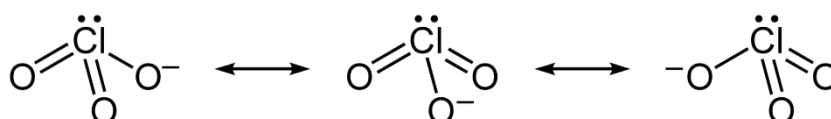


Figure 1: Resonance structures of chlorate

Since sodium chlorate is generally used in toxicity studies to assess chlorate toxicity, this section shortly summarizes the chemistry of sodium chlorate. Sodium chlorate has a white or colourless crystal structure and is highly soluble in water (Table 1). It has a melting point of 248 °C and a decomposition point of ~ 300 °C. Above 300 °C, sodium chlorate decomposes exothermically to NaCl releasing O_2 . Although sodium chlorate is a strong oxidizer and can be explosive when mixed with strong reducing agents, aqueous solutions of chlorate can be handled safely. In the environment and drinking water, chlorate can persist as a product from chlorine, chlorine dioxide and chlorite chemical reactions in an aqueous environment.

Table 1: Some relevant physico-chemical properties of sodium chlorate

Molecular formula: ClNaO_3	Density: 2.54 g/cm ³ (20.2 °C)
Molecular mass: 106.44 g/mol	Melting point: 248 °C
CAS Number: 7775-09-9	Boiling point: ~ 300 °C
Oxidations state of chlorine: +5	Solubility in water: 960-1 000 g/L dissociation into sodium an chlorate ions
Properties at room temperature: odourless, white or colourless crystal structure, hygroscopic	

1.2.3. Analytical methods

Analytical methods for the quantification of chlorate are typically based on spectrophotometric or colorimetric, electrochemical and chromatographic techniques, especially ion chromatography, also coupled with mass spectrometry (Michalski, 2006; Rao et al., 2010) These methods have been

¹³ Available at: <http://www.bfr.bund.de/cm/343/empfehlung-des-bfr-zur-gesundheitlichen-bewertung-von-perchlorat-rueckstaenden-in-lebensmitteln.pdf>

developed in the first line for relative clean matrixes, especially drinking water (summarized in Health Canada, 2008).

In complex matrixes of animal origin, liquid chromatography-mass spectrometry (LC-MS) utilizing a $\text{Cl}^{18}\text{O}_3^-$ internal standard has been demonstrated to be applicable to sensitively quantify chlorate (Smith and Taylor, 2011). In foods of plant origin chlorate is recommended to be analysed by a multi-residue method for polar pesticides (Quick Polar Pesticides Method, QuPPE). Chlorate is extracted from the test portion following water adjustment and the addition of acidified methanol. The mixture is centrifuged, filtered and directly analysed by liquid chromatography – tandem mass spectrometry (LC/MS-MS) (Anastassiades et al., 2013).

1.2.4. Legislation

Article 2 of Council Regulation (EEC) No 315/93¹⁴ stipulates that food containing a contaminant in an amount unacceptable for public health shall not be placed on the market, that contaminant levels should be kept as low as can reasonably be achieved and that, if necessary, the European Commission (EC) may establish maximum levels for specific contaminants. These maximum levels are laid down in the Annex of Commission Regulation (EC) No 1881/2006¹⁵ and may include limits for the same contaminants in different foods, analytical detection limits and reference to the sampling and analysis methods to be used. No maximum levels for chlorate are presented in this regulation.

Chlorate was previously listed as an active substance approved for use in plant protection products in Annex I of Directive 91/414/EC (now replaced by Regulation (EC) No 1107/2009.¹⁶ In accordance with Commission Decision 2008/865/EC¹⁷ the approval of chlorate for use in plant protection products has been withdrawn and thus chlorate cannot be used anymore in plant protection products.

In Annexes II, III, and V of Regulation (EC) No 396/2005 maximum residue levels (MRLs) for active substances currently or formerly used in plant protection products are listed. For those substances for which no specific MRLs are listed in these annexes, the default MRL value of 0.01 mg/kg is applicable to all food products listed in Annex I of that Regulation. For chlorate no specific MRLs were set, thus the default MRL is applicable.

The disinfection of drinking water, or surfaces in contact with food, falls within the scope of the Biocidal Product Regulation (EU) No 528/2012.¹⁸ For these uses, various active substances are currently under assessment in the review programme of biocidal active substances established under Regulation (EU) No 1062/2014, including chlorine, chlorine dioxide, active chlorine, sodium hypochlorite, calcium hypochlorite. Clarifications are also currently on-going within the biocides legislation with regards to the in-situ generation of biocides, which covers situations where the active substance is generated from the use of one or several chemical precursors. For instance, chlorine dioxide is currently under assessment as being generated from sodium chlorite or sodium chlorate. The placing on the market and use of all these biocidal products are subject to national rules of each Member State. Once a decision on the approval of the active substances is taken at European Union (EU) level, biocidal products will be subject to the evaluation and authorisation scheme established under the Biocidal Product Regulation.

¹⁴ Council Regulation (EEC) No 315/93 of February 1993 laying down Community procedures for contaminants in food. OJ L 37, 13.2.1993, p. 1–3.

¹⁵ Regulation (EC) No 1881/2006 of the European Parliament and the Council of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs. OJ L 364, 20.12.2006, p. 5–24.

¹⁶ Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

¹⁷ Commission Decision of 10 November 2008 concerning the non-inclusion of chlorate in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance OJ L 307, 18.11.2008, p. 7–8.

¹⁸ Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products. OJ L 167, 27.6.2012, p. 1–123.

According to Regulation (EC) No 852/2004¹⁹ for prevention of contamination of plant products potable or clean water should be used.

Regulation (EC) No 853/2004²⁰ laying down general rules for food business operators on the hygiene of foodstuffs stipulates that food business operators shall not use any substance other than potable water to remove surface contamination from products of animal origin besides those approved in accordance with the Committee procedure described in Art. 12 of this Regulation. Currently only lactic acid is approved.

Food business operators in the EU importing products of animal origin from third countries shall ensure that importation takes place only if (*inter alia*) the product satisfies the requirements laid down in the regulation.

Products used for decontamination of food of plant origin qualify as processing aids which are regulated under national legislation. Chlorate yielding substances such as chlorine (gas), chlorine dioxide or hypochlorite can fall under this definition. In the absence of EU rules it is possible for Member States to adopt specific measures to control microbial contamination. Such is the case for instance in France where the use of water treated with sodium hypochlorite for the washing of fruit and vegetables is listed in a positive list together with a mandatory rinsing of the treated product with water.

Sodium chlorate and potassium chlorate are used in industrial and manufacturing processes and are registered substances under Regulation (EC) No 1907/2006²¹ with a tonnage band of 100 000–1 000 000 tonnes per annum and 1 000–10 000 tonnes per annum, respectively.

Council Directive 98/83/EC²² on the quality of water intended for human consumption does not provide for maximum levels of chlorate.

For drinking water a guideline level of 0.7 mg/L chlorate in drinking water has been established by the WHO. However, this level is not legally binding in the EU.

2. Data and methodologies

2.1. Data

2.1.1. Occurrence data

Following a request of the European Commission to the European Food Safety Authority (EFSA) for a scientific opinion concerning the risks for public health related to the presence of chlorate in food, the EFSA Evidence Management Unit (DATA Unit) started an *ad hoc* collection of data on chlorate levels in food and drinking water. European national food authorities and similar bodies, research institutions, academia, and food business operators submitted analytical data. The data submission to EFSA followed the requirements of the EFSA Guidance on Standard Sample Description for Food and Feed (EFSA, 2010a).

¹⁹ Regulation (EC) No 852/2004 of the European Parliament and of the Council of 29 April 2004 on the hygiene of foodstuffs. OJ L 139, 30.4.2004, p. 1–54.

²⁰ Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for food of animal origin. OJ L 139, 30.4.2004, p. 55–96.

²¹ Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. OJ L 396, 30.12.2006, p. 1–98.

²² Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.98, p. 32–54.

By the end of March 2015, a total of 8 774 samples of food and drinking water with analytical data on chlorate were available in the EFSA database. Approximately 7 % of the samples were reported as drinking water and the rest as food samples. Data received after that date were not included in the dataset to estimate dietary exposure.

To guarantee an appropriate quality of the data used in the exposure assessment the initial dataset was carefully evaluated applying several data cleaning and validation steps (e.g. exclusion of duplicates and samples without complete information). When the information on the sampling strategy was described as ‘Suspect sampling’, the samples were excluded from the final dataset since they do not represent random sampling (644 samples). Samples collected outside Europe were not considered for the dietary exposure estimations (27 samples). Likewise, food samples codified as ‘Grain as crops’, which refer to unprocessed grains of undefined end-used, were also excluded (18 samples), together with 49 samples of ‘Drinking water’, some 48 reported as process water used in industry and one non-quantified sample that reported a limit of quantification (LOQ) of 1 000 µg/L.

For the food groups ‘Meat and meat products’, ‘Fish and other seafood’ and ‘Eggs and egg products’ (all at FoodEx Level 1) only eight samples were available in total. These samples refer to two samples of chicken, two of pork, and one each of beef, unspecified fish, prawns and egg powder. Due to the very limited number of samples, they were not considered representative of these food groups and they were also excluded.

2.1.1.1. Data collection on food including drinking water

After the quality assessment of the analytical data and their evaluation, a total of 8 028 samples of food and drinking water were available to estimate dietary exposure to chlorate. Most of the analytical data were derived from samples collected in Germany (4 838 samples). In total, 19 different European countries were reported as sampling country, with 1 513 samples reported as collected in the European Union without further details (Figure 2). The samples were mainly collected between 2013 (1 871 samples) and 2014 (6 096 samples), although few were also collected in 2011 (61 samples).

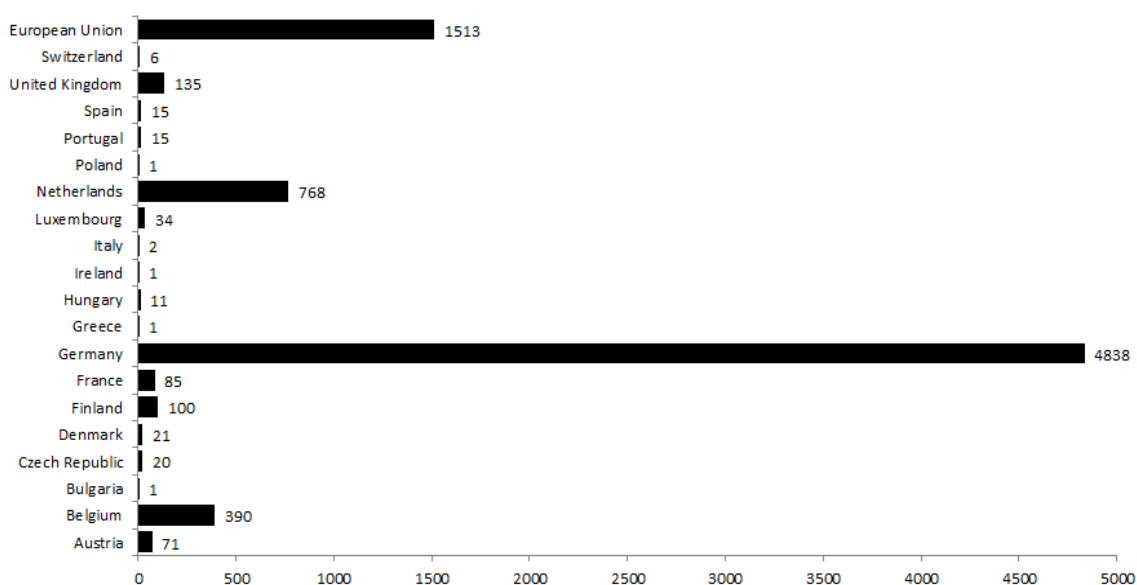


Figure 2: Country of sampling of food and drinking water samples analysed for chlorate

2.1.1.2. Analytical methods used

Figure 3 shows the analytical methods reported for the different samples of food and drinking water. Information on the analytical method was not provided for approximately 12 % of the samples. High performance liquid chromatography (HPLC) was the separation method selected for almost all samples that provided information on the analytical method used. For 161 samples the reported analytical method was ion chromatography with suppressed conductivity detection. The preferred option for detection was tandem mass spectrometry (MS/MS) with 6 695 samples (83 %), followed by electrical conductivity detection (ECD) and mass spectrometry detection (MS). Few samples only reported the use of HPLC without further information on the detection method.

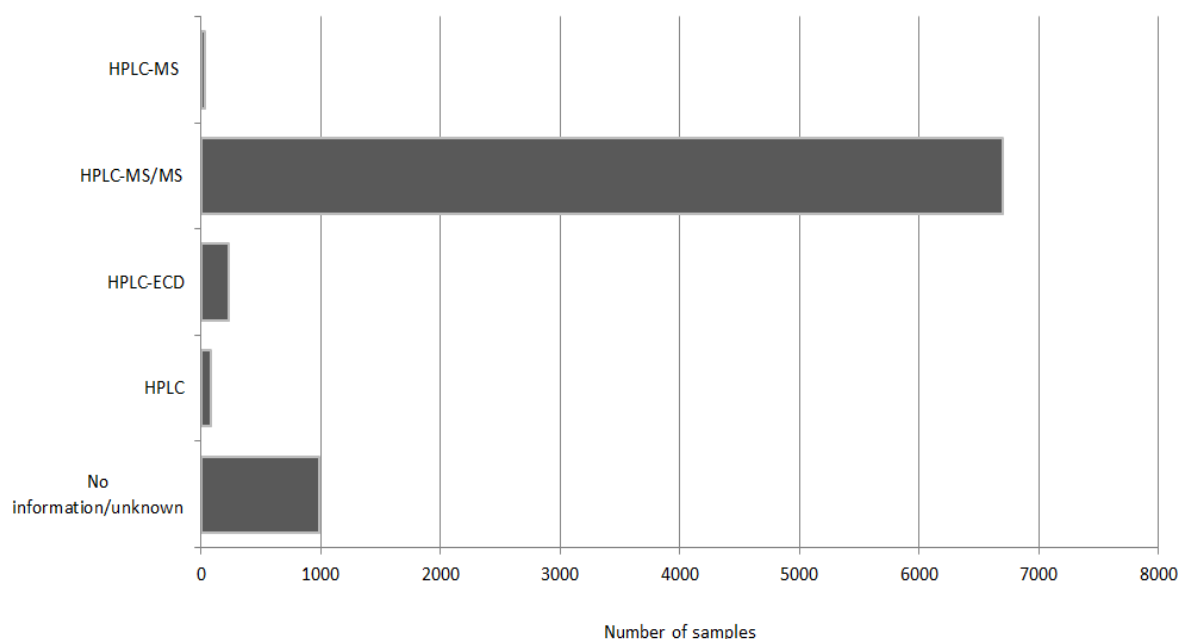


Figure 3: Analytical methods used in the analysis of chlorate in samples of food and drinking water

Among the samples that reported information, the most sensitive analytical method was HPLC-MS/MS that reported a minimum LOQ of 2 µg/kg in the analysis of ‘Fruit and fruit products’. The highest LOQ was also reported for HPLC-MS/MS (100 µg/kg) in the analysis of drinking water and diverse food commodities, such as ‘Vegetables and vegetable products’ and ‘Herbs, spices and condiments’, among others. The broadest ranges of LOQs within one specific food commodity was observed for ‘Fruit and fruit products’ (n= 2 366), with a range of LOQs between 2 µg/kg and 100 µg/kg, and for ‘Drinking water’ (n= 453) with a range between 3 µg/kg and 100 µg/kg, always using HPLC-MS/MS.

The left-censored data (analytical data below the limit of detection (LOD)/LOQ) accounted for 71 % of the analytical results on chlorate. The proportion of left-censored data among the different food groups (FoodEx Level 1) ranged between 0 % (Non-alcoholic beverages, n = 2) and 97 % (Alcoholic beverages, n = 37). More details for the different food groups are shown in Figure 4.

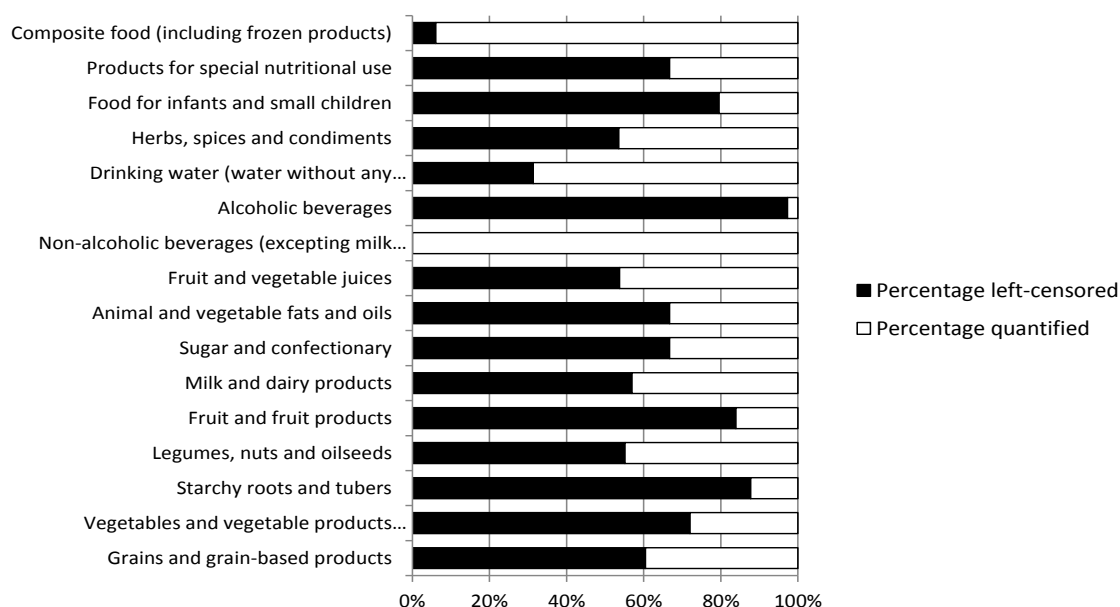


Figure 4: Percentage of quantified and left-censored data across different food groups (at FoodEx Level 1)

2.1.1.3. Food consumption data

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) provides a compilation of existing national information on food consumption at individual level. It was first built in 2010 (EFSA, 2011b; Huybrechts et al., 2011; Merten et al., 2011) and then updated in 2015 (EFSA, 2015). Details on how the Comprehensive Database is used are published in the Guidance of EFSA (EFSA, 2011a).

The database contains data from 41 surveys in 23 different European countries for a total of 78 990 participants (Appendix C). Data from six surveys were available for ‘Infants’ (< 12 months old), eleven for ‘Toddlers’ (≥ 12 months to < 36 months old), from 19 surveys for ‘Other children’ (≥ 36 months to < 10 years old), from 19 surveys for ‘Adolescents’ (≥ 10 years to < 18 years old), from 21 surveys for ‘Adults’ (≥ 18 years to < 65 years old), from 15 surveys for the ‘Elderly’ (≥ 65 years to < 75 years old) and from 13 surveys for the ‘Very elderly’ (≥ 75 years old). Two additional surveys provided information on specific population groups: ‘Pregnant women’ (Latvia) and ‘Lactating women’ (Greece).

In the surveys above, consumption data were collected using single or repeated 24- or 48-hour dietary recalls or dietary records covering from 3 to 7 days per subject. Owing to the differences in the methods used for data collection, direct country-to-country comparisons must be taken with caution.

2.1.2. Toxicokinetic and toxicological data

All data were obtained as described in Section 2.2.3.1.

2.2. Methodologies

2.2.1. Collection and appraisal of previous occurrence results

For the present evaluation the CONTAM Panel considered literature made publicly available until the 30 January, 2015. A comprehensive literature search was conducted in September 2014 and has since been updated in November 2014, December 2014 and January 2015 focusing on research and reports related to occurrence of chlorate, focusing on food and drinking water. The references obtained were screened using title and abstract to identify the relevant literature.

All information retrieved as described in the previous paragraph has been reviewed and used for the present assessment using expert judgement. No studies on the occurrence of chlorate in fruit, vegetables and food of animal origin were identified. Experimental studies on the direct treatment of fruit, vegetables and food of animal origin with ASC and chlorine dioxide, and for which the resulting chlorate levels in the food were reported, were considered. Studies on the administration of chlorate to livestock were not considered in the present opinion. For drinking water and other beverages, only data from European countries were considered.

2.2.2. Exposure assessment

The EFSA Panel on Contaminants in the food Chain (CONTAM Panel) considered that both chronic dietary and acute exposure to chlorate had to be assessed. As suggested by the EFSA Working Group on Food Consumption and Exposure (EFSA, 2011b), dietary surveys with only one day per subject were only considered for acute exposure as they are not adequate to assess repeated exposure. Similarly, subjects who participated only one day in the dietary studies, when the protocol prescribed more reporting days per individual, were also excluded for the chronic exposure assessment. Thus, for chronic exposure assessment, food consumption data were available from 35 different dietary surveys carried out in 19 different European countries (Appendix C). Six additional dietary surveys with only one day per subject from six different countries (covering all age classes except infants) were considered for acute exposure assessment (Appendix C). In the Appendix, the number of available days for each age class used in the acute exposure assessment are described beside the number of subjects available for the chronic exposure assessment.

In line with the outcome of the hazard characterization, the CONTAM Panel decided to estimate chronic and acute dietary exposure (see Table 2). First, dietary chronic exposure to chlorate was estimated using all available occurrence data (scenario A.1). Acute exposure was also estimated as total exposure and food by food using all available occurrence data (scenario B.1). Then, based on the Terms of Reference, a hypothetical MRL of 0.7 mg/kg for chlorate in food and drinking water was considered and all samples with reported higher concentrations were excluded before estimating dietary exposure (scenarios A.2 and B.2). Finally, a scenario assuming the presence of 0.7 mg/kg chlorate in all food commodities was also assessed (scenario B.3). For acute exposure assessments variability factors were not applied (see Section 3.2.3).

Table 2: Different scenarios used to estimate chronic and acute dietary exposures to chlorate

Dietary exposure scenarios	
A. Chronic exposure assessments	A.1. Chronic dietary exposure using the available occurrence data
	A.2. Chronic dietary exposure applying a cut-off of 0.7 mg/kg to the available occurrence data
B. Acute exposure assessments	B.1. Acute dietary exposure using the available occurrence data
	B.1.1. Total acute dietary exposure
	B.1.2. Acute dietary exposure food by food
	B.2. Acute dietary exposure applying a cut-off of 0.7 mg/kg to the available occurrence data
	B.2.1. Total acute dietary exposure
	B.2.2. Acute dietary exposure food by food
	B.3. Acute dietary exposure assigning a value of 0.7 mg/kg to all samples of food and drinking water
	B.3.1. Total acute dietary exposure
	B.3.2. Acute dietary exposure food by food

2.2.3. Hazard assessment

2.2.3.1. Strategy for literature search

For the present evaluation the CONTAM Panel considered literature made publicly available until 30 January 2015. A comprehensive search for literature was conducted for peer-reviewed original research pertaining to the occurrence of chlorate in food and drinking water and adverse health effects on (experimental) animals and humans. The search strategy was designed to identify scientific literature dealing with chemical analysis, chemistry, occurrence, exposure, toxicity, mode of action, toxicokinetics and epidemiology of chlorate.

Additionally, research or reports related to compounds that can yield chlorate upon transformation processes were considered, i.e. sodium chlorate, potassium chlorate, chlorine dioxide and hypochlorite. Literature search was not restricted to publications in English language, however, literature in other languages was only considered if an English abstract was available. A first literature search was performed in September 2014 and has since been updated in November 2014, December 2014 and January 2015. Web of Science²³ and Pubmed²⁴ were identified as databases appropriate for retrieving literature for the present evaluation. The references resulting from the literature search were imported and saved using a software package (EndNote²⁵), which allows effective management of references and citations. Additionally, reviews, relevant scientific evaluations by national or international bodies were considered for the current risk assessment i.e. previous evaluations of ECHA (2015a, b), BfR (2013), WHO (2005), FAO/WHO (2007, 2008, 2011), NTP (2002, 2005) and the US EPA (2002, 2006). Particular consideration has been given to the scientific opinion on perchlorate (EFSA CONTAM Panel, 2014). Furthermore, the unpublished original studies summarized in the Draft Assessment Report (EU DAR, 2008) have been reviewed for the present assessment as the data owner has granted full access to these.

2.2.3.2. Appraisal of studies

Information retrieved has been reviewed by the CONTAM WG on chlorate in food and used for the present assessment using expert judgement. Any limitations of the information used are clearly documented in this opinion. Human case-studies and reports, including accidental or intentional exposure followed by death or illness were only included in the assessment when the exposure to chlorate was well documented or recorded. The available epidemiological studies were only related to disinfection of drinking water by chlorination. Studies not providing information on chlorate concentrations were excluded. Studies solely focusing on the efficacy of chlorate as anti-microbial agent or herbicide were excluded from analysis.

2.2.4. Methodology applied for risk assessment

The CONTAM Panel applied the general principles of the risk assessment process for chemicals in food as described by WHO/IPCS (2009), which include hazard identification and characterization, exposure assessment and risk characterization. Additionally to the principles described by WHO/IPCS (2009), EFSA guidance pertaining to risk assessment (EFSA SC, 2012b) has been applied for the present assessment. In brief, the EFSA guidance documents cover the procedures currently used within EFSA for the assessment of dietary exposure to different chemical substances and the uncertainties arising from such assessments (EFSA, 2006b). For details on the specific EFSA guidance applied see Appendix A.

²³ Web of Science (WoS), formally ISI Web of Knowledge, Thomson Reuters. Available at: <http://thomsonreuters.com/thomson-reuters-web-of-science/>

²⁴ PubMed, Entrez Global Query Cross-Database Search System, National Center for Biotechnology Information (NCBI), National Library of Medicine (NLM), Department of the National Institutes of Health (NIH), United States Department of Health and Human Services. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/>

²⁵ EndNote X5, Thomson Reuters. Available at: <http://endnote.com/>

3. Assessment

3.1. Occurrence data

3.1.1. Previously reported occurrence results

3.1.1.1. Fruit and vegetables

No studies on the occurrence of chlorate in fruit and vegetables were identified in the scientific literature. Instead, only experimental studies on the direct treatment of fruit and vegetables with ASC and chlorine dioxide and the resulting chlorate levels in the fruit or vegetables were identified. Biocides such as chlorine dioxide are mainly used in the EU to maintain the quality of potable water used by food industry at an acceptable microbial level. This is allowed in some EU Member States under national legislation (see Section 1.3.4). Therefore, the CONTAM Panel considered these studies relevant for the current evaluation.

The JECFA evaluated the use of ASC as an antimicrobial agent on fruits and vegetables (see Section 1.3.1). The manufacturer had reported the residual chlorate levels in fruit and vegetables following treatment with ASC solutions applied under different conditions. Cut up and sliced carrots, melons, lettuce, strawberries, onions and potatoes were dipped in or sprayed with ASC (1 200 mg sodium chlorite/L, pH 2.5) for 30 seconds, followed by a washing step. Chlorate concentration was determined after 24 hours, and was below 10 µg/kg. Chlorate was detected at a concentration of 500 µg/kg in pre-processed produce (fruit or vegetable not specified) that was sprayed with ASC (1 200 mg sodium chlorite/L, pH 2.5) for 5–10 seconds and then immersed in water. Application of a high-volume wash for 30 seconds reduced the chlorate levels below the LOD of 100 µg/kg (FAO/WHO, 2008).

Chen et al. (2011) immersed mulberries in chlorine dioxide solutions at different concentrations (20, 60 and 80 mg/L) for 5, 10 or 15 minutes, followed by a rinsing step with potable water for 1 minute. The chlorate concentration was determined for the treatment with 60 mg/L during 15 minutes and was below the LOD (300 µg/kg).

Tomatoes (100 g/trial, three trials) were exposed to approximately 5 mg ³⁶Cl-labelled chlorine dioxide gas during 2 hours and rinsed afterwards. The Na³⁶ClO₃ concentration ranged between 0.4 and 1.3 mg/kg in the liquid fraction of tomato puree, between < 0.51 and 2.1 mg/kg in the solid fraction of tomato puree and between 117 and 125 mg/kg in the stem scar tissue (Smith et al., 2014).

3.1.1.2. Food of animal origin

No studies on the occurrence of chlorate in food of animal origin were identified in the scientific literature. Instead, only experimental studies on the direct treatment of food of animal origin with ASC and chlorine dioxide and the resulting chlorate levels were identified which are summarised below.

The AFC Panel evaluated the use of ASC as an antimicrobial agent on poultry carcasses (see Section 1.3.1). The manufacturer had reported chlorate levels in the carcasses between 11 and < 200 µg/kg depending on the treatment. For chlorine dioxide treatment, a residual chlorate concentration of 60 µg/kg was reported (EFSA, 2006a). The studies on ACS were also evaluated by the JECFA in 2007 (FAO/WHO, 2008).

The use of ASC as an antimicrobial agent on red meat was also evaluated by the JECFA. Chlorate levels of 45 and 220 µg/kg were reported by the applicant for different treatments (FAO/WHO, 2008).

For seafood and fish, the use of ASC as an antimicrobial agent resulted in chlorate levels < 100 µg/kg depending on the treatment (FAO/WHO, 2008).

The CONTAM Panel noted that the use of ASC and chlorine dioxide as antimicrobial agents on food of animal origin is not allowed in the EU (see Section 1.3.4).

3.1.1.3. Food supplements and flavour enhancing ingredients

Chlorate was analysed in dietary supplements ($n = 31$) and flavour enhancing ingredients (kelp granules, iodized salt, sea salt; $n = 4$) by LC-MS/MS (LOD = 4–30 $\mu\text{g/kg}$). Samples were collected from commercial vendors in the USA but no information was available on whether they had been treated with chlorine products. Chlorate was detected in 26 samples of dietary supplements at concentrations ranging from 25 to 10 300 $\mu\text{g/kg}$ and in all tested flavour enhancing ingredients at concentrations ranging from 45 to 65 $\mu\text{g/kg}$ (Snyder et al., 2006).

3.1.1.4. Drinking water

Fantuzzi et al. (2007) analysed chlorate in drinking water ($n = 1\,199$) from different Italian cities by ion chromatography with conductivity detection. Samples had been collected between October 1999 and September 2000. Chlorate was detected in 34 % of the samples (LOD = 20 $\mu\text{g/L}$) with a median concentration of 76 $\mu\text{g/L}$ (range: 20–1 500 $\mu\text{g/L}$).

Chlorate was measured by ion chromatography with conductivity detection (LOD = 1.0 $\mu\text{g/L}$) in 509 drinking water samples taken in 2007 and 2008 in Castilla y León, Spain. Chlorate was detected in 65 % of the samples with a mean concentration of 224 $\mu\text{g/L}$ (range: 2–4 340 $\mu\text{g/L}$) (García-Villanova et al., 2010).

In addition, studies on the occurrence of chlorate in drinking water and other beverages are available in the scientific literature for non-European countries. However, since the chlorate levels in drinking water and beverages depend on the drinking water treatment, these studies were not considered relevant for the current evaluation.

3.1.2. Food processing

There are two major sources of chlorate residues in food:

- i) the use of chlorinated water for various food processing steps (drinking water, potable water and processing water), and
- ii) the disinfection of surfaces and food processing equipment.

To ensure microbiological safety and to prevent contamination of food from the production process, surfaces and equipment are cleaned by disinfectants. Regarding milk for example, after use surfaces of equipment that are intended to come into contact with milk (utensils, containers, tanks, etc. intended for milking, collection or transport) must be cleaned and, where necessary, disinfected. According to Regulation (EC) No 853/2004 on specific hygiene rules for hygiene on foodstuffs, at least once a day, containers and tanks used for the transport of milk must be cleaned and disinfected before re-use.

Drinking water and potable water can contain substantial amounts of chlorate (CVUA, 2014a) and thus increase chlorate levels in food when used as ingredient water.

Various food commodities are rinsed, sprayed and washed with potable water, that can contain substantial amounts of chlorate as a consequence of water disinfection (e.g. chlorination). In a recent small study lettuce and green onions were washed for 1 minute with water supplemented with chlorate (0.66 mg/L) and subsequently homogenized and analysed by LC-MS/MS for chlorate. In the non-washed controls no chlorate ($< 0.01 \text{ mg/kg}$) was detectable. The washed lettuce ($n = 4$) contained chlorate concentrations of 0.068–0.078 mg/kg , the washed green onions ($n = 4$) 0.018–0.027 mg/kg . (Labor Friedle, 2014, unpublished report). Moreover, in EU countries the use of a chlorine-based disinfectant solution can be allowed for the dipping or spraying of fruits or vegetables under national legislation (see Section 1.3.4).

‘Hydro-cooling’ is a procedure, in which freshly harvested but also prepared vegetables/fruits are quickly cooled in ice water (to 10 °C), mainly to minimize the loss of moisture and to extend shelf life. The CVUA Stuttgart has recently shown that prepared carrots from the USA have high chlorate residue levels (up to 0.54 mg/kg), which likely result from the use of chlorinated water in the hydro-cooling process (CVUA, 2014b).

In a recent update the CVUA provided additional evidence, that especially the postharvest treatment contributes to the high levels of chlorate in processed and frozen carrots (CVUA, 2014c).

In frozen vegetables chlorate residues might originate from both washing procedures with potable water but also the use of processing water e.g. for blanching and hydro-cooling procedures (CVUA, 2014b, c). For the washing, blanching and cooling, a closed water circuit is applied. Since the water is not refreshed continuously it is repeatedly chlorinated to keep its microbial quality within safe limits. During the re-circulation chlorate therefore concentrates into the processing water as a by-product from chlorine disinfection.

Changes to the chlorate content might also take place during the preparation of food at private households. The CONTAM Panel has not identified reliable literature about this aspect. Nevertheless, from a chemical point of view it is likely that the washing with, and especially the cooking procedure in, drinking water decreases the chlorate levels in chlorate-polluted vegetables and fruits. In contrast, a non-appropriate use of chlorine-containing cleaning agents, e.g. for cookware and dinnerware, might increase chlorate levels in food.

3.1.3. Current occurrence results

The left-censored data were treated by the substitution method as recommended in the ‘Principles and Methods for the Risk Assessment of Chemicals in Food’ (WHO/IPCS, 2009). The same method is indicated in the EFSA scientific report ‘Management of left-censored data in dietary exposure assessment of chemical substances’ (EFSA, 2010b) as an option in the treatment of left-censored data. The guidance suggests that the lower-bound (LB) and upper-bound (UB) approach should be used for chemicals likely to be present in the food (e.g. naturally occurring contaminants, nutrients and mycotoxins). At the LB, results below the LOQ and LOD were replaced by zero; at the UB the results below the LOD were replaced by the LOD and those below the LOQ were replaced by the value reported as LOQ.

Despite the presence of a high percentage of left-censored data (71 %) no substantial differences were observed in most of the food groups when LB and UB estimations were compared at the different FoodEx levels. The highest differences between LB and UB estimates were for drinking water, and were around 26 % (LB = 28.3 µg/L; UB = 38.5 µg/L).

All analytical results were reported based on whole weight. In terms of number of samples the best represented food group was ‘Vegetable and vegetable products’ (n = 3 752), followed by ‘Fruit and fruit products’ (n = 2 607). Other food groups that were well represented were ‘Drinking water’ (n = 453) and ‘Herbs, spices and condiments’ (n = 374). Table 3 shows summary statistics for chlorate concentration (µg/kg) with the different food samples aggregated at FoodEx level 1.

Among ‘Vegetable and vegetable products’, the best represented food group was ‘Fruiting vegetables’ (n = 1 654). Within ‘Fruiting vegetables’ several food commodities stood out due to their mean high levels of chlorate, in particular ‘Chilli pepper’ (LB = 164 µg/kg, UB = 169 µg/kg, n = 27) and ‘Aubergines’ (LB = 157 µg/kg, UB = 164 µg/kg, n = 73). High levels of chlorate were also reported for ‘Vegetable and vegetable products, unspecified’ (LB = 216 µg/kg, UB = 222 µg/kg, n = 25) and ‘Brassica vegetables’ (LB = 160 µg/kg, UB = 165 µg/kg, n = 416). Detailed information on the chlorate levels in the different foods is shown in Appendix D. For certain food samples (~ 10 % of the total) information was reported on the fact that they underwent freezing processes. Most of these foods belong to the food group ‘Vegetable and vegetable products’ although samples of ‘Fruit and fruit products’ among others were also reported. It was noticed that for certain food groups there was an

association between high levels of chlorate and being reported as frozen. This was particularly evident for ‘Broccoli’ where all the samples with the highest concentrations (samples above 1 000 µg/kg, n = 15) were reported as being frozen products. A similar situation is found for ‘Carrots’ where the two samples with the highest concentrations were frozen products (720 µg/kg and 1 500 µg/kg) or for ‘Peppers, paprika’ where one of the samples with the highest chlorate levels were also reported as frozen product. However, it is important to indicate that in the above mentioned food categories many samples described as frozen presented levels of chlorate very low or below the LOD. For example, 60 % of the samples of ‘Peppers, paprika’ reported as frozen were below the LOQ. Chlorate levels in the frozen food samples seems to derive from the blanching/washing process carried out previous to freezing the foods, a process to stop enzyme actions which can cause loss of flavour, colour and texture. Since blanching/washing in chlorinated water prior to freezing seems to be a common practice in food industry, the differences in the reported chlorate levels in the frozen foods may be explained by the use of water with different concentrations of chlorine.

Table 3: Summary statistics for chlorate concentrations (µg/kg) with the different samples aggregated at FoodEx level 1 (detailed description of the occurrence values grouped at the appropriate FoodEx level to calculate dietary exposure is shown in Appendix D). Values were rounded off to the nearest whole number (0 decimal places).

FoodEx level 1 food groups	n	LC (%)	LB/UB	Concentration (µg/kg) ^(a)					
				Mean	P5	P25	P50	P75	P95
Grains and grain-based products	91	60	LB	27	0	0	0	22	180
			UB	31	2	5	10	22	180
Vegetables and vegetable products (including fungi)	3 756	72	LB	76	0	0	0	13	250
			UB	83	2	5	10	16	250
Starchy roots and tubers	122	88	LB	13	0	0	0	0	88
			UB	18	2	2	5	10	98
Legumes, nuts and oilseeds	263	55	LB	143	0	0	0	46	910
			UB	147	2	2	10	50	910
Fruit and fruit products	2 607	84	LB	8	0	0	0	0	31
			UB	13	2	2	5	10	41
Milk and dairy products	130	57	LB	85	0	0	0	54	510
			UB	91	10	10	10	54	510
Sugar and confectionary	12	67	LB	65	-	0	0	49	-
			UB	79	-	10	25	54	-
Animal and vegetable fats and oils	3	67	LB	85	-	-	-	-	-
			UB	92	-	-	-	-	-
Fruit and vegetable juices	67	54	LB	42	0	0	0	18	177
			UB	46	2	5	10	18	177
Non-alcoholic beverages (excepting milk based beverages)	2 ^(b)	0	LB	62	24	24	62	100	100
			UB	62	-	-	-	-	-
Alcoholic beverages	37 ^(c)	97	LB	-	-	-	-	-	-
			UB	3	2	2	2	2	5
Drinking water	453	31	LB	28	0	0	11	30	118
			UB	39	2	10	22	50	118
Herbs, spices and condiments	372	53	LB	413	0	0	0	125	2 700
			UB	417	2	5	10	125	2 700
Food for infants and small children	44	80	LB	5	-	0	0	0	-
			UB	9	-	5	5	10	-
Products for special nutritional use	3	67	LB	18	-	-	-	-	-
			UB	25	-	-	-	-	-
Composite food (including frozen products)	66	6	LB	111	0	25	42	84	566
			UB	112	10	25	42	84	566

LB: lower bound; LC: left-censored; n: number of samples; UB: upper bound.

(a): The different percentiles were only described when a minimum number of samples were available, 60 samples for the 5th and 95th percentile, 11 samples for 25th and 75th percentile, and six samples for the median. Otherwise, the percentiles may not be statistically robust (EFSA, 2011b).

(b): Before estimating dietary exposure the chlorate levels reported for 453 samples of drinking water were assigned to tea and coffee.

(c): Before estimating dietary exposure the chlorate levels reported for 453 samples of drinking water were assigned to beer.

In the FoodEx classification system (EFSA, 2011a) the different types of water (bottled water, tap water, water ice and well water) are grouped under the generic name 'Drinking water'. Therefore, the generic term 'Drinking water' as used in this opinion includes both water intended for human consumption (Council Directive 98/83/EC) and natural mineral waters (Commission Directive 2003/40/EC²⁶). Bottled water as used in this opinion includes natural mineral water, but also spring water and other bottled drinking water, products that must comply with Council Directive 98/83/EC.

Most of the samples of 'Drinking water' were reported as unspecified (83 %, $n = 376$) without further details. Only 28 and 46 samples of drinking water were reported as bottled and tap water, respectively. As most of the consumption data in the EFSA Comprehensive Database refers to tap water (63 %), and the chlorate levels in this type of drinking water did not differ much from those reported for unspecified drinking water, it was decided to group all samples at FoodEx level 1 before estimating dietary exposure.

To avoid underestimation of the dietary exposure to chlorate due to the lack of occurrence data, chlorate levels were imputed to particular foods that are relatively highly consumed. Accordingly, the 453 samples of drinking water were also used to derive chlorate levels for tea, coffee, and beer. In addition, when estimating the dietary exposure to chlorate it was also considered the potential contribution of the water used during the preparation of certain foods such as dry legumes, rice and pasta. The amount of water used for cooking was based on described weight yield factor for the different foods; for pasta and rice it was estimated that two parts of water per part of food are used while for dry legumes it should be 1.5 parts of water per part of food (Bognár, 2002). By doing this it is assumed that chlorate is non-volatile and that it remains stable during cooking as it has been recently reported (Asami et al., 2013).

Two samples of low-fat yoghurt (< 1 % fat) reported relatively high chlorate values (180 µg/kg and 380 µg/kg). The CONTAM Panel considers that these two samples are insufficient and not representative of a food commodity that is relatively highly consumed; therefore they were excluded before the dietary exposure to chlorate was estimated. Instead, the occurrence values reported for 'Liquid milk' were used when the consumption of yoghurt was reported (10-17 µg/kg, LB-UB).

One analytical result on infant/follow-on formula was received by EFSA, with a reported value of 2.5 mg chlorate/kg dry weight. This sample was not included in the exposure scenarios as it was received at a very late stage during the preparation of this scientific opinion, but is notable because of the high chlorate level. High levels of chlorate (in the order of mg/kg dry weight) have been reported also from infant/follow-on formula in Japan (Asami et al., 2013).

Appendix D shows a more detailed description of the occurrence values selected to calculate the dietary exposure to chlorate, and in the scenarios described in Table 2 and how the samples were grouped before the exposure estimations were carried out.

3.2. Exposure assessment

3.2.1. Previously reported exposure assessments

Both the AFC Panel (EFSA, 2006a) and the JECFA (FAO/WHO, 2008) estimated the potential dietary exposure to chlorate based on data submitted by an applicant for the use of biocides such as chlorine dioxide as a processing aid. However, this use is not allowed in the EU and the CONTAM Panel considered these exposure assessments not relevant for the current evaluation.

²⁶ Commission Directive 2003/40/EC of 16 May 2003 establishing the list, concentration limits and labelling requirements for the constituents of natural mineral waters and the conditions for using ozone-enriched air for the treatment of natural mineral waters and spring waters OJ L 126, 22.5.2003, p. 34–39.

Snyder et al. (2006) estimated the dietary exposure from dietary supplements and flavour enhancing ingredients (kelp granules, iodized salt, sea salt) (see Section 3.1.1.3). Based on the recommended daily dose of the supplements, it was estimated that the daily exposure to chlorate ranged from 0.046 to 20 µg per day. Exposure from the flavour enhancing ingredients considered in this study was estimated to be between 0.072 and 0.2 µg per serving.

3.2.2. Non-dietary exposure

In humans, there is a potential for additional exposure to chlorate from shower water and swimming pool water. Righi et al. (2014) analysed 24 water samples taken from indoor swimming pools in Italy and detected chlorate in all samples at concentrations ranging from 5 to 19 537 µg/L (mean: 3 661 µg/L and median: 1 235 µg/L). In Poland, also Michalski and Mathews (2007) detected chlorate in all water samples (n = 7) taken from indoor swimming pools and reported concentrations between 2 140 and 31 920 µg/L (mean: 19 086 µg/L and median: 22 230 µg/L).

3.2.3. Current exposure assessment

3.2.3.1. Chronic dietary exposure to chlorate

For calculating the chronic dietary exposure to chlorate, food consumption and body weight data at the individual level were accessed in the Comprehensive Database. Occurrence data and consumption data were linked at the lowest FoodEx level possible. In addition, the different food commodities were grouped within each food category to better explain their contribution to the total dietary exposure to chlorate. For each country, exposure estimates were calculated per dietary survey and age class. Chronic exposure estimates were calculated for 35 different dietary surveys carried out in 19 different European countries. Not all countries provided consumption information for all age groups, and in some cases the same country provided more than one consumption survey.

The mean and the high (95th percentile) chronic dietary exposures were calculated by combining chlorate mean occurrence values for food and drinking water samples collected in different countries (pooled European occurrence data) with the average daily consumption for each food at individual level in each dietary survey.

Chronic dietary exposure using the available occurrence data (Scenario A.1, see Table 2)

Table 4 shows summary statistics of the chronic exposure assessment to chlorate using the available occurrence data. Detailed mean and 95th percentile dietary exposure estimates calculated for each of the 35 dietary surveys are presented in Appendix F.

The highest chronic exposure to chlorate was estimated for the youngest population groups ('Infants', 'Toddlers' and 'Other children'). For the mean exposure, the estimates ranged between 0.5 µg/kg b.w. per day in adolescents (LB) and 4.1 µg/kg b.w. per day in 'Infants' (UB). In the highly exposed population (95th percentile) the lowest dietary exposure was estimated in 1.0 µg/kg b.w. per day (LB) in diverse age classes ('Elderly' and 'Very elderly') and 'Lactating women', and the highest exposure in 'Infants' (6.6 µg/kg b.w. per day, UB).

Overall, in all age classes and vulnerable population groups ('Pregnant and lactating women') the main average contributor to the dietary exposure to chlorate was 'Drinking water'. It is important to mention that when considering 'Drinking water' also the water used for cooking pasta, rice and legumes is included. In few dietary surveys drinking water was not the main contributor, as observed for instance in 'Toddlers' where soft drinks and fruit juices were the main contributors in two countries. In some dietary surveys the consumption of drinking water is missing ('Regional Crete', Diet Lactation GR, 'Childhealth') or underreported ('National Dietary Survey' and 'National Repr Surv') resulting in different food commodities becoming the main average contributors (further information on the contributors across the different dietary surveys and age classes is provided in Appendix E).

Further information of the different contributors to chlorate exposure, under this scenario and across the different age classes, is detailed in Appendix E.

The ranges of contribution of ‘Drinking water’ across age classes and vulnerable groups were as follow (at the LB estimations): ‘Infants’ (24.9–58 %), ‘Toddlers’ (11.6–47.8 %), ‘Other children’ (0.02–37.9 %), ‘Adolescents’ (0.03–37.9 %), ‘Adults’ (6.2–48 %), ‘Elderly’ (8.1–34.8 %), ‘Very elderly’ (5.5–39.1 %).

Since ‘Drinking water’ was the main contributor in most of the dietary surveys, the differences observed in the LB and UB exposure estimates (mean difference = 25 %) are in line with those reported at the occurrence level in drinking water (see Section 3.1.3.1).

With regards to the distribution of the level of contamination for drinking water, the Panel noted that the 95th percentile of 118 µg/L is approximately six times lower than the guideline level of 0.7 mg/L set by the WHO. It is also noted that the mean concentration level used in the exposure calculations (LB of 28 µg/L–UB of 39 µg/L) is approximately 20 times lower than this guideline level of 0.7 mg/L.

Table 4: Summary statistics of chronic exposure assessments to chlorate across European dietary surveys (µg/kg b.w. per day). Estimates were rounded to one decimal place.

Mean dietary exposure (µg/kg b.w. per day)							
Age class ^(a)	n	Lower bound (LB)			Upper bound (UB)		
		Min	Median	Max	Min	Median	Max
Infants	6	1.6	1.9	2.9	2.0	2.6	4.1
Toddlers	10	2.1	2.6	2.8	2.8	3.2	3.5
Other children	18	1.3	1.9	2.3	1.5	2.4	2.8
Adolescents	17	0.5	1.1	1.6	0.6	1.4	1.9
Adults	17	0.7	1.0	1.3	0.8	1.3	1.6
Elderly	14	0.6	0.9	1.1	0.7	1.1	1.4
Very elderly	12	0.6	0.9	1.2	0.7	1.1	1.6
Pregnant women	1	0.8	– ^(b)	– ^(b)	– ^(b)	– ^(b)	1.0
Lactating women	1	0.6	– ^(b)	– ^(b)	– ^(b)	– ^(b)	0.7
95th percentile dietary exposure ^(c) (µg/kg b.w. per day)							
Age class ^(a)	n	Lower bound (LB)			Upper bound (UB)		
		Min	Median	Max	Min	Median	Max
Infants	6	3.3	3.4	5.0	4.1	4.3	6.6
Toddlers	10	3.2	4.1	4.7	4.2	5.2	5.4
Other children	18	2.5	3.2	4.1	2.7	3.9	5.0
Adolescents	17	1.1	2.0	2.6	1.2	2.3	3.0
Adults	17	1.2	1.8	2.3	1.4	2.2	2.8
Elderly	14	1.0	1.5	2.0	1.2	1.9	2.5
Very elderly	12	1.0	1.4	1.7	1.2	1.8	2.2
Pregnant women	1	1.4	– ^(b)	– ^(b)	– ^(b)	– ^(b)	1.8
Lactating women	1	1.0	– ^(b)	– ^(b)	– ^(b)	– ^(b)	1.1

b.w.: body weight; LB: lower bound; n: number of samples; UB: upper bound.

(a): Section 2.1.1.3 describes the age range within each age class.

(b): Not calculated since estimates were only available from one dietary survey.

(c): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

Chronic dietary exposure applying a cut-off of 0.7 mg/kg to the available occurrence data (Scenario A.2, see Table 2)

Table 5 shows summary statistics of the chronic exposure assessment to chlorate based only on available occurrence data with chlorate levels equal to or lower than 0.7 mg/kg.

As compared to the chronic dietary exposure without applying any cut-off (Section 3.2.3.1, subsection on ‘Chronic dietary exposure using the available occurrence data (Scenario A.1, see Table 2)’), the estimates of exposure were only slightly lower. This is explained by the fact that only 143 foods reported values above 0.7 mg/kg, and they mainly belong to the food groups ‘Vegetables and vegetable products’ and ‘Herbs, spices and condiments’ that do not contribute substantially to the chronic dietary exposure to chlorate. Only one sample of ‘Drinking water’ was excluded by applying this cut-off.

Table 5: Summary statistics of the chronic exposure assessment to chlorate across European dietary surveys (µg/kg b.w. per day). Occurrence values above 0.7 mg/kg were excluded before calculating exposure. Estimates were rounded to one decimal place.

Mean dietary exposure (µg/kg b.w. per day)							
Age class ^(a)	n	Lower bound (LB)			Upper bound (UB)		
		Min	Median	Max	Min	Median	Max
Infants	6	1.3	1.7	2.7	1.8	2.3	3.9
Toddlers	10	1.8	2.1	2.3	2.5	2.7	3.1
Other children	18	1.1	1.7	2.0	1.3	2.1	2.4
Adolescents	17	0.4	1.0	1.4	0.5	1.2	1.7
Adults	17	0.5	0.9	1.1	0.7	1.1	1.5
Elderly	14	0.4	0.8	1.0	0.5	1.0	1.3
Very elderly	12	0.4	0.7	1.0	0.6	1.0	1.4
Pregnant women	1	0.7	– ^(b)	– ^(b)	– ^(b)	– ^(b)	0.9
Lactating women	1	0.4	– ^(b)	– ^(b)	– ^(b)	– ^(b)	0.5

95th percentile dietary exposure ^(c) (µg/kg b.w. per day)							
Age class ^(a)	n	Lower bound (LB)			Upper bound (UB)		
		Min	Median	Max	Min	Median	Max
Infants	6	2.6	2.9	4.6	3.5	4.0	6.2
Toddlers	10	2.8	3.5	4.3	3.9	4.4	5.1
Other children	18	2.2	2.8	3.4	2.5	3.4	4.4
Adolescents	17	0.9	1.8	2.4	1.0	2.1	2.8
Adults	17	1.0	1.5	2.0	1.2	2.0	2.5
Elderly	14	0.8	1.3	1.6	1.0	1.7	2.3
Very elderly	12	0.8	1.2	1.4	1.0	1.6	1.9
Pregnant women	1	1.2	– ^(b)	– ^(b)	– ^(b)	– ^(b)	1.6
Lactating women	1	0.8	– ^(b)	– ^(b)	– ^(b)	– ^(b)	0.9

b.w.: body weight; LB: lower bound; n: number of samples; UB: upper bound.

(a): Section 2.1.1.3 describes the age range within each age class.

(b): Not calculated since estimates were only available from one dietary survey.

(c): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

3.2.3.2. Consideration of the use of a variability factor for acute exposure assessment

The CONTAM Panel discussed whether it was necessary to apply, in its acute exposure assessments, variability factors for residues in fruit and vegetables with a large unit weight (> 25 g) as is commonly performed for pesticides to account for variation within composite samples (EFSA, 2005). The CONTAM Panel considered that in some instances where measurements of contaminants were carried out with composite samples of foods with a large unit size and depending on the route by which the contaminant enters the food, application of variability factors could be appropriate in acute exposure assessments.

Chlorate residues (unlike pesticide residues) usually arise post-harvest through food processing and, thus, local contamination resulting in high variation of residues within individual food samples is less likely to occur. The practices leading to the presence of chlorate are most likely the use of chlorinated water for various food processing (e.g. for blanching and hydro-cooling procedures), and the treatment of food processing equipment with chlorate containing/yielding substances. Due to the high solubility

of chlorine and chlorate in water an even distribution of chlorate residues in processing water is expected.

In addition, the acute dietary exposure estimations presented in the opinion are based on a data set of occurrence/monitoring data received upon a call for data. Variability in chlorate levels between samples is addressed by the use of the highest reliable percentile (often the 95th but for some of the food groups also the 99th percentile) for the assessment of acute exposure.

This approach is confirmed by the fact that food commodities with the highest reported levels of chlorate were mainly frozen vegetables (e.g. broccoli, cucumbers, carrots). The CONTAM Panel considers that these samples refer to small pieces of vegetables obtained from whole vegetables units that were washed, chopped, blanched, cooled and then blended. Therefore, the potential variability in the levels of chlorate during food processing is minimised.

Overall, the CONTAM Panel concludes that the use of variability factors for assessments of acute exposure to chlorate in food is not appropriate.

3.2.3.3. Acute dietary exposure

Acute exposure estimates were calculated for 41 different dietary surveys carried out in 23 different European countries. Acute dietary exposure to chlorate was estimated as total exposure and as exposure food by food. The different food commodities were grouped based on their occurrence values as done before estimating chronic dietary exposure (see Appendix D). Overall, foods were grouped at FoodEx level 2, although for certain commodities FoodEx level 1 (e.g. 'Drinking water') or level 3 (e.g. 'Aubergines', 'Broccoli') were used.

In each dietary survey, total acute dietary exposure was estimated for each individual and reporting day by multiplying the total daily consumption amount for each food by their mean occurrence level (UB estimate), except for one food where the highest reliable percentile (UB estimate) was used as occurrence value (see Appendix D). This food refers to that with the highest contribution to the exposure when using highest reliable percentile occurrence levels. To estimate the acute dietary exposure food by food, the highest reliable percentile (UB estimate) was selected as occurrence value for each food at the appropriate FoodEx level, and linked to individual consumption data of that food in one single day.

As in the estimation of the chronic dietary exposure to chlorate when considering 'Drinking water' as one of the contributors, the water used for cooking pasta, rice and legumes is also included.

Acute dietary exposure using the available occurrence data (scenario B.1)

Total acute dietary exposure (scenario B.1.1, see Table 2)

Using all available occurrence data estimates of mean acute exposure to chlorate ranged between 1.0 µg/kg b.w. per day and 13.2 µg/kg b.w. per day; for the 95th percentile exposure the estimates were between 2.6 and µg/kg b.w. per day and 30.9 µg/kg b.w. per day. The highest acute exposure to chlorate was estimated for the age class 'Infants', in both the average and the highly exposed population. Overall, the young population ('Infants', 'Toddlers' and 'Other children') showed the highest levels of acute exposure to chlorate. Table 6 shows the summary statistics of the total acute exposure assessment to chlorate using the available occurrence data.

Table 6: Summary statistics of the acute exposure assessment to chlorate (at the upper bound estimate) across European dietary surveys ($\mu\text{g/kg}$ b.w. per day). Estimates were rounded to one decimal place.

Age class ^(a)	n	Mean dietary exposure ($\mu\text{g/kg}$ b.w. per day)			95th percentile dietary exposure ^(c) ($\mu\text{g/kg}$ b.w. per day)		
		Upper bound					
		Min	Median	Max	Min	Median	Max
Infants	6	4.8	7.6	13.2	13.9	17.3	30.9
Toddlers	11	5.5	7.2	10.6	10.9	15.3	18.0
Other children	20	2.5	5.2	7.0	4.9	11.0	16.9
Adolescents	20	1.0	3.0	4.4	2.6	7.2	9.4
Adults	22	1.4	2.9	4.7	3.6	6.9	12.2
Elderly	16	1.3	2.9	3.9	3.6	6.0	8.0
Very elderly	14	1.3	2.7	4.1	2.9	5.3	10.4
Pregnant women	1	2.4	— ^(b)	— ^(b)	— ^(b)	— ^(b)	5.8
Lactating women	1	1.3	— ^(b)	— ^(b)	— ^(b)	— ^(b)	3.9

b.w.: body weight; n: number of samples.

(a): Section 2.1.1.3 describes the age range within each age class.

(b): Not calculated since estimates were only available from one dietary survey.

(c): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

Acute dietary exposure food by food (scenario B.1.2, see Table 2)

Table 7 shows the estimates of acute exposure, for consumers only, through the daily consumption of those 10 individual foods and food groups leading to the highest levels of acute exposure to chlorate. For each food, based on the number of samples reported, the highest reliable percentile was selected as the occurrence value and combined with the daily consumption of this specific food for each consumer.

Table 7: Estimates of acute exposure to chlorate (only consumers) through the daily consumption of individual foods/food groups and drinking water ($\mu\text{g/kg}$ b.w. per day). Estimates were rounded to one decimal place.

Food/Food group	$\mu\text{g/kg}$, UB estimate ^(a) (highest reliable percentile)	Average percentage of consuming days ^(b)	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(c)	
			Mean exposure	P95 dietary exposure ^(d)
Drinking water	196 (P99)	— ^(e)	0.0 ^(f) –12.6	0.2 ^(f) –31.6
Broccoli	2 400 (P95)	4.5	1.2–25.0	3.7–21.3
Whey and whey products (excluding whey cheese)	618 (P95)	4.3	0.0–8.1	0.0–18.8
Legumes, beans, green, without pods	1 100 (P95)	9.4	0.1–9.3	0.3–13.9
Tea (Infusion)	196 ^(g) (P99)	32.6	0.2–4.4	1.0–13.2
Beer and beer-like beverage	196 ^(g) (P99)	8.2	0.2–5.0	1.7–12.6
Herbs	8 500 (P99)	24.1	0.1–4.8	0.1–8.5
Peppers, paprika	1 400 (P99)	15.7	0.2–2.7	0.6–8.4
Fruiting vegetables (except peppers, chili peppers and aubergines)	420 (P99)	45.9	0.3–3.4	1.0–8.2

Food/Food group	$\mu\text{g/kg}$, UB estimate ^(a) (highest reliable percentile)	Average percentage of consuming days ^(b)	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(c)	
			Mean exposure	P95 dietary exposure ^(d)
Soft drinks	62 (mean)	23.9	0.1–1.7	0.4–5.3

b.w.: body weight; P95, 99: 95th, 99th percentile; UB: upper bound.

(a): The highest reliable percentiles (at the UB) for each food/food group is shown in brackets. The selection of the highest reliable percentiles was based on the number of samples available, 60 samples for the 5th and 95th percentile, 11 samples for 25th and 75th percentile, and six samples for the median. Otherwise, the percentiles may not be statistically robust.

(b): Average percentage of consumption days across dietary surveys and age classes.

(c): Range of acute exposure food by food across dietary surveys and age classes.

(d): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

(e): Not calculated as the contribution of drinking water also includes the water used for cooking;

(f): In specific dietary surveys the consumption of drinking water was missing ('Regional Crete', Diet Lactation GR and 'Childhealth') or underreported ('National Dietary Survey' and 'National Repr Surv')

(g): The 453 samples of drinking water were used to derive chlorate levels for tea and beer.

Acute dietary exposure applying a cut-off of 0.7 mg/kg to the available occurrence data (scenario B.2)

Total acute dietary exposure (scenario B.2.1, see Table 2)

Table 8 shows summary statistics of the total acute exposure assessment to chlorate using available occurrence data with chlorate levels equal or lower to 0.7 mg/kg.

As compared to the acute dietary exposure using the whole data set, only small differences were observed when applying the cut-off of 0.7 mg/kg. Estimates of mean acute exposure to chlorate ranged between 0.7 $\mu\text{g/kg}$ b.w. per day and 12.3 $\mu\text{g/kg}$ b.w. per day; for the 95th percentile exposure the estimates were between 1.5 and $\mu\text{g/kg}$ b.w. per day and 28.9 $\mu\text{g/kg}$ b.w. per day. The highest acute exposure to chlorate was estimated in the age class 'Infants', in both the average and the highly exposed population. Overall, the young population ('Infants', 'Toddlers' and 'Other children') showed the highest levels of acute exposure to chlorate. Table 8 shows summary statistics of the total acute exposure assessment to chlorate using available occurrence data with chlorate levels equal or lower to 0.7 mg/kg.

Table 8: Summary statistics of the acute exposure assessment to chlorate (at the upper bound estimate) across European dietary surveys ($\mu\text{g/kg}$ b.w. per day). Occurrence values above 0.7 mg/kg were excluded before calculating exposure. Estimates were rounded to one decimal place.

Age class ^(a)	n	Mean dietary exposure ($\mu\text{g/kg}$ b.w. per day)			P95 dietary exposure ^(c) ($\mu\text{g/kg}$ b.w. per day)		
		Min	Median	Upper bound Max	Min	Median	Max
Infants	6	3.7	6.8	12.3	10.0	14.1	28.9
Toddlers	11	4.2	6.1	9.6	9.6	13.6	16.5
Other children	20	2.0	4.5	6.0	3.9	9.6	14.6
Adolescents	20	0.7	2.6	4.1	1.5	6.3	8.6
Adults	22	1.1	2.6	4.2	2.9	6.3	11.3
Elderly	16	0.8	2.6	3.6	2.2	5.2	7.3
Very elderly	14	0.8	2.4	3.8	2.2	4.5	9.7
Pregnant women	1	2.1	— ^(b)	— ^(b)	— ^(b)	— ^(b)	5.2
Lactating women	1	0.9	— ^(b)	— ^(b)	— ^(b)	— ^(b)	2.3

b.w.: body weight; n: number of samples; P95: 95th percentile.

(a): Section 2.1.1.3 describes the age range within each age class.

(b): Not calculated since estimates were only available from one dietary survey.

(c): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

Acute dietary exposure food by food (scenario B.2.2, see Table 2)

As commented in Section 3.2.3.1 (subsection on ‘Chronic dietary exposure applying a cut-off of 0.7 mg/kg to the available occurrence data (Scenario A.2, see Table 2)’), the use of a cut-off of 0.7 mg/kg for all available occurrence data leads to the exclusion of only 143 samples, among them one sample of ‘Drinking water’.

Table 9 shows the same individual foods and food groups as reported in Table 7 when all occurrence data were used. It can be seen that the exposure estimations for certain groups such as ‘Drinking water’, ‘Tea (infusion)’, ‘Beer and beer-like beverage’ and ‘Soft drinks’ were similar to those reported in Table 7. This is because in these groups no samples or very few occurrence values were above 0.7 mg/kg. On the contrary, several samples of ‘Broccoli’, ‘Whey and whey products (excluding whey cheese)’, ‘Peppers, paprika’ ‘Legumes, beans, green, without pods’ were excluded as a consequence of applying the cut-off of 0.7 mg/kg. As a result the estimates of acute exposure from daily consumption of these foods decreased as compared to those considering all occurrence data.

Table 9: Estimates of acute exposure to chlorate (only consumers) through the daily consumption of individual foods/food groups and drinking water (µg/kg b.w. per day). Occurrence values above 0.7 mg/kg were excluded before calculating exposure. Estimates were rounded to one decimal place.

Food/Food group	µg/kg, UB estimate ^(a) (highest reliable percentile)	Average percentage of consuming days ^(b)	Range of acute exposure (µg/kg b.w. per day) ^(c)	
			Mean exposure	P95 dietary exposure ^(d)
Drinking water	183 (P99)	— ^(e)	0.0 ^(f) –11.7	0.2 ^(f) –29.5
Tea (infusion)	183 ^(g) (P99)	32.6	2.2–4.1	1.0–12.4
Beer and beer-like beverage	183 ^(g) (P99)	8.2	0.1–4.7	1.6–11.8
Whey and whey products (excluding whey cheese)	180 (P75)	4.3	0.0–2.4	0.0–5.5
Soft drinks	62 (mean)	23.9	0.1–1.7	0.4–5.3
Fruiting vegetables (except peppers, chili peppers and aubergines)	260 (P99)	45.9	0.2–2.1	0.6–5.1
Legumes, beans, green, without pods	300 (P95)	9.4	0.0–2.8	0.1–4.2
Broccoli	400 (P95)	4.5	0.2–4.2	0.6–3.6
Peppers, paprika	183 (P99)	15.7	0.1–1.0	0.2–3.2
Herbs	330 (P95)	24.1	0.0–0.2	0.0–0.3

b.w.: body weight; P95: 95th percentile; UB: upper bound.

(a): The highest reliable percentiles (at the UB) for each food/food group is shown in brackets. The selection of the highest reliable percentiles was based on the number of samples available, 60 samples for the 5th and 95th percentile, 11 samples for 25th and 75th percentile, and six samples for the median. Otherwise, the percentiles may not be statistically robust.

(b): Average percentage of consumption days across dietary surveys and age classes

(c): Range of acute exposure food by food across dietary surveys and age classes

(d): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

(e): Not calculated as the contribution of drinking water also includes the water used for cooking;

(f): In specific dietary surveys the consumption of drinking water is missing (‘Regional Crete’, Diet Lactation GR and ‘Childhealth’) or underreported (‘National Dietary Survey’ and ‘National Repr Surv’.

(g): The 453 samples of drinking water were used to derive chlorate levels for tea and beer.

3.2.3.4. Acute dietary exposure assuming an occurrence value of 0.7 mg/kg in all food commodities (scenario B.3)

In line with the terms of reference in this hypothetical scenario, acute exposures were estimated assuming that all food items and drinking water consumed have an occurrence value of 0.7 mg/kg in

order to assess the potential impact of applying the guidance value of 0.7 mg/kg²⁷ set by WHO (2005) for all food commodities included in the assessment covered by Regulation (EC) No 396/2005 and drinking water.

Total acute dietary exposure (scenario B.3.1, see Table 2)

Overall, the assumption of an occurrence value of 0.7 mg/kg for all commodities including drinking water led to substantially higher estimates of acute exposures in all age groups as compared to the scenario where actual occurrence levels were used. Highest relative increase (5.6-fold) of exposures applying this scenario was seen in ‘Infants’ at maximum mean dietary exposure, where exposure rose from 12.3 µg/kg b.w. per day (see Table 8, Section 3.2.3.3, subsection on ‘Total acute dietary exposure (scenario B.2.1, see Table 2)’) to 68.9 µg/kg b.w. per day.

For certain food commodities the selected value of 0.7 mg/kg is lower than the highest reliable percentile derived from the reported occurrence data (e.g. herbs, paprika, broccoli). This in principle should lead to lower exposure estimations. However, since these food commodities are not consumed in high amounts their impact on the acute exposure to chlorate was not important. Contrarily, the use of 0.7 mg/kg as occurrence value in some highly consumed commodities such as ‘Drinking water’ and ‘Liquid milk’ led to a dramatic increase of the acute exposure to chlorate. This is due to the fact that for ‘Drinking water’, for instance, the value of 0.7 mg/kg is almost more than 3.5 times higher than the highest reliable percentile derived from the reported occurrence data (99th percentile). Together with drinking water, other foods with relatively high consumption such as ‘Liquid milk’, ‘Beer’, ‘Tea (infusion)’ or ‘Soft drinks’ were important contributors to the acute exposure when using 0.7 mg/kg as chlorate level, a value far above the reported occurrence values.

Table 10 provides an overview on the summary statistics of acute exposures in the different age groups when applying an occurrence value of 0.7 mg/kg for all food commodities.

Table 10: Summary statistics of the acute exposure assessment to chlorate (at the UB estimate) across European dietary surveys (µg/kg b.w. per day). Occurrence values were all set up at 0.7 mg/kg before calculating exposure. Estimates were rounded to one decimal place.

Age class ^(a)	n	Mean dietary exposure ^(a)			P95 dietary exposure ^(c) (µg/kg b.w. per day)		
		Min	Median	Upper bound (UB) Max	Min	Median	Max
Infants	6	20.7	30.3	68.9	45.7	69.6	110.8
Toddlers	11	20.9	24.5	36.0	37.4	53.4	62.2
Other children	20	8.7	17.1	21.4	21.2	36.2	53.6
Adolescents	20	4.1	10.1	15.4	9.4	23.3	32.0
Adults	22	4.1	8.9	14.9	10.5	22.6	40.5
Elderly	16	2.6	8.5	11.8	5.9	17.9	25.1
Very elderly	14	2.9	7.8	13.2	6.9	15.1	35.1
Pregnant women	1	7.0	— ^(b)	— ^(b)	— ^(b)	— ^(b)	18.0
Lactating women	1	3.7	— ^(b)	— ^(b)	— ^(b)	— ^(b)	8.5

b.w.: body weight; n: number of samples; P95: 95th percentile.

(a): Section 2.1.1.3 describes the age range within each age class.

(b): Not calculated since estimates were only available from one dietary survey.

(c): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

²⁷ In analogy with the WHO guideline level for drinking water or 0.7 mg chlorate/L.

Acute dietary exposure food by food (scenario B.3.2, see Table 2)

An occurrence value of 0.7 mg/kg was used for all food commodities to estimate the acute exposure through the daily consumption of individual foods. The occurrence values were applied to all food commodities at FoodEx level 3 in order to assess the influence of individual foods in the acute exposure to chlorate.

The use of the occurrence value of 0.7 mg/kg results in 'Drinking water' and some foods such as milk, juice or soft drink being the commodities that lead to the highest estimates of acute exposure to chlorate (Table 11). Since for all foods the same occurrence value is assigned the exposure estimates are only driven by consumption. This makes that the highest acute exposures are estimated from foods consumed as liquids and with relative high consumption.

Table 11 shows the estimates of acute exposure, for consumers only, through the daily consumption of those ten individual food commodities (including drinking water) leading to the highest levels of acute exposure to chlorate. Estimates of acute exposure through the daily consumption (food by food) of all commodities at FoodEx level 3 are shown in Appendix G.

Table 11: Range of estimates of acute exposure to chlorate through the daily consumption of individual foods/food groups and drinking water ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. The ten commodities with the highest acute exposure estimates are shown.

FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. day) ^(a)	
	Mean exposure	95th percentile dietary exposure ^(b)
Drinking water	1.1 ^(c) –47.7	3.3 ^(c) –111.3
Cow milk	0.9–25.4	3.1–55.9
Beer and beer-like beverage	0.7–15.6	7.8–37.4
Flavoured milk	0.2–11.9	4.7–30.3
Juice, Apple	0.8–14.1	3.1–28.5
Tea (Infusion)	0.8–13.8	3.6–26.7
Soft drinks	0.2–12.3	2.9–26.2
Fruit purée for children	0.8–12.4	12.4–25.7
Juice, Orange	0.8–13.9	2.4–25.7
Concentrated fruit juice	0.0–6.2	0.5–24.8

b.w.: body weight; P95: 95th percentile.

(a): Range of acute exposure food by food across dietary surveys and age classes.

(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

(c): In specific dietary surveys the consumption of drinking water is missing ('Regional Crete', Diet Lactation GR, and 'Childhealth') or underreported ('National Dietary Survey' and 'National Repr Surv').

3.2.4. Potential contribution to dietary exposure to chlorate of infant/follow-on formula and yoghurt

As mentioned in Section 3.1.3, one analytical result on infant/follow-on formula and two of low-fat yoghurt (< 1 % fat) were not used in the assessments of the dietary exposure to chlorate reported in Section 3.2.

The analytical result on infant/follow-on formula was received by EFSA at a very late stage during the preparation of this scientific opinion, with a reported value of 2.5 mg chlorate/kg dry weight. The presence of chlorate in the order of mg/kg dry weight in infant/follow-on formula is supported by published studies carried out in Japan (Asami et al., 2013). EFSA is informed that further analyses are currently on-going to confirm the presence of these high levels of chlorate in infant/follow-on formula. If confirmed, these levels would result in a substantial increase in acute and chronic exposures in 'Infants' and 'Toddlers'.

The CONTAM Panel excluded the two samples of low-fat yoghurt (< 1 % fat) with relatively high chlorate values (180 µg/kg and 380 µg/kg) because they were considered as not representative of a food commodity that is relatively highly consumed. However, it is important to note that, in certain populations, the high consumption of yoghurt containing the above described levels of chlorate may result in a substantial increase in acute and chronic exposures, especially in ‘Infants’ and ‘Toddlers’.

3.3. Hazard identification and characterisation

3.3.1. Toxicokinetics

3.3.1.1. Laboratory animals

In 1925, Ross orally administered 500 mg/kg b.w. potassium chlorate (equivalent to 390 mg chlorate/kg b.w.) to dogs and provided evidence for a rapid absorption and excretion by assessing the chloride content before and after an acid-catalysed reduction of urinary chlorate. Of the total amount excreted in urine > 67 % was excreted within 6 hours of dosing. Subsequent studies utilized ^{36}Cl as a tracer for the chlorine and applied a fractionated or chromatographic methodology to separate the ^{36}Cl species in the respective body fluids (Abdel-Rahman et al., 1982, 1984; Hakk et al., 2007). After administering 0.065 mg/kg $^{36}\text{ClO}_3^-$ orally to male rats a peak ^{36}Cl plasma level was reached at 30 minutes (Abdel-Rahman et al., 1984). Gastrointestinal absorption rates after oral dosing chlorate salts are summarized in Table 12 and clearly indicate that in rats and livestock animals (Smith et al., 2006) after oral intake chlorate salts are rapidly and efficiently absorbed from the gastrointestinal tract.

Table 12: Gastrointestinal absorption after oral exposure assessed by urinary excretion of parent chlorate or of total radioactive residues (the sum of parent chlorate and metabolites) in studies in which $^{36}\text{ClO}_3^-$ salts were dosed

Species (number)	Dose residue measured	Collection time (hours)	Cumulative absorption (% of dose)	Reference
Dog (6)	500 mg/kg b.w. KClO_3 chlorate	4	46.0 ± 6.9	Ross et al. (1925)
		24	84.4 ± 7.0	
		48	88.9 ± 7.4	
Rat (4)	1.3 ^(a) mg/kg b.w. $\text{K}^{36}\text{ClO}_3$ TRR	8	21.6	Abdel-Rahman et al. (1984)
		24	37.4	
		48	40.1	
Rat (4)	3 mg/kg b.w. $\text{Na}^{36}\text{ClO}_3$ TRR	6	36.1	Hakk et al. (2007)
		24	70.5	
		48	74.9	
Swine (2)	20 mg/kg b.w. $\text{Na}^{36}\text{ClO}_3$	12	50.8 ± 5.9	Smith et al. (2006)
		24	77.7 ± 3.5	
	40 mg/kg b.w. $\text{Na}^{36}\text{ClO}_3$	12	62.7 ± 0.5	
		24	75.4 ± 12.8	
	60 mg/kg b.w. $\text{Na}^{36}\text{ClO}_3$	12	55.1 ± 13.5	
		24	81.0 ± 2.9	

b.w.: body weight; TRR: total radioactive residues.

(a): dose calculated assuming an average rat weight of 235 g.

Abdel-Rahman et al. (1980, 1982, 1984) reported that in rats chlorate is metabolized to chlorite (ClO_2^-) and chloride (Cl^-), which are, next to the parent chlorate, excreted into rat urine. The authors considered chlorite as a significant metabolite making up to 4 % of the initial dose of chlorate. Subsequent toxicokinetics studies in rats (Hakk et al., 2007) and livestock animals (Smith et al., 2005a, b, 2006, 2007) did not detect chlorite in tissue or excreta of animals. Furthermore, Hakk et al. (2007) demonstrated that the chemical methods used by Abdel-Rahman et al. (1980, 1982, 1984) which are based on the differential solubilities of chloride, chlorite and chlorate, were not capable of

distinguishing $^{36}\text{Cl}^-$, $^{36}\text{ClO}_2^-$ and $^{36}\text{ClO}_3^-$ in biological matrices. Applying ion chromatography with radiochemical detection Hakk et al. (2007) provided strong evidence that in contrast to chloride, chlorite is not a significant urinary chlorate metabolite in rats.

After absorption, both chlorate and its metabolite chloride are widely distributed throughout body tissues in animals. Distribution of radioactivity after $^{36}\text{ClO}_3^-$ administration showed that the highest concentrations were in plasma (0.68 %), followed by whole blood (0.57 %), and a total of 3.6 % in kidneys, lungs stomach, duodenum, ileum, liver, spleen, bone marrow, testes, skin and carcass (Abdel-Rahman et al., 1982). Nevertheless, because the chloride ion is actively retained and chlorate is rapidly excreted, meaningful generalizations based on total radioactive residues are difficult to make. Excretion of chlorate and its metabolite chloride is rapid and mainly via urine, with very small amounts being excreted in faeces (Smith et al., 2012).

In conclusion, following oral exposure chlorate is rapidly absorbed, widely distributed throughout the body, and evidence indicates that it undergoes metabolism to chloride. The main pathway of elimination is via urine.

3.3.1.2. Humans

The CONTAM Panel has not identified studies on the toxicokinetics of chlorate in humans after oral uptake. Two studies were identified in which chlorate concentrations in human urine and plasma after chlorate poisoning were quantified (Table 13).

Table 13: Chlorate concentrations in chlorate poisoning cases

Cases	Urinary concentrations ^(a)	Plasma concentrations ^(a)	Reference
26 year old women Intake of 150–200g NaClO ₃ in the form of the herbicide 'Unkraut-Ex'	1–3 hours: 86 mM ClO ₃ ⁻ 3–5 hours: 24 mM ClO ₃ ⁻ 5–7 hours: 18 mM ClO ₃ ⁻ 7–9 hours: 10 mM ClO ₃ ⁻ 9–11 hours: 5 mM ClO ₃ ⁻	< LOD of 5 mM ClO ₃ ⁻	Steffen and Seitz (1981)
Patient survived after several weeks of haemodialysis	70 mM ClO ₃ ⁻ (≈ 7.4 g NaClO ₃) were excreted before the production of urine subsided		
49 year old male Chlorate poisoning unclear Patient died 12 hours after admission to hospital	4 300 mg/L ClO ₃ ⁻	54 mg/L ClO ₃ ⁻	Eysseric et al. (2000)

b.w.: body weight; LOD: limit of detection.

(a): time points refer to hours after admission to the respective hospital.

In conclusion, the data obtained after chlorate poisoning demonstrate that chlorate is bioavailable in humans after oral ingestion and that it is eliminated via the urine.

3.3.2. Toxicity in experimental animals

3.3.2.1. Acute toxicity

Chlorate toxicosis has been reported in humans, horses, cows, sheep, chickens and dogs (Gregory et al., 1993). Chlorate compounds are locally irritating to the gastrointestinal tract. They are potent oxidizing agents and will cause methaemoglobin formation and haemolysis, followed by intravascular coagulation. Chlorate is toxic to renal tubules and may cause acute renal failure (Reubi, 1978). Reported clinical signs included nausea, vomiting, abdominal pain, ataxia, dyspnoea, cyanosis, haematuria, haemoglobinuria, and haemoglobinemia (Kaye, 1970; Sheaban et al., 1971; Steffen and

Seitz, 1981; Gregory et al., 1993). Affected animals can progress to anuria, coma, and death within hours of a lethal exposure.

The acute oral toxicity of sodium chlorate was tested by oral gavage in CD (SD) BR rats at single dose-levels of 1 470 (males), 2 150, 3 160, 4 640, 6 810 (both sexes) and 10 000 (females) mg/kg b.w. (vehicle: deionised water). Death and treatment-related effects (ataxia, lower motor activity, prostration, yellow soft faeces, yellow wetness of inguinal and/or perianal region) were observed in both sexes. The oral LD₅₀ was 4 950 mg sodium chlorate/kg b.w. in males and 6 250 mg sodium chlorate/kg b.w. in females (equivalent to 3 861 mg chlorate/kg b.w. in males and 4 875 mg chlorate/kg b.w. in females) (Damske and Meckler, 1981, unpublished study cited in EU DAR, 2008).

Sodium chlorate (50 % w/w solution in distilled water) was administered once by gavage to Sprague-Dawley rats at dose levels of 2 000 and 5 000 mg/kg b.w. (equivalent to 1 560 and 3 900 mg chlorate/kg b.w.). One dead animal was recorded in high-dose females and treatment-related effects were observed at both dose-levels (lethargy, hunched posture, slight to moderate red discoloration of the lungs). The LD₅₀ was higher than 5 000 mg sodium chlorate/kg b.w. in both sexes (equivalent to 3 900 mg chlorate/kg b.w.) (Shapiro, 1991, unpublished study cited in EU DAR, 2008).

Sodium chlorate (1 g/kg b.w. equivalent to 0.78 mg chlorate/kg b.w.) was administered to New Zealand white rabbits by gavage. No methaemoglobin was detected in the blood. No changes in serum values of urea, creatinine, aspartate, or alanine aminotransferase were observed during the observation period of 7 days. After this period, the animals were killed and no adverse histopathological effects were observed in the kidneys 7 days after dosing (Steffen and Wetzel, 1993).

Other publications reported oral LD₅₀ for sodium chlorate to be 8 350 mg/kg b.w. (equivalent to 6 513 mg chlorate/kg b.w.) in mice, 1 200 mg/kg b.w. (equivalent to 936 mg chlorate/kg b.w.) in rats, 7 200 mg/kg b.w. (equivalent to 5 616 mg chlorate/kg b.w.) in rabbits and 700 mg/kg b.w. (equivalent to 546 mg chlorate/kg b.w.) in dogs (Lewis, 1996; HSDB, 2003). The oral LD₅₀ of potassium chlorate for rats was 1 870 mg/kg b.w. (equivalent to 1272 mg chlorate/kg b.w.) (RTECS, 1994).

Four dogs were given 1 g/kg b.w. sodium chlorate in a gelatine capsule and four dogs were given 2 g/kg b.w. sodium chlorate (equivalent to 0.78 and 1.56 g/kg b.w. chlorate) in divided doses over a 45 minute period. All dogs vomited between 5 and 15 minutes after dosing. With the exception of one dog receiving 2 g/kg b.w. which showed slight increases in methaemoglobin 1 hour after dosing, no significant change was noticed in methaemoglobin levels (Heywood et al., 1972).

One female dog was offered a solution of sodium chlorate equivalent to 3.3 g/kg b.w. (equivalent to 2.57 g/kg b.w. chlorate) over a 24 hour period and was found dead. *Post-mortem* examination showed the mucous membranes to be blue, the blood was dark chocolate brown, the liver was dark brown and all serous surfaces were blue-tinged. The appearance was consistent with acute sodium chlorate poisoning (Heywood et al., 1972).

3.3.2.2. Short term toxicity

Sodium chlorate was administered by drinking water to male and female B6C3F1 mice (10 animals/group) at concentrations of 0, 125, 250, 500, 1 000 or 2 000 mg/L for 22 days, resulting in daily doses of 0, 20, 45, 90, 175 and 350 mg/kg b.w. per day for males and 0, 20, 45, 95, 190 and 365 mg/kg b.w. per day for females. These doses were equivalent to 0, 16, 35, 70, 137 and 273 mg chlorate/kg b.w. per day for males and 0, 16, 35, 74, 148 and 285 mg chlorate/kg b.w. per day for females. No effect was observed on body weight, body weight gain or water consumption. No clinical alteration was induced and only mean cell haemoglobin concentration was slightly reduced at high dose in males and females, but in absence of haemolysis it was not considered relevant. No exposure-related lesions occurred in treated animals and in particular thyroid alterations were not present. The NOAEL was 350 mg/kg b.w. per day in males and 365 mg/kg b.w. per day in females, the highest dose tested (equivalent to 273 mg chlorate/kg b.w. per day for males and 285 mg chlorate/kg b.w. for females) (Hooth et al., 2001; NTP, 2005).

Female B6C3F1 mice (6 animals/group) were exposed to 0, 500, 1 000, 2 000, 4 000, or 6 000 mg/L sodium chlorate (equivalent to about 0, 50, 100, 200, 400 and 600 mg chlorate/kg b.w. per day) dissolved in deionized water for 105 days. There were no effects on thyroid histology, but no other details were reported (Hooth et al., 2001).

Sodium chlorate was administered by drinking water to male and female F344/N rats (10 animals/group) at concentrations of 0, 125, 250, 500, 1 000 or 2 000 mg/L for 22 days, resulting in daily doses of 0, 20, 35, 75, 170 and 300 mg/kg b.w. per day for males and 0, 20, 40, 75, 150 and 340 mg/kg b.w. per day for females. These doses were equivalent to 0, 16, 27, 59, 133 and 234 mg chlorate/kg b.w. per day in males and 0, 16, 31, 59, 117 and 265 mg chlorate/kg b.w. per day in females. No effect was observed on body weight, body weight gain or water consumption. At day 22, limited decrease in erythrocytes, haemoglobin and haematocrit were observed in males at high dose and haemoglobin was reduced in females at the two highest doses. In both males and females, segmented neutrophils were decreased. Heart weights (absolute and relative) were decreased by 15 % in males at high dose. Dose-related minimal to mild thyroid gland follicular cell hypertrophy occurred in males and females at doses ≥ 75 mg/kg b.w. per day. Significant increase in colloid depression and in follicular cell hyperplasia were also observed in males at doses ≥ 75 mg/kg b.w. per day and in females at doses ≥ 150 mg/kg b.w. per day. The NOAEL was 35 mg/kg b.w. per day in males and 40 mg/kg b.w. per day in females (equivalent to 27 mg chlorate/kg b.w. per day in males and 31 mg chlorate/kg b.w. per day in females) (Hooth et al., 2001).

Additional male and female F344/N rats (10 animals/group) were exposed via drinking water for 4, 21 or 90 days to 0, 125, 1 000 or 2 000 mg sodium chlorate/L (equivalent to 0, 16, 133 and 234 mg chlorate/kg b.w. per day in males and 0, 16, 117 and 265 mg chlorate/kg b.w. per day in females). Thyroid hormone levels were altered significantly in male and female rats after 4 days (decreases of triiodothyronine (T3) and T4 and increases in TSH) at the two higher concentrations, and after 21 days at the highest dose. TSH levels also increased significantly in male rats after 21 days of treatment with 1 000 mg sodium chlorate/L. TSH levels were higher in males than in females after 21 days of treatment. Although serum T3 and T4 levels were not different from controls in treated animals after 90 days, TSH levels were increased in the high dose groups. Thyroid follicular cell hyperplasia (with mild severity) and significant colloid depletion were present in all males and females at the two higher doses following 21 days of treatment. These effects were not present in animals from the control or low dose groups. The NOAEL was 16 mg chlorate/kg b.w. per day (Hooth et al., 2001).

Sodium chlorate was administered by drinking water to male and female F344/N rats (20 animals/group) at concentrations of 0, 125, 1 000 or 2 000 mg/L for 14 weeks, resulting in daily doses of 0, 11, 89 and 178 mg/kg b.w. per day for males and 0, 12, 93 and 186 mg/kg b.w. per day for females (equivalent to 0, 9, 69 and 139 mg chlorate/kg b.w. per day for males and 0, 9, 73 and 145 mg chlorate/kg b.w. per day for females). These additional groups were added to the 2-year study for thyroid hormone evaluations and histopathology. Serum concentrations of T4 and T3 were significantly reduced in 1 000 and 2 000 mg/L males and females on day 4 and in 2 000 mg/L males and females at week 3. Serum concentrations of TSH generally increased with exposure concentration and were significantly increased in 1 000 and 2 000 mg/L males on day 4 and at week 3, in 1 000 and 2 000 mg/L females on day 4, in 2 000 mg/L females at week 3, and in 2 000 mg/L males and females at week 14. Slightly enlarged thyroid glands were observed in 1 000 and 2 000 mg/L male rats and 2 000 mg/L female rats at 14 weeks. All rats in the 1 000 and 2 000 mg/L groups had follicular cell hypertrophy at 3 and 14 weeks; this lesion did not occur in control rats (NTP, 2005).

Male F344 rats (10 animals/group) were exposed to 0, 1, 10, 100, 1 000, or 2 000 mg/L sodium chlorate (0, 0.07, 0.7, 7, 70 and 140 mg chlorate/kg b.w. per day) dissolved in deionized water for 90 days. Sodium chlorate treatment induced a concentration-dependent increase in the incidence and severity of thyroid follicular cell hyperplasia. The increases were statistically significant at doses ≥ 1 000 mg/L. Significant colloid depletion was diagnosed in most treated animals but the incidences were similar in all groups. Follicular cell hypertrophy was present in most animals, but the incidence did not increase in a concentration manner (Hooth et al., 2001).

Female F344 rats (six animals/group) were exposed to 0, 500, 1 000, 2 000, 4 000, or 6 000 mg/L sodium chlorate (equivalent to 0, 35, 70, 140, 281 and 421 mg chlorate/kg b.w. per day) dissolved in deionized water for 105 days. Sodium chlorate treatment induced a statistically significant increase in the incidence and severity of thyroid follicular cell hyperplasia and colloid depletion at doses $\geq 2\,000$ mg/L. Follicular cell hypertrophy was observed at doses $\geq 2\,000$ mg/L, but the increase was statistically significant at the highest dose only (Hooth et al., 2001).

Sodium chlorate was administered by oral gavage (vehicle: distilled water) to groups of 15 male and 15 female Sprague-Dawley rats at dose levels of 0, 10, 100 and 1 000 mg/kg b.w. per day during 13 weeks. These doses were equivalent to 0, 8, 79 and 780 mg chlorate/kg b.w. per day. No treatment-related effects were observed in mortality, physical appearance or behaviour, food consumption, clinical chemistry, gross necropsy or organ histopathology. Body weights were significantly lower in females, without dose-response relationship. There was a slight, not statistically significant decrease in erythrocyte count and in haemoglobin in high dose males. Lower significant erythrocyte count (-4%), haemoglobin (-6%) and haematocrit (-9%) were recorded in high dose females, indicative of anaemia. Statistically significant decreases in adrenal weights were observed in high dose males and females (decrease of 22 % and 20 % absolute weights and 17 % and 11 % relative weights, respectively). The NOAEL was 100 mg sodium chlorate/kg b.w. per day (79 mg chlorate/kg b.w. per day) (Barrett, 1987a, unpublished study cited in EU DAR, 2008 and FAO/WHO, 2008).

Sodium chlorate was administered via drinking water to groups of five male and five female Sprague-Dawley rats during 13 weeks at concentrations of 3, 12 and 48 mM, corresponding to 38, 128 and 654 mg sodium chlorate/kg b.w. per day for males and 53, 202 and 1 022 mg sodium chlorate/kg b.w. per day for females (based on water consumption) (30, 100 and 510 mg chlorate/kg b.w. per day for males and 41, 158 and 797 mg chlorate/kg b.w. per day for females). Each drinking water sample was completed with sodium chloride to reach the same sodium concentration in each group (48 mM). Two control groups were used, one distilled water control and one saline control (sodium chloride). Higher mean water consumption was noted in high dose females. Food consumption was lower in both sexes at the high dose and terminal body weights were significantly lower in high dose males (-24%) and females (-16%). Significant decreased organ weights were observed in high dose animals for heart (males and females), kidney (males), spleen (females), adrenals (females), thymus (females) and liver (males). Testes and brain weights were increased in high dose males and brain weights in females. Statistically significant differences were noted in haematological (haematocrit concentration, red and white blood cell counts) and blood biochemistry (aspartate aminotransferase (AST), alanine aminotransferase (ALT), calcium, creatinine, phosphorus and cholesterol) parameters in high dose males, however as values stayed within physiological limits, the effects were not considered to be biologically relevant. Higher severity (males) or incidence (females) of cytoplasmic vacuolization of chromophobic and acidophilic cells in the *pars distalis* of the pituitary gland was noted in the high dose groups. There was also a dose-related increase in severity and incidence of moderate to marked thyroid colloid depletion in both sexes. The authors established a NOAEL of 38 mg/kg b.w. per day in males and 53 mg/kg b.w. per day in females (corresponding to 30 mg chlorate/kg b.w. per day for males and 41 mg chlorate/kg b.w. per day for females) (McCauley et al., 1995).

Male Sprague-Dawley rats (4 animals/group) were given 0, 10 or 100 mg/L chlorate per day in drinking water (equivalent to 0, 0.9 and 9 mg/kg b.w. per day) for 4 months. At 2 months, blood glutathione levels were decreased significantly in both exposed groups. At 4 months, blood osmotic fragility was decreased significantly in the high dose group and abnormal erythrocyte morphology, including the presence of codocytes and echinocytes, was observed in both exposed groups (Abdel-Rahman et al., 1980).

Couri and Abdel-Rahman (1980) studied the glutathione-dependent enzyme system in the erythrocytes of male Sprague-Dawley rats (4 animals/group) after exposure to chlorate in drinking water at 0, 10 or 100 mg/L (equivalent to 0, 0.9 and 9 mg/kg b.w. per day) for up to 12 months. At 6 months, rats exhibited no change in glutathione reductase activity, an increase in glutathione peroxidase and a decrease in catalase activity at high dose and a decrease in glutathione concentration at both doses.

After 12 months, there was no significant difference in the activity of glutathione reductase, glutathione peroxidase or catalase in treated groups and the glutathione concentration was significantly higher in both exposed groups.

Male Sprague- Dawley rats (10, 7 or 10 animals/group; measures generally represent means from 4 animals/group) were exposed to drinking water containing 0, 10 or 100 mg chlorate/L (equivalent to 0, 0.9 and 9 mg/kg b.w. per day) for up to one year. Mean body weights were significantly decreased (10 % to 20 %) in both treatment groups throughout the experiment. Blood osmotic fragility was significantly decreased in both exposed groups after 7 or 9 months. Reduced fragility of red blood cells was attributed to cross-linking of membrane components with haemoglobin and subsequent precipitation of haemoglobin. Reductions in blood glutathione levels were observed in the high dose group after 2, 7 and 9 months and in the low dose group after 2 and 9 months. At 2, 4 and 6 months, no significant haematologic changes were noted in treated rats compared to control. After 9 months, red blood cell count, haematocrit, and haemoglobin content were all significantly decreased at both dose levels. Evaluation of ³H-thymidine incorporation into the organs of rats exposed to 10 mg/L chlorate for 3 months indicated a decrease in incorporation in the testes but not in the liver, kidney, or intestinal mucosa (Couri et al., 1982; Abdel-Rahman et al., 1985).

Adult male F344 rats (10 animals/group) were exposed, via their drinking water, to 0, 10, 100 and 1 000 mg sodium chlorate/L or to 0.1, 1.0 or 10 mg/L ammonium perchlorate (containing 0.5, 0.65, 0.82 and 0.51 mg sodium chlorate/L)²⁸ for 7 days. Actual concentrations of sodium chlorate were 0.5, 25, 119 and 931 mg sodium chlorate/L corresponding to 0.06, 3.3, 16 and 120 mg/kg b.w. per day (equivalent to 0.05, 2.6, 12 and 93 mg chlorate/kg b.w. per day). Actual concentrations of ammonium perchlorate were 0.17, 1.5 and 8.7 mg/L (corresponding to 0.024, 0.2 and 1.2 mg/kg b.w. per day (equivalent to 0.02, 0.17 and 1.01 mg perchlorate/kg b.w. per day). Serum T3 and T4 levels were not altered by treatment and TSH was only increased after the highest dose treatment with sodium chlorate. Histological examination of the thyroid gland showed colloid depletion of follicular epithelial cells and an increase in the incidence and severity of follicular cell hyperplasia in high-dose treated animals. Hypertrophy of thyroid follicular epithelial cells was present at all doses of sodium chlorate (in 5/6, 6/6 and 5/6 animals, respectively, compared to 1/6 in controls) and in high dose of ammonium perchlorate (in 6/6 animals). There was also an apparent increase in the number of basophils in rats treated at the high dose of both compounds. For ammonium perchlorate, the NOAEL was 0.17 mg/kg b.w. per day and the lowest-observed-adverse-effect level (LOAEL) was 1.01 mg/kg b.w. per day expressed as perchlorate. The LOAEL was 3.3 mg sodium chlorate/kg b.w. per day equivalent to 2.6 mg chlorate/kg b.w. per day (Khan et al., 2005). This study is the only study where chlorate and perchlorate were tested at the same time. However, it is a poorly reported study, with limitations in the number of animals examined (only six/dose group for histopathology), in the number of examinations and only 7 days of exposure. The study results did not allow a dose-response comparison of the two compounds.

Sodium chlorate (as a commercial preparation) was administered by gavage over a 5-day period to four male and four female beagle dogs at doses of 200 to 326 mg/kg b.w. per day (equivalent to 156 to 254 mg chlorate/kg per day). Two animals receiving more than 300 mg/kg b.w. per day (equivalent to 234 mg chlorate/kg b.w. per day) displayed loss of appetite and body weight and had blood in their urine or faeces, and one died after 4 days of exposure. The surviving animal was allowed a 7-day recovery period. *Post mortem* examination of both animals revealed classic signs of chlorate poisoning, including cyanotic kidney surface and evidence of haemolysis in the liver. Dogs receiving less than 300 mg/kg per day sodium chlorate survived the exposure period and were allowed a week of recovery before necropsy. Three of these animals displayed slight weight loss. Some of these dogs exhibited extramedullary haematopoiesis in the spleen and evidence of haemolysis in the liver. Packed cell volume, haemoglobin content, and red blood cell count were all reduced in animals treated with greater than 200 mg/kg per day compared to pre-treatment values for each animal. Reticulocyte counts

²⁸ The source of sodium chlorate in the deionized water supply was not determined.

were increased in all animals treated with greater than 200 mg/kg per day. Methaemoglobin values were little affected, the only animal showing significant elevation being the animal that died (Heywood et al., 1972).

Sodium chlorate was administered by oral gavage (vehicle: distilled water) to groups of four male and four female Beagle dogs at dose levels of 0, 10, 60 and 360 mg/kg b.w. per day (0, 8, 47 and 284 mg chlorate/kg b.w. per day) during 13 weeks. The maximal dose was chosen because it produced emesis in a former range-finding study. No treatment-related effects were observed on clinical signs, body weight, food consumption, blood biochemistry parameters, organ weights or at necropsy. No relevant haematological effect was observed except individual increase in methaemoglobinemia in the two highest dose female groups at week 6 and in all treated female groups at week 13. This was judged to be within normal limits and therefore not treatment-related. The NOAEL was 360 mg/kg b.w. per day (281 mg chlorate/kg b.w. per day), the highest dose tested (Barrett, 1987b, unpublished study cited in EU DAR, 2008).

Twelve adult African green monkeys (five males and seven females) were exposed to solutions of sodium chlorate at concentrations of 0, 25, 50, 100, 200 or 400 mg/L. If water consumption of 580 mL/day and a mean body weight of 5 kg are assumed, the sodium chlorate consumption would be equivalent to 0, 3, 6, 12, 23 and 46 mg/kg b.w. per day (equivalent to 0, 2.3, 4.7, 9.4, 18, 36 mg chlorate/kg b.w. per day), respectively (FAO/WHO, 2008); the authors cited the top dose as being equal to 54 ± 38 mg/kg b.w. per day. The test substance was administered for 30–60 days at rising doses to the same group of animals with a 6- to 9-week resting period between testing of consecutive doses. Sodium chlorate induced a slight dose-dependent decrease in red blood cell count, reticulocytes and haemoglobin. Sodium chlorate did not induce significant changes in thyroid hormone (serum T4) levels (Bercz et al., 1982). Since this study was poorly conducted and reported it was not possible to precisely define the doses in mg/kg b.w. per day.

Conclusions

The thyroid gland and the haematological system are the primary target organs of toxicity of chlorate identified in animal species after repeated oral exposure. Decreases in erythrocytes, haemoglobin and haematocrit were observed in mice, rats, dogs and monkeys. Histopathological changes were noted in the thyroid gland of rats (follicular cell hypertrophy, increase in colloid depression and in follicular cell hyperplasia). Thyroid hormone levels were also altered significantly (decreases in T3 and T4 and increases in TSH).

3.3.2.3. Long term toxicity and carcinogenicity

Sodium chlorate was administered by drinking water to male and female B6C3F1 mice (50 animals/group) at concentrations of 0, 500, 1 000 or 2 000 mg/L for two years, resulting in daily doses of 0, 40, 80 and 160 mg/kg b.w. per day for males and 0, 30, 60 and 120 mg/kg b.w. per day for females (equivalent to 0, 31, 62 and 125 mg chlorate/kg b.w. per day for males and 0, 23, 47 and 94 mg chlorate/kg b.w. per day for females). Survival of exposed mice was similar to that of the control groups. Mean body weights of exposed groups of males were similar to those of the control group throughout the study. Mean body weights of 500 and 1 000 mg/L females were less than those of the controls after week 84 (88 % and 90 % of control at the end of the study) and those of 2 000 mg/L females were less after week 88 of the study (90 % of control at the end of the study). Water consumption by exposed mice was generally similar to that by controls throughout the study. No clinical findings related to sodium chlorate exposure were observed. There was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice that was composed primarily of adenomas (three of four neoplasms in the 2 000 mg/L group). The incidences of pancreatic islet adenoma and adenoma or carcinoma (combined) in 2 000 mg/L females exceeded the historical ranges for drinking water controls (adenoma: 0 %, 4 %, 4 % and 6 %, adenoma or carcinoma: 0 %, 4 %, 4 % and 8 %, historical incidence: $1.4 \% \pm 2.3 \%$, range: 0–4 %). The incidences of pancreatic hyperplasia decreased with increasing exposure concentration. The incidences of hepatocellular carcinoma were significantly greater in 500 and 1 000 mg/L females than in the control

group (3/49, 13/50, 15/49 and 9/50). Although not statistically significant, the incidence in 2 000 mg/L females was also increased. The incidences in all exposed groups of females exceeded the historical range for drinking water controls (8 %, range 4–14 %). When incidences of hepatocellular adenoma (30/49, 19/50, 26/49, 23/50) and carcinoma were combined (31/49, 26/50, 31/49, 26/50), there was no effect. Due to this fact and because the increases were not exposure concentration-related, these carcinomas were not considered to be induced by sodium chlorate. The incidence of minimal thyroid follicular cell hypertrophy was significantly increased in 2 000 mg/L female mice when compared to the control group (3/48, severity grade 1.3; 2/50, severity grade 2.0; 5/49, severity grade 1.0; 14/50, severity grade 1.4). The incidence of thyroid gland cystic degeneration was significantly increased in 1 000 mg/L females when compared to the control group (25/48, 28/50, 34/49, 32/50). Thyroid gland cystic degeneration was considered an aging change and not related to sodium chlorate administration. The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of female mice when compared to the control group (14/50, 28/50, 29/50, 31/50). The severity of this lesion in exposed females was slightly greater than in the controls (2.4, 2.6, 2.9 and 2.7). The incidence of granulosa cell hyperplasia of the ovary was significantly increased in 2 000 mg/L female mice when compared to the control group (0/45, 0/45, 3/47, 7/50). In general, these were considered not to be preneoplastic lesions.

In conclusion, there was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice. Thyroid gland follicular cell hypertrophy was significantly increased in 2 000 mg/L females. The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of females. There was no evidence of carcinogenic activity of sodium chlorate in male B6C3F1 mice. There was equivocal evidence of carcinogenic activity of sodium chlorate in female B6C3F1 mice based on marginally increased incidences of pancreatic islet neoplasms. A NOAEL was not identified in this study based on the decrease in body weight gain and the increase in incidence of pancreatic islet cell adenoma in females observed at the lowest dose. The LOAEL was 30 mg sodium chlorate/kg b.w. per day (equivalent to 23 mg chlorate/kg b.w. per day) (NTP, 2005).

Sodium chlorate was administered by drinking water to male and female F344/N rats (50 animals/group) at concentrations of 0, 125, 1 000 or 2 000 mg/L for 2 years, resulting in daily doses of 0, 5, 35 and 75 mg/kg b.w. per day for males and 0, 5, 45 and 95 mg/kg b.w. per day for females (equivalent to 0, 4, 27 and 59 mg chlorate/kg b.w. per day for males and 0, 4, 35 and 74 mg chlorate/kg b.w. per day for females). Survival of exposed rats was similar to that of the control groups. Mean body weights of all exposed groups were similar to those of the control groups throughout the study. Water consumption by exposed rats was generally similar to that by controls throughout the study. No clinical findings were attributed to sodium chlorate exposure. There were positive trends in the incidences of thyroid follicular cell carcinoma in male rats and in follicular cell adenoma or carcinoma (combined) in males and females. The incidences of follicular cell adenoma, follicular cell carcinoma, and follicular cell adenoma or carcinoma (combined) in 2 000 mg/L males and females (males: 2/47, 4/47 and 6/47 compared to 1/47, 0/47 and 1/47 in controls; females: 2/46, 2/46 and 4/46 compared to 0/47, 1/47 and 1/47 in controls) exceeded the historical ranges²⁹ for drinking water controls. The incidences of follicular cell hypertrophy in all exposed groups of males and in 1 000 and 2 000 mg/L females at two years were significantly greater than those in the control groups and the severity was increased in 2 000 mg/L males and females. The incidences of focal follicle mineralization in 1 000 and 2 000 mg/L females were significantly greater than that in the control group and the severity was increased in the 2 000 mg/L group. This is a common aging change, but the increased incidences may have been exacerbated by exposure to sodium chlorate. In the spleen, the incidence of hematopoietic cell proliferation was significantly increased in 2 000 mg/L males when compared to the control group (2/48, 6/49, 4/49 and 11/50, respectively). The incidences

²⁹ Historical incidence follicular cell adenoma or carcinoma: males: adenomas: mean: 2.2 %, range: 2 %; carcinomas: mean: 1.0 ± 1.4 %, range: 0–2 %; combined: mean: 3.2 ± 1.1%, range 2–4 %; females: adenomas: mean: 1.0 ± 1.4 %, range: 0–2 %; carcinomas: mean: 2.1 ± 0.2 %, range: 2 %; combined: mean: 3.1 ± 1.3 %, range 2–4 %.

of bone marrow hyperplasia were significantly increased in 1 000 and 2 000 mg/L males when compared to the control group (28/48, 35/48, 41/50 and 40/49, respectively). The severity grades of this lesion were greater in all treatment groups when compared to controls (1.9, 2.3, 2.4 and 2.7). The increases in hyperplasia incidence and severity suggest this was a treatment-related effect. The incidence of mononuclear cell leukaemia was significantly increased in the male 2 000 mg/L group when compared to controls (13/50, 21/50, 16/50, 23/50). However, the incidences of this lesion in all exposed groups fell within the historical range in controls (all routes) $43.1 \% \pm 12.8 \%$, range 22–68 %. Because the incidence of mononuclear cell leukaemia in the control group was at the low end of the historical control range and near average in the exposed groups, this lesion was not attributed to sodium chlorate administration.

In conclusion, a NOAEL was not identified in this study due to the increased incidence of follicular cell hypertrophy in males at the lowest dose. The LOAEL was 5 mg sodium chlorate/kg b.w. per day (equivalent to 4 mg chlorate/kg b.w. per day) (NTP, 2005). There was some evidence of carcinogenic activity of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms (NTP, 2005).

Sodium chlorate and potassium chlorate were tested in male F344 rats (15/group) for potential promoting effects in two-stage rat renal carcinogenesis studies. Renal carcinogenesis was initiated with 500 mg/L N-ethyl-N-hydroxyethylnitrosamine in the drinking water three times per week for 2 weeks. Rats were then treated with 10 g/L sodium chlorate, 10 g/L potassium chlorate in the drinking water, or distilled water for 25 weeks. Three other groups were treated similarly, except that drinking water was given in the initiation phase. Based on drinking-water consumption, the doses were reported to be 686 mg sodium chlorate/kg b.w. per day and 675 mg potassium chlorate/kg b.w. per day in the initiated rats and 654 mg sodium chlorate/kg b.w. per day and 667 mg potassium chlorate/kg b.w. per day in the rats consuming sodium or potassium chlorate without initiator equivalent to 535 or 510 and 459 or 460 mg chlorate/kg b.w. per day. No animals died during the course of the experiment. Animals were necropsied at 27 weeks. Sodium or potassium chlorate showed no promoting effect on the incidences of renal neoplastic lesions, including dysplastic foci and renal cell tumours (Kurokawa et al., 1985).

Conclusions

Long-term oral exposure to sodium chlorate resulted in non-neoplastic lesions in the thyroid gland (follicular cell hypertrophy) of male and female rats and female mice, bone marrow (hyperplasia) of male rats and female mice, and spleen (hematopoietic cell proliferation) of male rats.

There was no evidence of carcinogenic activity of sodium chlorate in male B6C3F1 mice. There was equivocal evidence of carcinogenic activity of sodium chlorate in female B6C3F1 mice based on marginally increased incidences of pancreatic islet cell adenoma and carcinoma (combined). There was some evidence of carcinogenic activity of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms.

3.3.2.4. Genotoxicity

The genotoxic potential of sodium chlorate has been evaluated *in vitro* and *in vivo* (somatic and germ cells). *In vitro*, in a majority of tests, sodium chlorate had no mutagenic activity on *S.typhimurium* or *E. coli* WP2 hcr. It was positive in one of the tests performed in TA1535 and negative in two others. Sodium chlorate was negative in a V79 hprt gene mutation assay, in an unscheduled DNS synthesis (UDS) on human epitheloid cervix carcinoma cell line (HeLa) S3 cells and in a micronucleus test in human hepatocyte carcinoma cell line (HepG2) cells. The result of a Comet assay in HepG2 cells is unclear. *In vivo*, sodium chlorate was negative in several mice micronucleus test. It was also negative in a chromosomal aberration test and in a sperm abnormality assay, however, the dose levels were low and there was no proof of exposure of the target cells. Positive results were observed in *Drosophila* and in plants. Tables 14 and 15 present an overview of the available genotoxicity studies with sodium and potassium chlorate *in vitro* and *in vivo* respectively.

Table 14: *In vitro* genotoxicity tests with sodium chlorate or potassium chlorate

Type of test	Experimental test system	Substance tested	Exposure conditions	Result	Reference
Reverse mutation assay	<i>S. typhimurium</i> TA98, TA100, TA1535, TA1537 and TA1538	Sodium chlorate	50–5 000 µg/plate +/- S9 Plate incorporation test Controls ^(a)	Negative	May and Hodson-Walker (1989)*
Reverse mutation assay	<i>S. typhimurium</i> TA98, TA100 and TA1537	Sodium chlorate	10–10 000 µg/plate +/- S9 Controls ^(b)	Negative	Hossack et al. (1978)*
Reverse mutation assay	<i>S. typhimurium</i> TA98, TA100, TA1535 TA1537 and TA1538	Sodium chlorate	up to 3 600 µg/plate +/-S9	+ S9: Positive at 12 µM/plate in TA1535	Gocke et al. (1981)
Reverse mutation assay	<i>S. typhimurium</i> TA97, TA98, TA100, TA1535, TA102 and TA104	Sodium chlorate	100–10 000 µg/plate +/- S9 **	Negative	NTP (2005)
Reverse mutation assay	<i>S. typhimurium</i> BA-13 (araD531, hisG46, ΔuvrB, pKM101)	Potassium chlorate	5–100 mM	Negative	Prieto and Fernandez (1993)
Lethal DNA damage	<i>E. coli</i> WP2, WP67 and CM871	Sodium chlorate	100–10 000 µg/mL +/- S9 Pre-incubation (2 hours or 18 hours) Controls ^(c)	2 hours Pre-incubation –S9 mix: suggestive of DNA damage in WP67 and CM871 (conc. 1 000–10 000 µg/mL) +S9 mix: suggestive of DNA damage	May and Hodson-Walker (1989b)*
Gene mutation assay (HPRT locus)	Chinese hamster V79 cells	Sodium chlorate	8–5 000 µg/mL +/- S9 Controls ^(d)	Negative (sensitivity of the test is low)	Hodson-Walker and Bootman (1989)*
Gene mutation assay (HPRT locus)	Chinese hamster ovary (CHO) cells	Sodium chlorate	10–5 000 µg/mL +/- S9 Controls ^(e)	Negative	ECHA (2015a)
Unscheduled DNA synthesis (UDS)	Human HeLa S3 cells	Sodium chlorate	100–10 000 µg/mL +/- S9 Controls ^(f)	Negative	Seeberg (1989)*

Type of test	Experimental test system	Substance tested	Exposure conditions	Result	Reference
Comet assay	Human HepG2 cells (ATCC HB 8065)	Chlorate solution	0.001–0.2 mg/L -S9 Incubation: 24 hours Controls ^(g) 0.001–0.2 mg/L -S9 Controls ^(g)	Increase % tail intensity at 0.001 mg/L only Dose-dependent decrease in tail intensity	Feretti et al. (2008)
Micronucleus test	Human HepG2 cells	Chlorate solution		Negative	

b.w.: body weight; HepG2: human hepatocyte carcinoma cell line; HeLa: human epitheloid cervix carcinoma cell line.

+/-S9: with/without supernatant fraction obtained from an organ (usually liver) homogenate by centrifuging 9 000 g for 20 minutes in a suitable medium; this fraction contains cytosol and microsomes.

(a): Positive controls were sodium azide (-S9), 2-aminoanthracene (\pm S9), 9-aminoacridine (-S9), 2-nitrofluorene (-S9) and benzo(a)pyrene (\pm S9).

(b): Solvent control (distilled water); three compounds served as positive controls in presence of metabolic activation: β -naphthylamine (10 μ g/plate), 2-acetylaminofluorene (20 μ g/plate) and neutral red (10 μ g/plate). No positive control was tested in absence of S9.

(c): Solvent/negative controls: distilled water, ampicillin; Positive controls: mitomycin C (MMC) for - S9 mix, 2-aminoanthracene (2-AA) for + S9 mix.

(d): Negative control: distilled water; Positive controls: Ethylmethanesulfonate (EMS), 7,-12 dimethylbenzanthracene (DMBA).

(e): Solvent/vehicle controls: medium; Positive controls: Ethylmethanesulfonate (EMS), benzo(a)pyrene (B(a)P)

(f): Negative control: distilled water, Positive controls: 4-nitroquinoline-N-oxide (4-NQO), benzo(a)pyrene (B(a)P), 7,-12 dimethylbenzanthracene (DMBA).

(g): Negative control: untreated; Positive control: benzo(a)pyrene (B(a)P).

* Unpublished study cited in EU DAR (2008).

** Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver.

Table 15: *In vivo* genotoxicity tests with sodium chlorate

Type of test	Experimental test system	Substance tested	Experimental conditions	Result	Reference
Micronucleus Test	NMRI mice	Sodium chlorate	Intraperitoneal: 530–2 120 mg/kg Gavage: 2 128–4 265 mg/kg Animals treated at 0 and 24 hours Smears prepared at 30 hours	Negative	Gocke et al. (1981)
Sex-linked recessive lethal assay	<i>Drosophila melanogaster</i> (Berlin K, wild type and Basic)	Sodium chlorate	0.25 M feeding solution	Positive	

Table continued overleaf.

Table 15: *In vivo* genotoxicity tests with sodium chlorate (continued)

Type of test	Experimental test system	Substance tested	Experimental conditions	Result	Reference
Micronucleus test	CD-1 mice Bone marrow cells	Sodium chlorate	Oral gavage	Negative	Mackay and Bootman (1989)*
			Preliminary cytotoxicity test: 625–5 000 mg/kg b.w.	No relevant cytotoxicity	
			Main test: 200–5 000 mg/kg b.w.	Clinical signs of toxicity Preliminary test: 2 500 and 5 000 mg/kg b.w.	
			Sacrifice: 24, 48 or 72 hours after treatment	Main test: 5 000 mg/kg b.w.	
			Controls ^(a)		
Micronucleus test	CD-1 mice Bone marrow cells	Sodium chlorate	7–33 mg/kg b.w.	Negative	Meier et al. (1985)
			5 days oral gavage	But: dose levels extremely low, no proof of exposure, clinical signs of exposure not reported, no data on PCE/NCE	
			Sacrifice: 6 hours after last administration		
			Controls ^(b)		
Chromosomal aberrations test	CD-1 mice Bone marrow cells	Sodium chlorate	Single or 5 days oral gavage	Negative	
			Sacrifice single administration: 6, 24 and 48 hours after administration 5 days: 6 hours after last administration	But: dose levels extremely low, no proof of exposure, clinical signs of exposure not reported, MI not reported	
			Controls ^(b)		
Sperm-head abnormality assay	Male B6C3F1 mice	Sodium chlorate	5 days oral gavage	Negative	
			Sacrifice: 1, 3 and 5 weeks after last administration	But: dose levels extremely low, no proof of exposure, clinical signs of exposure not reported	
			Controls ^(c)		

Table continued overleaf.

Table 15: *In vivo* genotoxicity tests with sodium chlorate (continued)

Type of test	Experimental test system	Substance tested	Experimental conditions	Result	Reference
Micronucleus test	B6C3F1 mouse Peripheral blood	Sodium chlorate	3-week oral administration in drinking water Up to 350–365 mg/kg b.w. per day	Negative	NTP (2005)
Chromosomal aberration test	<i>Allium cepa</i>	Sodium chlorate solution (45 %)	0.01–0.8 mg/L for 6 hours 0.01–0.2 mg/L for 24 hours Controls ^(d)	After 6 hours: increase chromosome aberrations (0.15–0.8 mg/L) After 24 hours: negative cytotoxic at 0.1 and 0.2 mg/L	Feretti et al. (2008)
Micronucleus test	<i>Tradescantia</i> (clone #4430)	Sodium chlorate solution (45 %)	0.1–0.8 mg/L 24 hours exposure Controls ^(d)	Positive at 0.4 mg/L only	

b.w.: body weight; NCE: normochromatic erythrocytes; PCE: polychromatic erythrocytes

(a): Solvent control: distilled water. Positive control: chlorambucil (CP).

(b): Solvent/negative control: deionized water. Positive control: triethylenemelamine (TEM).

(c): Solvent/negative control: deionized water. Positive control: ethylmethanesulfonate (EMS).

(d): Negative control: distilled water. Positive control: Maleic hydrazide.

* Unpublished study cited in the EU DAR (2008).

Conclusions

Based on the available data, the CONTAM Panel concluded that chlorate is not of concern with regard to genotoxicity.

3.3.2.5. Developmental and reproductive toxicity

In a one-generation dose-range finding study, Sprague Dawley rats (groups of six males and six females) were given sodium chlorate in purified water by gavage at 0, 40, 200 and 1 000 mg/kg b.w. per day (equivalent to 0, 31, 156 and 780 mg chlorate/kg b.w. per day) (Gaoua, 2004a, unpublished study cited in EU DAR, 2008). The treatment started when the animals were 6 weeks old, during 10 weeks pre-mating, during mating and in females during pregnancy and lactation. Males were sacrificed at the end of the mating period and females at weaning or at day 25 *post-coitum* if they had not delivered. Litters were culled on day 4 *post partum* (pp) to obtain four males and four females per litter. Other pups were sacrificed at weaning. The parental data showed no treatment-related clinical signs, and there were no adverse effects on reproductive performance. The reproduction NOAEL was 1 000 mg/kg b.w. per day (equivalent to 780 mg chlorate/kg b.w. per day). Treatment related thyroid epithelial cell hyperplasia was observed at 200 and 1000 mg/kg b.w. per day in males and at 1 000 mg/kg b.w. per day in females. Higher incidence and severity of presence of vacuolated cells in the pituitary gland *pars distalis* were observed in both sexes at 1 000 mg/kg b.w. per day. The parental NOAEL was 40 mg/kg b.w. per day in males (equivalent to 31 mg chlorate/kg b.w. per day) and 200 mg/kg b.w. per day in females (equivalent to 156 mg chlorate/kg b.w. per day). The litter data

showed treatment related lower foetal b.w. and decreased b.w. gain at 1 000 mg/kg b.w. per day. The offspring NOAEL was 200 mg/kg b.w. per day (equivalent to 156 mg chlorate/kg b.w. per day).

In a two-generation study following OECD guideline 416 (OECD, 2001), Sprague Dawley rats were given sodium chlorate in purified water at dose levels 0 (controls), 10, 70 and 500 mg/kg per day (equivalent to 0, 8, 55 and 390 mg chlorate/kg b.w. per day) by gavage (n = 25 males and 25 females in each dose group) from age 6 weeks (Gaoua, 2004b, unpublished study cited in EU DAR, 2008). F0 adults were treated 10 weeks before mating, during mating, throughout gestation and lactation (females) until sacrifice at weaning of the F1 pups. F1 pups were culled at day 4 pp, and weaned on day 21 pp, when couples were randomly selected to produce F2 litter. From day 22 pp the F1 generation was treated under the same experimental conditions as their parents. They were sacrificed at weaning of the F2 litter. F2 pups were culled at day 4 pp and sacrificed at weaning at day 22 pp.

Parental data of the F0 and F1 generation showed that the oestrus cycle and the female reproductive parameters were not altered by treatment. Sperm parameters were not affected in F0 or F1 males. In F0 animals at sacrifice, there were small dose-related decreases in haematology values (RBC count, haemoglobin concentration, packed cell volume, mean cell haemoglobin concentration) that were statistically significant in both males and females at the 500 mg/kg b.w. per day dose, and for RBC count and haemoglobin concentration also at the 70 mg/kg b.w. per day dose in females. They were, however, within the range of the historical background data. No haematology analysis was performed in F1 animals. There was a dose-related increase in male spleen weights in F0 (+ 1 %, + 15 %, + 25 %, relative weights), this was also seen in F1 males (+ 2 %, + 5 %, + 25 %), and is expected when damaged RBCs are destroyed in the spleen. Higher incidences of thyroid follicular hyperplasia at 500 mg/kg b.w. per day was seen in F0 and F1 males and females, as well as dose-related increase in grading of follicular hyperactivity, particularly in males. The NOAEL was 10 mg/kg b.w. per day for thyroid hyperactivity in males and 70 mg/kg b.w. per day in females.

No other notable treatment-related effects were reported for the F0 or F1 parental generation. No effects were reported for progeny of F0 or F1 (survival or development). No significant lesions were observed in thyroid glands of F2 pups. The NOAEL for reproduction and offspring was 500 mg/kg b.w. per day, the highest dose tested.

In a dose range finding study on teratogenicity in rats (Schroeder, 1987a, unpublished report cited in EU DAR, 2008), sodium chlorate was administered at 0, 10, 50, 100, 500 and 1 000 mg/kg b.w. per day (equivalent to 0, 8, 39, 78, 390 and 780 mg chlorate/kg b.w. per day; five animals per dose group) in distilled water by oral gavage to pregnant Sprague Dawley rats from day 6 to 15 of gestation. The treatment induced no maternal toxicity, embryotoxicity, foetotoxicity or malformations. The NOAEL was the highest dose tested at 1 000 mg/kg b.w. per day.

In a teratogenicity study sodium chlorate was administered at 0, 10, 100 and 1 000 mg /kg b.w. per day (equivalent to 0, 8, 78 and 780 mg chlorate/kg b.w. per day; 24 animals per dose group) in distilled water by gavage to pregnant Sprague Dawley rats from day 6 to 15 of gestation (Schroeder, 1987b, unpublished report cited in EU DAR, 2008). No adverse effects were reported and therefore the NOAEL was set at the highest dose tested, 1 000 mg/kg b.w. per day (corresponding to 780 mg chlorate/kg b.w. per day).

Pregnant New Zealand white rabbits (24 animals/group) were administered 0, 100, 250, or 475 mg sodium chlorate/kg b.w. per day (equivalent to 0, 78, 195 and 371 mg chlorate/kg b.w. per day) by oral gavage in distilled water from gestation day 6 to 29 (NTP, 2002). Dams were necropsied on gestation day 30. Transient changes in maternal food intake, urine colour, and/or output were noted at doses of 100 mg/kg per day and greater. Sodium chlorate did not cause any statistically significant treatment-related developmental toxicity under the conditions of this study.

In a 96 hours developmental toxicity test in *Xenopus laevis* Brennan et al. (2005) assessed four individual drinking water disinfection by-products, including sodium chlorate. Two replicates of

25 embryos were used. No chlorate-associated malformations were seen at concentrations < 5 000 mg/L. At 5 000 mg/L and 6 000 mg/L, gut malformation (gut coiling) was seen in 35 % and 96 % of the embryos, respectively. The LC_{50} was 5 778 mg/L and the EC_{50} for embryonic malformation was 4 865 mg/L.

Conclusions

Four studies on reproductive and developmental toxicity in rats were identified. The lowest reported NOAEL was 200 mg/kg b.w. per day, equivalent to 156 mg chlorate/kg b.w. per day for lower weight gain in offspring in a one-generation study (Gaoua, 2004a, unpublished study cited in EU DAR, 2008). Toxicity could be observed in the parental generation without reproductive or developmental toxicity. The parental effects observed at lowest level were thyroid epithelial cell hyperplasia (male parental NOAEL 40 mg/kg b.w. per day, equivalent to 31 mg chlorate/kg b.w. per day) and thyroid hyperactivity (male parental NOAEL 10 mg/kg b.w. per day, equivalent to 8 mg chlorate/kg b.w. per day).

3.3.3. Observations in humans

3.3.3.1. Acute effects

Death or illness resulting from accidental or intentional ingestion of herbicides containing sodium chlorate has been reported in the literature several times since the 1960s (Knight et al., 1967; Lee et al., 1970; Bloxham et al., 1979; Helliwell and Nunn, 1979; NRC 1980, 1987; Ranghino et al., 2006). Symptoms and signs of sodium chlorate intoxication include vomiting, abdominal pain, cyanosis, methaemoglobinaemia, anuria, and renal failure. According to NRC (1980) 'the lethal dose in adults is estimated to be 20 to 35 g for sodium chlorate and 5 to 30 g for potassium chlorate. For a 70-kg human, the oral lethal dose for these salts is 71 to 500 mg/kg'. Helliwell and Nunn (1979) reported 14 cases of sodium chlorate poisoning, with ingested amounts (1–2 g to 300 g) known in 12 of the cases. Nine of the cases died, and in all these the amount ingested was unknown or exceeded 100 g. Death occurred regardless of treatment, which in several cases included haemodialysis and exchange transfusion. The patient who had ingested the lowest amount (1–2 g, which corresponds to 11–23 mg chlorate/kg b.w.) survived. He received initial management with sodium thiosulphate (an antidote that inactivates the chlorate ion) and thereafter supportive management alone. Methaemoglobinaemia was seen in 13 of the 14 patients. It is not indicated which patient did not have methaemoglobinaemia, but the CONTAM panel assumes that this was the patient with the lowest dose ingested.

Matchsticks may contain 55 % potassium chlorate. After ingestion of approximately 2 g potassium chlorate from 120 matchstick heads or three matchstick boxes (corresponding to 20 mg chlorate/kg b.w. when assuming a b.w. of 70 kg) in an attempted suicide, toxicity was reported (Mutlu et al., 2003). The patient had decreased level of consciousness when he was brought in 24 hours after ingestion, and had increased blood potassium (21 mM/L), urea (21 mM/L) aspartate aminotransferase (58 U/L), creatine kinase (209 U/L) and low bicarbonate (4 mM/L). Methaemoglobinaemia was not reported. The patient underwent gastric lavage, haemodialysis and hyperbarbic oxygen treatment and recovered within a week.

Matchstick head consumption has also been reported as 'an old army trick' against insect bites. Ingestion of one pack of matchsticks every 4 days during field training, corresponding to approximately 45 mg potassium chlorate every 4 days (equivalent to 437 µg/kg b.w. chlorate assuming a b.w. of 70 kg), was apparently without short term toxic symptoms (Thurlow et al., 2013).

3.3.3.2. Controlled clinical trials

In a controlled clinical evaluation (Lubbers et al., 1981), 10 healthy male volunteers participated in an acute rising-dose tolerance study (Study I). They drank one litre (0.5 L consumed within 15 minutes and administered twice with 4-hour intervals) of water containing increasing chlorate concentrations (0.01, 0.1, 0.5, 1.0, 1.8 and 2.4 mg/L) every 3rd day for 16 days. A control group consisted of 10 volunteers. Several biochemical parameters, grouped into serum chemistry, blood count, urinalysis,

special tests and physical exam, were assayed every third day. In a separate study (Study II), 10 healthy male volunteers received 2.5 mg chlorate per day administered in 0.5 L water for 12 weeks (corresponding to 36 µg chlorate/kg b.w. per day assuming a b.w. of 70 kg). Physical examination and collection of blood and urine was conducted weekly during the treatment period and in an 8-week follow-up period. According to the authors, no clinically important impact was observed. Some changes in total bilirubin, iron and methaemoglobin was seen in Study I, whereas a trend of change in urea nitrogen was seen in Study II (relative slope was per week 1 % of the normal physiological range). The authors concluded that no physiological importance may be attributed with confidence to the observations. The no-observed-effect level (NOEL) in the study was the highest dose tested, approximately 36 µg chlorate/kg b.w. per day.

3.3.3.3. Epidemiological studies

Several epidemiological studies have addressed possible associations between exposures to chlorination disinfection by-products (DBPs) and different health outcomes. The formation and occurrence of DBPs is dependent on many variables. Epidemiological results from one study area may not be extended to others because the mixtures of DBPs present in water may be different as a result of differences in for instance water treatment, organic content in water or pH (Nieuwenhuijsen et al., 2009). In several epidemiological studies the type of water disinfection method has been used as a surrogate for chlorite and chlorate exposure. However, only studies with information on chlorate levels in water have been summarized below.

A case-control study was performed in nine Italian towns (Genoa, Udine, Modena, Parma, Siena, Rome, L'Aquila, Naples, Catania) in 1999-2000, addressing chlorination by-products in drinking water and adverse pregnancy outcomes (n = 1 194, 343 preterm births, 239 small for gestational age at term, 612 controls) (Aggazzotti et al., 2004). Water was sampled at the mothers' home and they filled in a questionnaire addressing personal habits including use of tap water, swimming pool attendance, shower and bath habits. Median water chlorate concentration was 76.5 µg/L (range 20–1 500) in the samples above the LOD (34 %). No associations were found with concentration of chlorate in water and adverse pregnancy outcomes.

Righi et al. (2012) studied associations between exposure to disinfection by-products (including chlorate) during first trimester of pregnancy and congenital anomalies in the period 2002-2005 in a case-control study in Emilia-Romagna, Italy. Data on 1 917 congenital anomalies were extracted from the regional malformation registry. For each case, four controls matched by pregnancy period were randomly selected from the regional birth register. The network supplying water was linked to maternal address, and they used historical tap water data provided by local authorities. The chlorate concentration in water was 283 ± 79 µg/L. Maternal exposure to chlorate at concentrations of > 200 µg/L in drinking water appeared to be associated with obstructive urinary defects (odds ratio (OR) 2.88, 95th percentile, confidence interval (CI) 1.09–7.63), cleft palate (OR 9.60, 95th percentile, CI 1.04–88.9) and *spina bifida* (OR 4.94, 95th percentile, CI 1.10–22.0) in newborns. There was no information on factors such as e.g. maternal diet, alcohol and coffee consumption, smoking habits, tap water consumption, swimming pool attendance, shower and bath habits. Furthermore, the number of cases for each outcome was small (n = 13–36) and the authors concluded that the results need confirmation in other studies.

3.3.3.4. Biomarkers

The CONTAM Panel has not identified studies on biomarkers for chlorate in humans.

3.3.4. Mode of action

Most of the potential acute adverse health effects of exposure towards NaClO₃ are associated with blood oxidation. The primary mechanism of chlorate toxicity is rupture of the red blood cell membranes with intravascular haemolysis. Steffen and Wetzel (1993) proposed that subsequent to initial formation of methaemoglobin, chlorate inactivates glucose-6-phosphate dehydrogenase and

glyceraldehyde phosphate dehydrogenase and thus interrupts the capacity of the erythrocyte to generate nicotinamid adenine dinucleotide phosphate (NADPH), which is also a cofactor required for methaemoglobin reductase. Without cellular NADPH a cascade of protein denaturation and a crosslinking of erythrocyte membrane proteins occurs, finally resulting in erythrocyte haemolysis.

Chlorate-induced methaemoglobin formation is most likely caused by an autocatalytic reaction and thus depends on the initial methaemoglobin concentration (Steffen and Wetzel, 1993). Jung (1965) describes it as the rapid formation of a $\text{Hb}^{3+}\text{-ClO}_3$ complex that decomposes to methaemoglobin, chloride and oxygen radicals. Methaemoglobin formation also depends on the availability of other oxidisable substrates, such as glutathione (GSH) that could protect haemoglobin from oxidation (Allen and Jandl, 1961). Erythrocytes deficient in glucose-6-phosphate-dehydrogenase have low GSH levels due to the outward transport of oxidised glutathione (GSSG) and are therefore quite sensitive towards chlorate (Srivasta and Beutler, 1969). The formation of methaemoglobin is followed by its denaturation, a cross-linking of erythrocyte membrane proteins and an inactivation of membrane enzymes.

The mechanisms causing renal failure await further clarification. Early studies considered chlorate induced renal effects as secondary to haemolysis and acidosis (Bing, 1943, 1944) but postulated also direct toxic effects of chlorate on the nephron (Oliver et al., 1951; Jackson et al., 1961). A more recent study provided evidence that a direct oxidative attack on the tubular epithelium is likely to be of minor importance. To separate indirect and direct effects of chlorate on the kidney Steffen and Wetzel (1993) used rabbits which are known to have a high methaemoglobin reduction capacity and thus the animals did not develop methaemoglobinaemia after intragastral administration of 1 g/kg b.w. sodium chlorate (equivalent to 0.78 g chlorate/kg b.w.). In spite of quite high serum (up to 16 ± 4.3 mM) and urine (246 ± 99 nM) chlorate concentrations, no changes in serum values of urea, creatinine, aspartate and alanine aminotransferase during the 7-day observation period were observed. The histopathological examination of the kidneys showed no pathological findings. The authors therefore concluded that it seems probable that methaemoglobinaemia is required for chlorate to exert a nephrotoxic effect.

Chlorate is chemically similar to perchlorate, which is a well-known thyroid gland toxicant and chemical oxidant. Chlorate inhibits the active transport of iodine from the blood to the follicular cells of the thyroid via the sodium iodine symporter (NIS). This can result in decreased serum thyroid hormones, increased release of TSH and consequent stimulation of thyroid cell proliferation and thyroid gland growth (ATSDR, 2008). It is unlikely that chlorate induces thyroid gland follicular cell tumours through a direct genotoxic mode of action (see Section 3.3.4). Nevertheless, chlorate might cause oxidative damage.

The pituitary-thyroid system is qualitatively similar in rats and humans in that the HPT feedback pathway maintains homeostasis in both species, however the dynamics of the system in both species differ substantially (NRC, 2005; FAO/WHO, 2011; Fisher et al., 2012).

There are differences in the binding proteins for the thyroid hormones T3 and T4 between rats and humans. In humans the principal binding protein for T4 is thyroxine-binding globulin (TBG), however, in rats, T4 mainly binds to albumin and transthyretin. The rat binding proteins have a 100-times lower binding affinity, than TBG in humans, which contributes to a higher clearance rate of T4 in rats, causing a higher production of T4 in order to maintain normal T4 concentrations. The plasma half-life of T4 in rats is 12–24 hours compared with 5–9 days in humans (NRC, 2005). The higher T4 production in rats is reflected in a more functionally active histological appearance of the rat thyroid. Follicular epithelium in rats is cuboidal, compared with a more flattened appearance in primates (NRC, 2005).

Rats are thus considered to be highly sensitive to the effects of agents that disrupt thyroid hormone homeostasis. Humans are likely to be less sensitive than rats to these effects.

In *in vitro* studies comparative potency of different ions to inhibit thyroid uptake has been investigated. Van Sande et al. (2003) measured the uptake of ^{125}I in FRTL5 cells (expressing rat NIS) and in COS NIS-6 cells (expressing human NIS) and studied the inhibition of the transport of ^{125}I by competing anions e.g. ClO_4^- , ClO_3^- and I^- . They showed that the order of inhibitory potency, reflecting the affinity of the transporter was $\text{ClO}_4^- > \text{I}^- > \text{ClO}_3^-$. The IC_{50} on relative uptake (concentration that reduce the relative uptake of ^{125}I used to half of its maximal value) of ^{125}I was 0.62 and 1 368, respectively in FRTL5 cells and 0.43 and 131, respectively in COS NIS-6 cells for perchlorate and chlorate. These cells exhibit similar transport properties as thyroid cells in slices. Di Bernardo et al. (2011) studied *in vitro* a yellow fluorescent protein variant, YFP-H148Q/I152L, as a biosensor to monitor the cellular uptake of NIS substrates like chlorate and perchlorate. Exposure of FRTL-5 cells with stable YFP-H148Q/I152L expression to extracellular anions like ClO_3^- and ClO_4^- resulted in a time- and concentration-dependent decrease in cellular fluorescence. The affinity of perchlorate for uptake was much higher than that of chlorate.

These investigations also suggest a lesser inhibitory potency of chlorate as compared to perchlorate.

3.4. Consideration of critical effects, dose response assessment and derivation of health-based guidance values

Following oral exposure, chlorate is rapidly absorbed, widely distributed throughout the body and evidence indicates that it undergoes metabolism to chloride. The main pathway of elimination is via urine.

As described in the previous sections, the thyroid gland and the erythrocytes are the primary target organs of toxicity of chlorate identified in animal species. In repeated toxicity studies in mice, rats, dogs and monkeys, decreases in number of erythrocytes and haemoglobin and haematocrit levels were observed. Signs of accelerated erythrocytes degradation, such as spleen weight increase or signs of haematopoiesis in spleen or bone marrow hyperplasia were also seen after long-term exposure. The most sensitive toxicological effects consisted of histopathological changes in the thyroid gland (e.g. colloid depletion, follicular cell hypertrophy and hyperplasia) and in thyroid hormones in rats. Male rats were more sensitive than females. Based on the negative *in vivo* genotoxicity data and the nature of the histopathological observations, the CONTAM Panel concluded that a non-genotoxic mode of action was likely for the induction of thyroid tumours in rats by sodium chlorate. Sodium chlorate is of minimal toxicity toward reproduction in rats and not toxic toward development in rats or rabbits. No indication for neurotoxic effects of sodium chlorate has been seen in repeated dose studies.

In comparison with rats, healthy adult humans have lower thyroid hormone turnover rates and larger reserves of iodinated thyroglobulin, allowing them to compensate for reduced hormone synthesis in the thyroid. Due to these differences in thyroid hormone physiology, the data from toxicological studies in rats are of limited relevance for humans.

Like perchlorate, the chlorate anion is a competitive inhibitor of iodine uptake into the thyroid. (Goodman et al., 1980). Iodine uptake in the thyroid is a key step in the synthesis of thyroid hormones and its inhibition may result in the disruption of the thyroid hormone synthesis leading eventually to the development of hypothyroid symptoms.

Chronic adaptive changes to compensate for a sustained inhibition of thyroid iodine uptake can lead to long term effects such as the development of multinodular toxic goitre, in particular in populations with mild to moderate iodine deficiency. Human fetuses, neonates and individuals with low iodine intake or genetically predisposed to develop hypothyroidism are potentially more susceptible to the effects of exposure to chlorate.

Potential acute effects for fetuses in the late gestation period and for infants may therefore be postulated like in the case of perchlorate. However, no data are available to support this hypothesis. These life stages are identified as being particularly sensitive to inhibition of thyroid iodine uptake,

because they do not have the reserve capacity existing in adult humans (Zoeller, 2003; Scinicariello et al., 2005; Ginsberg et al., 2007).

Thyroid hormones play a key role in foetal and neonatal neurological development (Zoeller et al., 2002; Morreale de Escobar et al., 2004), and thus a transient fall in the thyroid hormone levels, as result of acute exposure to chlorate, could result in an adverse neurodevelopmental effect. With regard to the fetus, the limitations in the reserve capacity are mitigated by the maternal supply of thyroidal hormones. On the other hand, neonates can rely only on their hormone synthesis and thus could be considered as the more vulnerable population (Clewett et al., 2003; Ginsberg et al., 2007).

In the previous assessment of perchlorate (EFSA, CONTAM Panel 2014) it was concluded that a complete thyroid iodine uptake inhibition for one day only would not result in a severe depletion of the thyroid iodine depot even in the more vulnerable population. By similarity with perchlorate, the CONTAM Panel noted that a single acute exposure to chlorate at levels found in food and water is unlikely to cause adverse effects on thyroid function, including the more vulnerable groups of the population. Therefore, the CONTAM Panel concluded that the establishment of an ARfD is not warranted based on the thyroid toxicity of chlorate.

The information on the toxic effects of chlorate in humans comes from reports on cases of poisoning after oral intake. Sodium chlorate typically induces local irritation of the gastrointestinal mucous membranes in humans after acute exposure, which has not been reported in studies with laboratory rodents performed with comparable doses. Such an effect has also been observed in several animal species such as horses, sheep, chickens and dogs after ingestion. However, the main toxic effect in humans is methaemoglobin formation, and its subsequent consequences including haemolysis and haemoglobinuria with subsequent renal failure (acute renal tubular necrosis). Rodent species appear to be poorly relevant for quantification of the toxicity level of sodium chlorate.

In humans, the acute oral toxicity of chlorate is high. US EPA (2006) reports that lethal poisonings occur at a dose of ca. 7.5 g or ca. 110 mg/kg b.w. or higher (US EPA, 2006). According to NRC (1980) 'the lethal dose in adults is estimated to be 20 to 35 g for sodium chlorate and 5 to 30 g for potassium chlorate'. Based on these estimates, the lowest oral lethal dose for chlorate would be approximately 50 mg chlorate/kg b.w. when a body weight of 70 kg is assumed. In rats, however, chlorate shows only a slight acute oral toxicity ($LD_{50} \geq 3\,861$ mg/kg b.w.).

In controlled clinical studies with adult volunteers, oral chlorate doses up to 34 µg/kg b.w. administered for 3 days or doses up to 36 µg/kg b.w. per day administered for 12 weeks were tolerated without any harmful effects (Lubbers et al., 1981). Bloxham et al. (1979) described a 29-year-old man who had ingested about 20 g sodium chlorate (equivalent to 230 mg chlorate/kg b.w.) who became cyanotic, had a severe drop in haemoglobin, and methaemoglobin and methaemalbumin were detected in his plasma. A case of severe sodium chlorate poisoning was also observed within 5 hours after suicidal ingestion of 150–200 g sodium chlorate (117–156 mg chlorate/kg b.w.). Methaemoglobinaemia was the early symptom of the intoxication. Helliwell and Nunn (1979) reported 14 cases of sodium chlorate poisoning, with ingested amounts (1–2 g to 300 g) known in 12 of the cases. The patient who had ingested the lowest amount (1–2 g, which corresponds to 11–23 mg chlorate/kg b.w.) survived. Methaemoglobinaemia was seen in 13 of the 14 patients. It is not indicated which patient did not have methaemoglobinaemia, but the CONTAM Panel assumes that this was the patient with the lowest dose ingested.

Based on the acute hematological and renal toxicity of chlorate in humans, the CONTAM Panel considers that it is necessary to establish an ARfD.

3.4.1. Derivation of a chronic health-based guidance value

There are no *in vivo* human studies on the inhibition of iodine uptake by chlorate. However, perchlorate has a similar mode of action, and there are several observations in humans, including clinical studies and case reports from the medicinal use of perchlorate, volunteer studies and both

occupational and ecological epidemiological studies on the effects of exposure to perchlorate (EFSA CONTAM Panel, 2014). Both JECFA (FAO/WHO, 2011) and EFSA CONTAM Panel (2014) based the hazard characterization of perchlorate on the available human data and selected the human volunteer study of Greer et al. (2002) as the pivotal study for the dose-response assessment. They both considered the inhibition of thyroid iodine uptake as the critical effect for the dose-response assessment. The CONTAM Panel established a TDI of 0.3 µg/kg b.w. per day for perchlorate on basis of the reference point (RP) of 0.0012 mg/kg b.w. per day, based on a BMDL₀₅ for thyroid iodine uptake inhibition and applying an overall uncertainty factor of 4 to the RP (EFSA CONTAM Panel, 2014).

As it was shown in the EFSA perchlorate opinion (2014), the available data indicate that a substantial part of the EU population, including children and pregnant and lactating women, is subject to a mild to moderate deficiency in iodine intake, and therefore may be more sensitive to goitrogenic effects of chlorate in comparison to population groups with an adequate iodine intake. The CONTAM Panel considered that a 5 % inhibition of iodine uptake would not lead to adverse effects in any subgroup of the population, and therefore no additional uncertainty factor was considered for intraspecies differences in toxicodynamics.

In order to establish a chronic health based guidance value for chlorate, and as the toxicity of chlorate and perchlorate are both related to the inhibition of iodine uptake, the CONTAM Panel decided to use the TDI established for perchlorate and to apply an extrapolation factor for the difference in potency between chlorate and perchlorate. When comparing the NOAEL and LOAEL for thyroid follicular cell hypertrophy in rats, perchlorate is about 10 times more potent than chlorate (see Appendix B).

In addition *in vitro* studies comparing the inhibition of thyroid iodine transport by chlorate and perchlorate showed that perchlorate is a more potent inhibitor than chlorate.

On this basis, the CONTAM Panel established a TDI for chlorate of 3 µg/kg b.w. per day, based on the TDI established for perchlorate (0.3 µg/kg b.w. per day) and by multiplying by a factor of 10 for the difference in potency between the two substances.

3.4.2. Derivation of an acute reference dose

As explained previously, formation of methaemoglobin is the critical acute toxic effect which was identified in cases of poisoning. Infants (and presumably the fetus) are much more sensitive than adults to intracellular methaemoglobin inducers. This is due to a relative deficiency in methaemoglobin reductase in red blood cells of newborns, because the foetal form of haemoglobin is more sensitive to reducing agents, and because the fetus has a greater oxygen demand. A large proportion of haemoglobin in neonates and infants is in the form of foetal haemoglobin, which is more readily oxidized to methaemoglobin than adult haemoglobin (Steinberg and Benz, 1991; Mensinga et al., 2003; Sadeq et al., 2008). Also the gastric environment in infants is more alkaline than in adults, providing optimal conditions for growth of bacteria that promotes methaemoglobin formation and gastroenteritis with vomiting and diarrhoea, which is more common in infants than adults, enhances conditions for methaemoglobinaemia formation (ECETOC, 1988; Wright et al., 1999). However, it is not clear whether the newborn or the fetus may be more sensitive to the haemolytic effect of chlorate than adults. The extracellular autooxidative formation of methaemoglobin from lysed cells is irreversible and complete in both adults and fetuses, so there would be no difference in sensitivity in this step.

Persons with pre-existing blood conditions, especially anaemia, or those with kidney diseases, might be more sensitive. Persons with genetic diseases such as hereditary methaemoglobinaemia and glucose-6-phosphate dehydrogenase deficiency (which increases the haemolytic susceptibility of humans to oxidizing agents), and other persons who may be unusually susceptible to oxidants may also be at greater risk than the general population.

The only controlled clinical study available is the study of Lubbers et al. (1981) who considered the impact on normal subjects (10/group) of daily ingestion of 500 mL water containing 5 mg/L sodium chlorate (equivalent to 36 µg chlorate/kg b.w. per day) for 12 consecutive weeks. The subjects were followed for 8 weeks following cessation of treatment. A control group received untreated water. An extensive battery of parameters was monitored to assess the biochemical and physiological response to the oral ingestion of sodium chlorate. No adverse physiological effects were identified. The NOEL was 36 µg chlorate/kg b.w. per day.

The CONTAM Panel considers that this study can be the basis for the establishment of an ARfD. Lethal poisonings have been reported to occur at doses of approximately 50 mg chlorate/kg b.w. The NOEL from the controlled clinical study (Lubbers et al., 1981) is about 1 400-fold lower than the lowest lethal dose. Furthermore, it is at least 300 fold lower than the toxic level in a poisoning case (11–23 mg chlorate/kg b.w.) where induction of methaemoglobinaemia was not reported. Taking into account also that the NOEL was the highest dose tested in a study with administration daily for 12 weeks, the CONTAM Panel concluded that these differences are sufficiently large that no uncertainty factor is required for more vulnerable individuals (e.g. glucose-6-phosphate dehydrogenase-deficient individuals or hereditary methaemoglobinaemia) and establishes an ARfD of 36 µg chlorate/kg b.w.

3.5. Risk characterisation

Mean and high chronic and acute dietary exposure levels to chlorate were based on the occurrence dataset obtained after an ad hoc call for data on chlorate levels in food and drinking water.

3.5.1. Risk characterisation based on current occurrence data

3.5.1.1. Chronic

The chronic effects of chlorate are mediated by its activity as a competitive inhibitor of iodine uptake via the NIS in the thyroid. Hence, the adverse effects of chlorate have to be considered in conjunction with the iodine status of the exposed population. The CONTAM Panel noted that a sustained and marked inhibition of thyroid iodine uptake could lead to the development of toxic multinodular goitre as a result of thyroid autoregulation to overcome the lower iodine bioavailability. This chronic effect is particularly relevant for populations with mild to moderate iodine intake. For this chronic effect of chlorate, the CONTAM Panel established a TDI of 3 µg/kg b.w. per day.

The mean and 95th percentile chronic exposure estimates for ‘Adolescents’, ‘Adults’, ‘Elderly’, ‘Very elderly’, ‘Pregnant women’ and ‘Lactating women’ do not exceed the TDI.

In ‘Infants’, the age group with the highest exposure estimates, the levels for mean and 95th percentile chronic dietary exposure ranged from 1.6 to 4.1 µg/kg b.w. per day and from 3.3 to 6.6 µg/kg b.w. per day (minimum LB–maximum UB across different dietary surveys), respectively. In ‘Toddlers’, mean exposure levels in the range 2.1–3.5 µg/kg b.w. per day and 95th percentile exposure levels in the range 3.2–5.4 µg/kg b.w. per day were calculated.

In these younger populations (‘Infants’ and ‘Toddlers’), the TDI was exceeded at the 95th percentile in all surveys and in some surveys for the mean exposure estimates.

At the 95th percentile at median and maximum UB, the TDI was also exceeded in the group ‘Other children’. The 95th exposure levels were in the range of 2.5–5 µg/kg b.w. per day (minimum LB – maximum UB across different dietary surveys).

In all these populations groups where estimates are exceeding the TDI, the Panel noted that the main contributing food source is drinking water at up to 60 % in ‘Infants’, up to 50 % in ‘Toddlers’ and up to 40 % in ‘Other children’.

Overall, the CONTAM Panel concluded that the chronic dietary exposure to chlorate is of potential concern in particular for the high consumers in the younger age groups of the population with mild to moderate iodine deficiency. Fetuses, neonates, and individuals with low iodine intake or genetically predisposed to develop hypothyroidism are likely to be more sensitive to the effects of exposure to chlorate. Individuals who have sufficient iodine intake are less likely to develop adverse effects at such exceedances of the TDI. The effects of chlorate could be exacerbated by concurrent exposure to other substances that also act as antithyroid substances (e.g. perchlorate, thiocyanate and nitrate, among others).

3.5.1.2. Acute

By similarity with perchlorate, the CONTAM Panel noted that a single acute exposure to chlorate at levels found in food and water is unlikely to cause adverse effects on thyroid function, including the more vulnerable groups of the population. Even a one-day complete thyroid iodine uptake inhibition would not deplete the thyroid iodine content in infants with mild to moderate iodine deficiency, and therefore, the CONTAM Panel concluded that the establishment of an ARfD is not warranted based on the thyroid toxicity of chlorate.

Because of the acute haematological and renal toxicity of chlorate in humans the CONTAM Panel derived an ARfD of 36 µg/kg b.w. The CONTAM Panel considered that this ARfD covered also the more vulnerable individuals (e.g. Glucose-6-phosphate dehydrogenase deficient individuals or hereditary methaemoglobinemia).

The mean and 95th percentile acute exposure estimates for all age groups are below the ARfD. In 'Infants', the age group with the highest exposure estimates, the levels for 95th percentile acute dietary exposure ranged from 13.9–30.9 µg/kg b.w. per day (minimum to maximum UB).

3.5.2. Risk characterization based on a hypothetical maximum residue level of 0.7 mg/kg

3.5.2.1 Chronic

For chronic exposures based on the current occurrence data, removing foods and drinking water containing more than 0.7 mg/kg chlorate from the data set would have a minimal impact and consequently on the risk characterisation since most of the occurrence levels in food commodities are substantially below 0.7 mg/kg. Thus mean and 95th percentile chronic exposure estimates for 'Adolescents', 'Adults', 'Elderly', 'Very elderly', 'Pregnant women' and 'Lactating women' would not exceed the TDI. In 'Infants' and 'Toddlers', the TDI would be exceeded at mean exposures and in addition at 95th percentile also in 'Other children'.

It should be emphasised that the mean occurrence data set applies to current practice in the food industry under which the occurrence is, in general, substantially lower than 0.7 mg/kg. It cannot be predicted whether application of a MRL of 0.7 mg/kg would result in different practices leading to higher residue levels and higher exposures to chlorate.

3.5.2.2. Acute

For acute exposure based on the current occurrence data removing foods containing more than 0.7 mg/kg chlorate from the data set would also have a minimal impact on the exposure. The level for average and 95th percentile acute dietary exposure would all remain below the ARfD.

3.5.3. Risk characterization assuming an occurrence value of 0.7 mg/kg in all commodities

Assuming an occurrence value of 0.7 mg/kg for all foods covered by Annex I of Regulation 396/2005 and drinking water, acute exposure would increase by up to five-fold, primarily due to drinking water and cow's milk. The ARfD would be exceeded at mean exposure in 'Infants', and at the 95th percentile also in 'Toddlers', 'Other children' and 'Adults'. However, although an individual food commodity could contain chlorate at the hypothetical MRL of 0.7 mg/kg on some eating occasions, it

is implausible that all foods consumed on a single day would contain chlorate at 0.7 mg/kg and therefore such exceedances of the ARfD are unlikely. A potential exception would be drinking water which by itself contributes to a large extent to the intake of chlorate.

When considering food commodities one by one, mean acute chlorate exposure did not exceed the ARfD from any food item, with the exception of drinking water. The scenario indicated that if the chlorate concentration in drinking water would be 0.7 mg/kg, the exposure to chlorate could be similar to the ARfD at mean water consumption and up to 3-fold the ARfD at high (95th percentile) water consumption.

3.6. Uncertainty analysis

The evaluation of the inherent uncertainties in the assessment of exposure to chlorate in food and drinking water has been performed following the guidance of the Opinion of the Scientific Committee related to Uncertainties in Dietary Exposure Assessment (EFSA, 2006b). In addition, the report on 'Characterizing and Communicating Uncertainty in Exposure Assessment' has been considered (WHO/IPCS, 2008). According to the guidance provided by the EFSA opinion (2006b), the following sources of uncertainties have been considered: assessment objectives, exposure scenario, exposure model, and model input (parameters).

3.6.1. Assessment objectives

The objectives of the assessment were clearly specified in the terms of reference.

3.6.2. Exposure scenario/Exposure model

A total of 8 028 samples of which about 5 % were drinking water samples were available to estimate dietary exposure to chlorate. In total, 19 different European countries were reported as sampling country, with most of the analytical data derived from samples collected in Germany (4 839 samples); therefore, most probably, the dataset is not fully representative for food on the EU market. This lack of representativeness also affects the samples of 'Drinking water', which were mostly collected in one single country. The use of different disinfectants for drinking water disinfection across Europe could lead to very different levels of chlorate depending on the country or region of origin of the samples.

No or very limited occurrence data on some food commodities such as non-alcoholic beverages (e.g. coffee or tea), infant/follow-on formula and beer were submitted to EFSA. Likewise, some available data on specific commodities such as yoghurt, meat, fish and eggs and eggs based products were not considered sufficiently robust to be included in the final dataset used for exposure estimation. A particular uncertainty arises from the indication that high levels of chlorate might be present in yoghurt and infant/follow-on formula.

3.6.3. Other uncertainties

The CONTAM Panel established a TDI of 3 µg/kg b.w. per day extrapolated from a TDI of 0.3 µg/kg b.w. per day derived for perchlorate (EFSA CONTAM Panel, 2014). The TDI for perchlorate was based on the lowest BMDL₀₅ calculated for the thyroid iodine uptake inhibition measured in a human volunteer study. The CONTAM Panel concluded, based on the overall weight of evidence, that this effect was also the most relevant chronic effect caused by uptake of chlorate. However, since no human studies on inhibition of iodine uptake for chlorate exist, this conclusion adds to the overall uncertainty.

In addition, all uncertainties incurred with derivation of the TDI for perchlorate and described in the respective opinion (EFSA CONTAM Panel, 2014) also apply for the TDI derived for chlorate and are described in the opinion on perchlorate.

Based on a comparative analysis of dose levels of perchlorate and chlorate respectively inducing hypertrophy in the thyroid gland in subacute and subchronic rat studies supported by *in vitro* studies

suggesting a more pronounced inhibition of iodine transport of perchlorate as compared to chlorate, the CONTAM Panel concluded that perchlorate is about 10 times more potent than chlorate with respect to this effect. Different rat strains have been used for the tests with the two compounds and there is further uncertainty in the extrapolation of the potency difference in rats to humans and between endpoints (induction of thyroid hypertrophy in rats versus iodine uptake inhibition in humans). The *in vitro* studies were designed to elucidate mechanistic effects and potential differences in toxicokinetics and toxicodynamics of the two compounds are not reflected in their results. All these limitations add substantially to the overall uncertainty.

The effects of chlorate could be exacerbated by concurrent exposure to other substances that also act as antithyroid substances (e.g. perchlorate, thiocyanate and nitrate, among others).

An ARfD was set on the basis of a NOEL of 36 µg chlorate/kg b.w. per day in a human repeat dose study with a small number of male healthy volunteers. The NOEL was the highest dose tested and there is uncertainty about how much higher a LOAEL would be. An uncertainty factor was not applied since the NOEL from the controlled clinical study is at least 300-fold lower than the toxic level in a poisoning case where induction of methaemoglobinaemia was not reported. However, this difference of 300 was derived from a single poisoning case. This adds to the overall uncertainty.

3.6.4. Summary of uncertainties

In Table 16, a summary of the uncertainty evaluation for chlorate is presented highlighting the main sources of uncertainty and indicating an estimate of whether the respective source of uncertainty might have led to an over- or underestimation of the exposure or the resulting risk.

Table 16: Summary of qualitative evaluation of the impact of uncertainties on the risk assessment of the dietary exposure to chlorate

Sources of uncertainty	Direction ^(a)
Lack of representativeness of occurrence data for whole Europe, including 'Drinking water'	+/-
Missing occurrence data on particular food commodities	-
Imputation of occurrence data for drinking water to beer, tea and coffee	+/-
All uncertainties incurred with derivation of tolerable daily intake for perchlorate as used as a basis for chlorate TDI	+/-
Use of different rat strains and induction of thyroid hypertrophy as endpoint for derivation of differential potency factor for inhibition of iodine uptake in humans	+/-
Use of a NOEL from a human repeat dose study in the absence of any established effect level for derivation of ARfD	+
Small number of volunteers (healthy males) in study used for derivation of ARfD	-
Use of a 12 week human study to set an ARfD	+
Effect dose in humans derived based on one poisoning case	+/-
The effects of chlorate could be exacerbated by concurrent exposure to other substances that also act as antithyroid substances (e.g. perchlorate, thiocyanate and nitrate, among others).	-

ARfD: acute reference dose; NOEL: no-observed-effect level; TDI: tolerable daily intake.

(a): +: uncertainty with potential to cause over-estimation of exposure/risk; -: uncertainty with potential to cause under-estimation of exposure/risk.

Overall, the CONTAM Panel concluded that the impact of the uncertainties on the risk assessment is large.

4. Conclusions

General

- Chlorate is formed as a by-product when using chlorine, chlorine dioxide or hypochlorite for the disinfection of drinking water or water for food production.

- In processed food two routes of exposure are conceivable for chlorate residues, the disinfection of surfaces and food processing equipment, and the use of chlorinated water for washing and other food processing steps.
- For the washing, blanching and cooling of vegetables, a closed water circuit is applied. Here the re-circulating water is repeatedly chlorinated to keep its microbial quality within safe limits and thus chlorate concentrates in the processing water. This might explain the high chlorate levels in frozen vegetables.
- In foods of plant origin chlorate is frequently analysed after extraction with methanol by liquid chromatography-tandem mass spectrometry (LC-MS/MS) detection.
- In complex matrices of animal origin, liquid chromatography-mass spectrometry (LC-MS) utilising a $\text{Cl}^{18}\text{O}_3^-$ internal standard has been demonstrated to be applicable to quantify chlorate at low levels.

Occurrence data

- After a quality assessment of the analytical data and their evaluation, a total of 8 028 samples of which about 5 % were drinking water samples were available to estimate dietary exposure to chlorate.
- In total, 19 different European countries were reported as sampling country, with most of the analytical data derived from samples collected in Germany (4 839 samples). The samples were mainly collected between 2011 and 2014.
- The left-censored data (analytical data below the limit of detection/limit of quantification (LOD/LOQ)) accounted for 71 % of the analytical results on chlorate. The largest difference between lower bound (LB) and upper bound (UB) concentrations was for drinking water, at around 26 %.
- The most represented food groups were 'Vegetable and vegetable products' (n = 3 756), followed by 'Fruit and fruit products' (n = 2 607). The highest mean concentrations were observed for 'Chilli pepper' (lower bound, LB = 164 µg/kg, upper bound, UB = 169 µg/kg), 'Aubergines' (LB = 157 µg/kg, UB = 164 µg/kg,) and 'Vegetable and vegetable products, unspecified' (LB = 216 µg/kg, UB = 222 µg/kg).
- A total of 453 samples of 'Drinking water' were available, most of them reported as unspecified. Mean chlorate values for 'Drinking water' were 28 µg/L and 39 µg/L at the LB/UB scenarios, respectively. The 99th percentile at the UB scenario used to estimate acute exposure was 196 µg/L.
- Overall, food commodities reported as 'frozen' showed the highest levels of chlorate within one particular food group. However, in many samples reported as 'frozen' the chlorate levels were below the limit of quantification, indicating that chlorate levels may depend on how processing is done in the food industry (levels of chlorine in water and rinsing)
- There were indications that high levels of chlorate might be present in yoghurt and infant/follow-on formula but the data were insufficient for exposure assessment.

Exposure assessment

- The youngest population groups ('Infants', 'Toddlers' and 'Other children') showed the highest dietary exposure to chlorate.

- The CONTAM Panel concluded that a variability factor accounting for residue variation within composite samples of food commodities for acute exposure assessment of chlorate is not needed, mainly since the unit weight in frozen vegetables is small. Additionally, chlorate residues are highly soluble and an even distribution in processing water is expected.
- Considering all available occurrence data, the mean chronic dietary exposure ranged between 0.5 µg/kg body weight (b.w.) per day in 'Adolescents' (LB) and 4.1 µg/kg b.w. per day in 'Infants' (UB). At the 95th percentile, the lowest dietary exposure of 1.0 µg/kg b.w. day (LB) was estimated in the age classes 'Elderly' and 'Very elderly'. The highest 95th percentile exposure was in 'Infants' (6.6 µg/kg b.w. per day, UB).
- The estimates of chronic dietary exposure to chlorate in the available dietary survey on 'Pregnant women' and the one on 'Lactating women' are similar or lower than those calculated in the general population.
- Overall, in all age classes and vulnerable groups of population (pregnant and lactating women) the main average contributor to the chronic dietary exposure to chlorate was 'Drinking water'. Range of contribution at the LB estimation: 'Infants' (25–58 %), 'Toddlers' (12–48 %), 'Other children' (0–38 %), 'Adolescents' (0–38 %), 'Adults' (6.2–48 %), 'Elderly' (8.1–35 %), 'Very elderly' (5.5–39 %).
- Considering all available occurrence data, mean acute exposure (UB) ranged between 1.0 µg/kg b.w. day in 'Adolescents' and 13 µg/kg b.w. day in 'Infants'. At the 95th percentile, the estimates of acute exposure were between 2.6 µg/kg b.w. per day in 'Adolescents' and 31 µg/kg b.w. per day in 'Infants'.
- Acute exposure through the daily consumption of individual foods, at 95th percentile (UB) was highest for 'Drinking water' (32 µg/kg b.w. per day), 'Broccoli' (21 µg/kg b.w. per day), and 'Whey and whey products, excluding whey cheese' (19 µg/kg b.w. per day).
- Acute and chronic estimates of exposure when excluding the occurrence data above a hypothetical MRL of 0.7 mg/kg were only slightly lower than those using all available occurrence data. This is explained by the fact that only few commodities were excluded and most of them belong to food groups with a relatively low contribution to the exposure.
- In a hypothetical scenario, acute exposures were estimated assuming that all food items consumed have an occurrence value of 0.7 mg/kg. This led to a substantial increase of the acute exposure estimates as compared to the scenario using the reported occurrence levels.
- Estimating acute exposure assuming an occurrence value of 0.7 mg/kg for individual food commodities generally results in lower acute exposure as compared to the use of the reported occurrence data. Important exceptions were the estimates of acute exposure calculated through the daily consumption of 'Drinking water' and 'Cow milk' that reached values up to 111 µg/kg and 56 µg/kg b.w. per day, respectively.

Hazard identification and characterization

Toxicokinetics

- Following oral exposure in experimental animals, chlorate is rapidly absorbed, widely distributed throughout the body and evidence indicates that it undergoes metabolism to chloride. The main pathway of elimination is via urine.
- The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) has not identified literature studies on the toxicokinetics of chlorate by humans after ingestion. The data

obtained after chlorate poisoning indicate that chlorate is bioavailable in humans after oral ingestion and that it is eliminated via the urine.

Toxicity in experimental animals

- The thyroid gland and the haematological system are the primary targets of toxicity of chlorate identified in animal species after repeated oral exposure. Decreases in erythrocytes, haemoglobin and haematocrit were observed in mice, rats, dogs and monkeys. Histopathological changes were noted in the thyroid gland of rats (follicular cell hypertrophy, increase in colloid depression and in follicular cell hyperplasia). Thyroid hormone levels were also altered significantly (decreases in triiodothyronine (T3) and thyroxine (T4) and increases in thyroid stimulating hormone (TSH)).
- Long-term oral exposure to sodium chlorate resulted in non-neoplastic lesions in the thyroid gland (follicular cell hypertrophy) of male and female rats and female mice, bone marrow (hyperplasia) of male rats and female mice, and spleen (hematopoietic cell proliferation) of male rats. There was no evidence of carcinogenic activity of sodium chlorate in male B6C3F1 mice. There was equivocal evidence of carcinogenic activity of sodium chlorate in female B6C3F1 mice based on marginally increased incidences of pancreatic islet cell adenoma and carcinoma (combined). There was some evidence of carcinogenic activity of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms.
- Chlorate is unlikely to pose a genotoxic hazard.
- Chlorate has not been shown to have reproductive effects in rats or developmental effects in rats or rabbits.
- No neurotoxic effects of chlorate have been demonstrated.

Observations in humans

- Death from acute oral sodium or potassium chlorate poisoning in adults has been reported from 5 g and above (50 mg chlorate/kg b.w.), caused by formation of methaemoglobinaemia, followed by lysis of red blood cells and renal failure.
- Toxicity has been reported in case studies where individuals acutely ingested approximately 11–23 mg chlorate/kg b.w. and above.
- In a controlled clinical trial male participants received 2.5 mg chlorate (36 µg/kg b.w. per day) in drinking water daily for 12 weeks. No physiologically relevant effects were detected by biochemical parameters and physical examination.

Mode of action

- Chlorate-induced methaemoglobin formation is most likely caused by an autocatalytic reaction. Subsequently, chlorate disturbs the capacity of the erythrocyte to form nicotinamid adenine dinucleotide phosphate (NADPH), resulting in a cascade of protein denaturation, crosslinking of membrane proteins and finally haemolysis.
- Chlorate-induced renal failure appears to be secondary to haemolysis.
- Like perchlorate, the chlorate ion is a competitive inhibitor of iodine uptake via the sodium-iodine symporter (NIS) in the thyroid resulting in decreased serum thyroid hormones T4 and T3 and increased release of TSH. Persistent stimulation of the thyroid gland by elevated levels

of TSH results in increases in thyroid gland size and weight, decreased colloid, hypertrophy and hyperplasia of thyroid follicle cells and thyroid tumours in rats.

Hazard characterization

Chronic

- Chronic adaptive changes to compensate for a sustained inhibition of thyroid iodine uptake could lead to long term effects such as the development of toxic multinodular goiter, in particular in populations with mild to moderate iodine deficiency.
- The CONTAM Panel considered the inhibition of thyroid iodine uptake as the critical effect for the chronic hazard characterization.
- Rats are highly sensitive to the effects of agents that disrupt thyroid hormone homeostasis. Humans are likely to be less sensitive than rats to these effects. Due to the differences in thyroid hormone physiology, the dose response data from toxicological studies in rats are of limited relevance for humans. However, there are no *in vivo* human studies on the inhibition of iodine uptake by chlorate.
- In order to establish a chronic health-based guidance value for chlorate, the CONTAM Panel decided to use the tolerable daily intake (TDI) established for perchlorate and to apply an extrapolation factor for the difference in potency between chlorate and perchlorate. When comparing the no-observed-adverse-effect level (NOAEL) and the lowest-observed-adverse-effect level (LOAEL) for thyroid follicular cell hypertrophy in rats, perchlorate is about 10 times more potent than chlorate.
- The CONTAM Panel established a TDI for chlorate of 3 µg/kg b.w. per day, based on the TDI established for perchlorate and by multiplying by a factor of 10 for the difference in potency between the two substances in rats.

Acute

- As for perchlorate, the CONTAM Panel noted that a single acute exposure to chlorate at levels found in food and water is unlikely to cause adverse effects in thyroid function, including in the more vulnerable groups of the population.
- Based on the acute haematological and renal toxicity of chlorate in humans observed in poisoning cases, the CONTAM Panel considered that it is necessary to establish an acute reference dose (ARfD).
- Formation of methaemoglobin is the critical acute toxic effect which was identified in cases of poisoning. The CONTAM Panel considered that the no-observed-effect level (NOEL) of 36 µg chlorate/kg b.w. per day from the controlled clinical study can be the basis for the establishment of an ARfD. The CONTAM Panel concludes that the differences between the NOEL in the controlled clinical study and the effect levels in poisoning cases are sufficiently large that no uncertainty factor is required for more vulnerable individuals (e.g. glucose-6-phosphate dehydrogenase deficient individuals or hereditary methaemoglobinemia) and establishes an ARfD of 36 µg chlorate/kg b.w.

Risk characterization based on current occurrence data

- The mean and 95th percentile chronic exposure estimates for surveys from adolescent and adult age classes did not exceed the TDI.

- In the younger populations ('Infants' and 'Toddlers'), the TDI exceeded at the 95th percentile in all surveys and in some surveys for the UB mean exposure estimates. At the 95th percentile at median (LB), the TDI was also exceeded in the group 'Other children'.
- Overall, the CONTAM Panel concluded that the chronic dietary exposure to chlorate is of potential concern in particular for the high consumers in the younger age groups of the population with mild to moderate iodine deficiency. Fetuses, neonates, and individuals with low iodine intake or genetically predisposed to develop hypothyroidism are likely to be more sensitive to the effects of exposure to chlorate. Individuals who have sufficient iodine intake are less likely to develop adverse effects at such exceedances of the TDI.
- The mean and 95th percentile acute exposure estimates for all age groups are below the ARfD.

Risk characterisation based on a hypothetical MRL of 0.7 mg/kg

- For chronic exposure based on the current occurrence data removing foods containing more than 0.7 mg/kg chlorate from the data set would have a minimal impact on the exposure and consequently on the risk.
- For acute exposure based on the current occurrence data removing foods containing more than 0.7 mg/kg chlorate from the data set would also have a minimal impact on the exposure. The level for mean and 95th percentile acute dietary exposure would all remain below the ARfD.
- It should be emphasised that the occurrence data set applies to current practice in the food industry under which the occurrence is, in general, substantially lower than 0.7 mg/kg. It cannot be predicted whether application of a MRL of 0.7 mg/kg would result in different practices leading to higher residue levels and higher exposures to chlorate.

Risk characterisation assuming an occurrence value of 0.7 mg/kg in all commodities

- Assuming an occurrence value of 0.7 mg/kg for all foods covered by Annex I of Regulation 396/2005 and drinking water, acute exposures would increase by up to approximately five-fold, and the ARfD would be exceeded at mean exposure in 'Toddlers' and at 95th percentile also in 'Infants', 'Other children' and 'Adults'.
- The CONTAM Panel considers that such exceedances of the ARfD resulting from this scenario are unlikely, because it is highly implausible that that all foods consumed on a single day would have chlorate concentrations in the range of 0.7 mg/kg. A potential exception would be drinking water which by itself contributes to a large extent to the intake of chlorate.
- Chlorate concentrations of 0.7 mg/kg in drinking water could lead to exposures similar to the ARfD at mean water consumption and up to 3-fold the ARfD at high (95th percentile) water consumption.

5. Recommendations

- There is a need for human data on inhibition of iodine uptake by chlorate and relative potency compared to perchlorate.
- There is a need for information on levels of chlorate in humans and association with possible effects.
- More information about the impact of food processing (e.g. blanching) on chlorate residues in food is needed.

- Occurrence data are needed for foods for which there are currently no data (e.g. animal derived foods, tea, coffee, beer).
- More data on chlorate in foods are required where there are currently indications of high chlorate levels such as infant/follow-on formula and yoghurt.
- Efforts to reduce chlorate residues in food should take into account whether these would have an impact on microbiological food safety.
- There is a need for a better understanding of the contribution of various dietary factors and contaminants to the overall thyroid iodine uptake inhibition.

DOCUMENTATION PROVIDED TO EFSA

Documents made available by the European Commission

- Data and comments for the Standing Committee on the Food Chain and Animal Health (SCOFAH) pesticides residues of 24-25 February 2014, point 16.01:
 - BFR opinion
 - Germany (DE) occurrence data and comments
 - Spain (ES) occurrence data and comments
- Data and comments for the SCOFAH pesticides residues of 12-13 June 2014, point A. 04:00:
 - Belgium (BE) occurrence data and comments
 - The Czech Republic (CZ) occurrence data and comments
 - Studies provided by Germany (DE)
 - Occurrence data from Food Drink Europe
 - Occurrence data from the European Fresh Produce Association - Freshfel
 - Occurrence data from the European Association of Fruit and Vegetable Processing Industries - PROFEL
 - Overview of the Rapid Alert System for Food and Feed (RASFF) notifications
 - Comments from Sweden (SE) and the United Kingdom (UK)

Unpublished documents made available by the data owner of the original study reports of the EU sodium chlorate – EU DAR (2008)

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Unpublished study made available by the owner of study report (Labor Friedle GmbH)

Labor Friedle GmbH, 2014, Chlorat-Kontamination von pflanzlichen Lebensmitteln durch Waschwasser, Tegernheim, 13.05.2014.

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APPENDICES

Appendix A. EFSA guidance documents applied for the assessment

- EFSA (European Food Safety Authority), 2006. Guidance of the Scientific Committee on a request from EFSA related to uncertainties in Dietary Exposure Assessment. The EFSA Journal 2006, 438, 1–54.
- EFSA (European Food Safety Authority), 2009. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: General principles. The EFSA Journal 2009, 1051, 1–22.
- EFSA (European Food Safety Authority), 2010. Management of left-censored data in dietary exposure assessment of chemical substances. EFSA Journal 2010;8(3):1557, 96 pp. doi:10.2903/j.efsa.2010.1557
- EFSA (European Food Safety Authority), 2011. Guidance of EFSA on the use of the EFSA Comprehensive European Food Consumption Database in Intakes Assessment. EFSA Journal 2011;9(3):2097, 34 pp. doi:10.2903/j.efsa.2011.2097
- EFSA (European Food Safety Authority), 2011. Overview of the procedures currently used at EFSA for the assessment of dietary exposure to different chemical substances. EFSA Journal 2011;9(12): 2490, 33 pp. doi:10.2903/j.efsa.2011.2490
- EFSA SC (EFSA Scientific Committee), 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. doi:10.2903/j.efsa.2012.2579
- EFSA SC (EFSA Scientific Committee), 2012. Scientific Opinion on Risk Assessment Terminology. EFSA Journal 2012;10(5):2664, 43 pp. doi:10.2903/j.efsa.2012.2664

Appendix B. Comparative evaluation of the potency of chlorate and perchlorate to induce thyroid gland follicular cell hypertrophy in rats

B1. Chlorate

For chlorate, the data included in NTP (2005) were considered. These were a 3-week dose range finding study, a 14-weeks study (satellite group of the 2-year study) and the 2-year chronic study in rats in male and female F344/N rats. In addition the 7-day study of Khan et al. (2005) in male F344/N rats was considered.

Table B1: Results from 3-week study in F344/N rats (NTP, 2005)

	Doses (mg sodium chlorate/kg b.w. per day)					
	0	20	35	75	170	300
Males						
Incidence of thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	1/10	5/10	10/10	10/10
	Doses (mg sodium chlorate/kg b.w. per day)					
	0	20	40	75	150	340
Females						
Incidence of thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	1/10	8/10	6/10	10/10

b.w.: body weight.

A no-observed-adverse-effect level (NOAEL) of 35 mg sodium chlorate/kg body weight (b.w.) per day, equivalent to 0.33 mM chlorate/kg b.w. per day and a lowest-observed-adverse-effect level (LOAEL) 75 mg sodium chlorate/kg b.w. per day, equivalent to 0.70 mM chlorate/kg b.w. per day were established from this study.³⁰

Table B2: Results from the interim 14-week study in F344/N rats (satellite group of the 2-year study) (NTP, 2005)

	Doses (mg sodium chlorate/kg b.w. per day) ^(a)			
	0	11	89	178
Males				
Incidence thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	10/10	10/10
	Doses (mg sodium chlorate/kg b.w. per day)			
	0	12	93	186
Females				
Incidence thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	10/10	10/10

b.w.: body weight.

(a): The NTP report does not indicate estimated doses for the satellite groups of the chronic study examined after 14 weeks of exposure. Doses reported in the table were converted considering the EFSA default factors for subchronic exposure via drinking water (i.e. 0.089 and 0.093 for male and female rat, respectively) (EFSA, 2012a) applied to the tested concentrations of sodium chlorate (0, 125, 1 000 and 2 000 mg/L, respectively).

A NOAEL of 11 mg sodium chlorate/kg b.w. per day, equivalent to 0.10 mM chlorate/kg b.w. per day and a LOAEL 89 mg sodium chlorate/kg b.w. per day, equivalent to 0.84 mM chlorate/kg b.w. per day were established in this study.

³⁰ A conversion factor of 0.0094 used to convert doses from mg to mM (MW NaClO₃ = 106.44 g/mol).

Table B3: Results from the 2-year study in F344/N rats (NTP, 2005)

	Doses (mg sodium chlorate/kg b.w. per day)			
	0	5	35	75
Males				
Incidence of thyroid gland follicular cell hypertrophy/number of animals	4/47	13/44	33/43	40/47
	Doses (mg sodium chlorate/kg b.w. per day)			
	0	5	45	95
Females				
Incidence of thyroid gland follicular cell hypertrophy/number of animals	3/47	7/47	27/43	42/46

b.w.: body weight.

A LOAEL of 5 mg sodium chlorate/kg b.w. per day, equivalent to 0.047 mM chlorate/kg b.w. per day was established in this study.

Table B4: Results from 7-day study in male F344/N rats (Khan et al., 2005)

	Doses (mg sodium chlorate/kg b.w. per day)			
	0.06	3.3	16	120 ^(a)
Incidence of thyroid gland follicular cell hypertrophy/number of animals	1/6	5/6	6/6	5/6

b.w.: body weight.

(a): Exposure to measured concentrations in drinking water containing background concentrations of chlorate.

A LOAEL of 3.310 mg sodium chlorate/kg b.w. per day, equivalent to 0.03 mM chlorate/kg b.w. per day was established in this study.

B.2. Perchlorate

For perchlorate, results reported from a 2-week study with perchlorate in male SD rats (McLanahan et al., 2007), a 2-week and a 13-week study with ammonium perchlorate in male and female SD rats (Siglin et al., 2000) and from a 7-day study in with ammonium perchlorate in male F344/N rats (Khan et al., 2005) were considered.

Table B5: Results from the 2-week study in male SD rats (McLanahan et al., 2007)

	Doses (mg perchlorate/kg b.w. per day)			
	0	0.01	0.1	1.0 ^(a)
Incidence of thyroid gland follicular cell hypertrophy/number of animals	0/8	0/8	0/8	0/8

b.w.: body weight.

(a): Poorly reported study. The authors state that no significant changes from control were observed during histopathological analysis of the thyroid, without further detail.

A NOAEL of 0.01 mg perchlorate/kg b.w. per day, equivalent to 0.01 mM perchlorate/kg b.w. per day was established in this study.³¹

³¹ Conversion factor of 0.010 used to convert doses of perchlorate from mg to mM (MW ClO₄⁻ = 99.45 g/mol).

Table B6: Results from the 2-week study in male and female SD rats (Siglin et al., 2000)

Males	Doses (mg ammonium perchlorate/kg b.w. per day)					
	0	0.01	0.05	0.2	1.0	10.0
Incidence of thyroid gland follicular cell hypertrophy/number of animals	1/8	0/10	1/10	0/10	0/10	10/10
Females	Doses (mg ammonium perchlorate/kg b.w. per day)					
	0	0.01	0.05	0.2	1.0	10.0
Incidence of thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	0/10	0/10	0/10	7/10

b.w.: body weight.

A NOAEL of 1.0 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.0085 mM perchlorate/kg b.w. per day and a LOAEL 10 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.085 mM perchlorate/kg b.w. per day were established in this study.³²

Table B7: Results from the 13-week study with ammonium perchlorate in male and female SD rats (Siglin et al., 2000)

Males	Doses (mg ammonium perchlorate/kg b.w. per day)					
	0	0.01	0.05	0.2	1.0	10.0
Incidence of thyroid gland follicular cell hypertrophy/number of animals	2/10	0/10	0/10	0/10	1/10	8/10
Females	Doses (mg ammonium perchlorate/kg b.w. per day)					
	0	0.01	0.05	0.2	1.0	10.0
Incidence of thyroid gland follicular cell hypertrophy/number of animals	0/10	0/10	0/10	0/10	0/10	9/10

b.w.: body weight.

A NOAEL of 1.0 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.0085 mM perchlorate/kg b.w. per day and a LOAEL of 10 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.085 mM perchlorate/kg b.w. per day were established in this study.

Table B8: Results from the 7-day study with ammonium perchlorate in male F344/N rats (Khan et al., 2005)

	Doses (mg ammonium perchlorate/kg b.w. per day)			
	0	0.024	0.2	1.2 ^(a)
Incidence of thyroid gland follicular cell hypertrophy/number of animals	1/6	0/5	1/6	6/6

b.w.: body weight.

(a): Exposure via drinking water containing background concentrations of chlorate. The dose of chlorate (expressed as mg sodium chlorate/kg b.w. per day) was estimated to be 0.069, 0.091, 0.112 and 0.069 for the control group and the three dose groups, respectively.

A NOAEL of 0.205 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.0017 mM perchlorate/kg b.w. per day and a LOAEL of 1.170 mg ammonium perchlorate/kg b.w. per day, equivalent to 0.0099 mM perchlorate/kg b.w. per day were established in this study.

³² Conversion factor of 0.0085 used to convert doses from mg to mM (MW NH₄ClO₄ = 117.49 g/mol).

Table B9: Summary table comparing results from studies with similar duration on induction of thyroid gland follicular cell hypertrophy with chlorate and perchlorate

Study duration; Compound; Strain; Reference	NOAEL mM/kg b.w. per day			LOAEL mM/kg b.w. per day		
	perchlorate	chlorate	factor	perchlorate	chlorate	factor
1 week; Perchlorate and chlorate; F334 rats; Khan et al. (2005)	0.002	n.d.	n.a.	0.010	0.030	3
2 weeks; Perchlorate; SD rats; Siglin et al. (2000)	0.009	0.330	37	0.085	0.700	8
3 weeks; Chlorate; F334 rats; NTP (2005)						
13 weeks; Perchlorate; SD rats; Siglin et al. (2000)	0.009	0.100	11	0.085	0.840	10
14 weeks; Chlorate; F334 rats; NTP (2005)						
105 weeks; Chlorate, F334 rats; NTP (2005)	n.t.	n.d.	n.a.	n.t.	0.047	n.a

b.w.: body weight; LOAEL: lowest-observed-adverse-effect level; n.a.: not applicable; n.d.: not derived; NOAEL: no-observed-adverse-effect level; n.t.: not tested.

Appendix C. Dietary surveys used for the estimation of chronic and acute dietary exposure to chlorate

Country	Survey acronym	Survey period	No of days per subject	No of subjects/No of days						
				Infants	Toddlers	Other children	Adolescents (mean age)	Adults	Elderly	Very elderly
Austria	ASNS - Adults	2010–2012	2					308/726	67/181	25/85
	ASNS - Children	2010–2012	3			128/384	237/706			
Belgium	Regional Flanders	2002–2002	3		36/108	625/1 875	–	–	–	–
Belgium	Diet National 2004	2004	2		–	-	576/1 187 (16a)	1 292/2 648	511/1 045	704/1 408
Bulgaria	NSFIN	2004	1				–/162	–/691	–/151	–/200
Bulgaria	NUTRICHILD	2007	2	861/1 720	428/856	433/867	–	-	-	-
Cyprus	Childhealth	2003	3		–	-	303/909 (13a)	-	-	-
Czech Republic	SISP04	2003–2004	2		–	389/778	298/596 (13a)	1 666/3 332	-	-
Denmark	DANSDA 2005-08	2005–2008	7		–	298/2 085	377/2 622 (13a)	1 739/12 127	274/1 916	12/84
Denmark	IAT 2006 07	2006–2007	7	826/5 771	917/6 388	-	–	–	–	–
Estonia	NDS 1997	1997	1					–/1 866	–	–
Finland	DIPP 2001 2009	2001–2009	3	500/1 500	500/1 500	750/2 250	–	–	–	–
Finland	NWSSP07 08	2007–2008	4		–	–	306/1 186 (13a)	–	–	–
Finland	FINDIET2012	2012	2		–	–	–	1 295/2 590	413/826	–
France	INCA2	2007	7		–	482/3 315	973/6 728 (14a)	2276/15 727	264/1 824	84/571
Germany	VELS	2001–2002	6	159/927	348/1 947	293/1 610	–	–	–	–
Germany	EsKiMo	2006	3		-	835/2 498	393/1 179 (11a)	–	–	–
Germany	National Nutrition Survey II	2007	2		-	–	1 011/2 022 (16a)	10 419/20 838	2 006/4 012	490/980
Greece	Regional Crete	2004–2005	3			838/2 508	-	-	–	–
Greece	DIET LACTATION GR	2005–2007	3		-	-	-	65/350	–	–
Hungary	National Repr Surv	2003	3		-	-	-	1 074/3 222	206/618	80/240
Ireland	NANS 2012	2008–2010	4		-	-	-	1 274/5 096	149/596	77/308
Italy	INRAN SCAI 2005 06	2005–2006	3	16/48	36/108	193/579	247/741 (14a)	2313/6 939	290/870	228/684

Country	Survey acronym	Survey period	No of days per subject	No of subjects/No of days						
				Infants	Toddlers	Other children	Adolescents (<i>mean age</i>)	Adults	Elderly	Very elderly
Latvia	EFSA TEST	2008	2			187/377	453/979 (14a)	1 271/2 655	–	–
Latvia	FC PREGNANTWOMEN 2011	2011	2		–	–	–	1 002/2 005	–	–
Netherlands	VCP kids	2006–2007	3		322/644	957/1 914	–	–	–	–
Netherlands	VCPBasis AVL2007 2010	2007–2010	2		–	447/894	1 142/2 284 (14a)	2 057/4 114	173/346	
Netherlands	VCP-Elderly	2010–2012	2		–	–	–	–	289/578	450/900
Poland	IZZ FAO 2000	2000	1		–/79	–/409	–/666 (14a)	–/2 527	–/329	–/124
Romania	Dieta Pilot Children	2012	1		–	–/205	–/567 (14a)	–	–	–
Romania	Dieta Pilot Adults	2012	7		–	–	–	1 254/8 770	83/581	45/315
Slovakia	SK MON 2008	2008	1		–	–	–	2 761	–	–
Slovenia	CRP 2008	2007–2008	1		–	–	–	407	–	–
Spain	enKid	1998–2000	2		17/34	156/312	209/418 (12a)	-	–	–
Spain	AESAN	1999–2001	3		–	–	–	410/828	–	–
Spain	NUT INK05	2004–2005	2			399/798	651/1 302 (14a)	-	–	–
Spain	AESAN FIAB	2009	3		–	–	86/226 (17a)	981/2 748	-	–
Sweden	NFA	2003	4		–	1 473/5 875	1 018/4 047 (12a)	–	-	–
Sweden	Riksmaten 2010	2010–2011	4		–	–	-	1 430/5 680	295/1 167	72/288
United Kingdom	NDNS- RollingProgrammeYears1-3	2008–2011	4		185/737	651/2 595	666/2 653 (14a)	1 266/5 040	166/662	139/552
United Kingdom	DNSIYC 2011	2011	4	1 369/5 446	1 314/5 217	–	–	–	–	–

Appendix D. Chlorate occurrence values in different food commodities

Table D: Chlorate occurrence values in different food commodities (µg/kg). Foods were grouped at different FoodEx levels depending on their occurrence values before estimating dietary exposure.

Groups ^(a) (FoodEx level 1)	Food Commodities ^(b)	N	% LC ^(c)	Mean		Highest reliable percentile ^(d)
				LB	UB	
Grains and grain-based products	Grains for human consumption (except rice)	36	70	12	13	25 (P90)
	<i>Rice</i>	12	92	57	59	5 (P75)
	Grain milling products	31	52	26	33	100 (P90)
	Pasta (Raw)	6	0	75	75	75 (mean)
	Breakfast cereals	5	80	41	46	46 (mean)
	Fine bakery wares	1	0	33	33	33 (mean)
Vegetables and vegetable products (including fungi)	Vegetables and vegetable products, unspecified	25	40	216	222	100 (P75)
	Root vegetables	245	78	35	41	150 (P95)
	Bulb vegetables (except garlic)	81	90	16	21	15 (P95)
	<i>Garlic, bulb</i>	10	70	201	208	208 (mean)
	Fruiting vegetables (except peppers, chili pepper and aubergines)	1 150	80	22	29	420 (P95)
	<i>Peppers, paprika</i>	400	76	63	70	1 400 (P99)
	<i>Chilli pepper</i>	27	81	164	169	10 (P75)
	<i>Aubergines (egg plants)</i>	73	47	157	164	480 (P95)
	Brassica vegetables (except broccoli)	243	80	23	28	64 (P95)
	<i>Broccoli</i>	173	30	351	358	2 400 (P95)
	Leaf vegetables (except Lettuce, excluding iceberg-type lettuce)	591	70	44	48	560 (P99)
	<i>Lettuce, excluding Iceberg-type lettuce</i>	298	66	138	144	600 (P95)
	Legume vegetables	78	86	22	35	100 (P95)
	Stem vegetables (Fresh) (except celery)	178	90	9	13	45 (P95)
	<i>Celery</i>	35	80	240	253	100 (P90)
	Sugar plants	9	56	41	46	46 (mean)
	Tea and herbs for infusions (Solid)	10	50	108	112	112 (mean)
	Cocoa beans and cocoa products	3	67	73	107	107 (mean)
	Vegetable products	24	50	31	41	60 (P75)
	Fungi, cultivated	66	64	29	33	162 (P95)
	Fungi, wild, edible	33	58	43	45	77 (P90)
Starchy roots and tubers	Potatoes and potatoes products	103	91	5	11	34 (P95)
	Other starchy roots and tubers	19	68	53	59	26 (P75)
Legumes, nuts and oilseeds	Legumes, beans, green, without pods	167	50	185	189	1 100 (P90)
	Legumes, beans, dried	79	62	84	88	560 (P90)
	Tree nuts	14	71	8	10	10 (P75)
	Legumes, beans, green, with pods	3	67	6	9	9 (mean)
Fruit and fruit products	Fruit and fruit products, unspecified	4	50	79	84	84 (mean)
	Citrus fruits	383	88	3	9	100 (P99)
	Pome fruits	416	82	4	13	100 (P99)
	Stone fruits	332	88	4	8	100 (P99)
	Berries and small fruits	897	87	8	13	270 (P99)
	Miscellaneous fruits	455	83	7	13	110 (P99)
	Dried fruits	99	43	35	37	134 (P95)
	Jam, marmalade and other fruit spreads	1	100	0	2	-
	Other fruit products (excluding beverages)	20	55	38	40	76 (P75)

Groups ^(a) (FoodEx level 1)	Food Commodities ^(b)	N	% LC ^(c)	Mean		Highest reliable percentile ^(d)
				LB	UB	
Milk and dairy products	Milk and dairy products, unspecified	43	74	16	23	67 (P90)
	Liquid milk	38	71	10	17	39 (P90)
	Milk based beverages	2	100	0	10	–
	Concentrated milk	6	67	128	135	135 (mean)
	Whey and whey products (excl. whey cheese)	23	9	347	348	618 (P75)
	Cream and cream products	6	33	32	36	36 (mean)
	Fermented milk products	38	71	10	17	38.5 (P90)
	Milk derivatives	7	43	40	44	44 (mean)
	Cheese	3	67	76	83	83 (mean)
Sugar and confectionary	Sugars	6	67	109	116	116 (mean)
	Chocolate (Cocoa) products	4	50	32	57	57 (mean)
	Honey	2	100	0	10	–
Animal and vegetable fats and oils	Animal fat	3	67	85	92	92 (mean)
Fruit and vegetable juices	Fruit juice	33	48	55	57	127 (P90)
	Concentrated fruit juice	4	50	11	16	16 (mean)
	Fruit nectar	27	59	34	39	12 (P75)
	Mixed fruit juice	3	67	8	12	12 (mean)
Non-alcoholic beverages (excepting milk based beverages)	Soft drinks	2	0	62	62	62 (mean)
	Tea (Infusion)	— ^(e)	31	28	39	196 (P99)
	Coffee (Beverage)	— ^(e)	31	28	39	196 (P99)
Alcoholic beverages	Beer and beer-like beverage	— ^(e)	31	28	39	196 (P99)
	Wine	37	97	0	3	5 (P90)
Drinking water	Drinking water	453	31	28	39	196 (P99)
Herbs, spices and condiments	Herbs	325	51	450	454	8 500 (P99)
	Spices (except paprika powder)	30	90	8	17	72 (P90)
	<i>Paprika powder</i>	11	27	5 118	5 119	5 119 (mean)
	Herb and spice mixtures	7	0	450	450	450 (mean)
	Seasoning or extracts	1	100	0	10	–
	Flavourings or essences	1	100	0	10	–
	Baking ingredients	1	0	26	26	26 (mean)
Food for infants and small children	Cereal-based food for infants and young children	3	100	0	2	–
	Ready-to-eat meal for infants and young children	20	55	10	13	23 (P75)
	Fruit juice and herbal tea for infants and young children	21	100	0	5	–
Products for special nutritional use	Dietary supplements	3	67	18	25	25 (mean)
Composite food (including frozen products)	Rice-based meals	1	0	120	120	120 (mean)
	Vegetable-based meals	1	0	55	55	55 (mean)
	Ready to eat soups	11	18	27	29	29 (mean)
	Prepared salads	53	4	129	130	491 (P90)

LB: Lower bound; P75, 90, 95: 75th, 90th, 95th percentile; UB: Upper bound.

(a): Food samples were grouped at FoodEx level 1 to better explain their contribution to the dietary exposure.

(b): Within each food group and depending on their reported occurrence values, the samples were grouped at FoodEx level 1 (**bold**), level 2 (normal), level 3 (*italic*), before being linked with the EFSA Comprehensive Food Consumption Database.

(c): Percentage of left-censored data.

(d): The selection of the highest reliable percentiles (at the UB) in each food/food group was based on the number of samples available, 60 samples for the 5th and 95th percentile, 11 samples for 25th and 75th percentile, and six samples for the median. Otherwise, the percentiles may not be statistically robust.

(e): Mean value obtained from the average concentration of 453 samples of 'Drinking water' at FoodEx level 1.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Infants	Grains and grain-based products		3	3			
	Vegetables and vegetable products (including fungi)		2		4		
	Starchy roots and tubers	3	3				
	Legumes, nuts and oilseeds	3	1	2			
	Fruit and fruit products		6				
	Milk and dairy products				4	2	
	Sugar and confectionary	2	3	1			
	Animal and vegetable fats and oils	4	2				
	Fruit and vegetable juices	2	3	1			
	Non-alcoholic beverages (excepting milk based beverages)	2	3		1		
	Alcoholic beverages	6					
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)					3	3
	Herbs, spices and condiments	6					
	Food for infants and small children	1	3	1	1		
	Products for special nutritional use	6					
	Composite food (including frozen products)	4	2				
Toddlers	Grains and grain-based products			7	3		
	Vegetables and vegetable products (including fungi)			9	1		
	Starchy roots and tubers	5	5				
	Legumes, nuts and oilseeds	1	6	3			
	Fruit and fruit products		10				
	Milk and dairy products				9	1	
	Sugar and confectionary	2	8				
	Animal and vegetable fats and oils	7	3				

Table continued overleaf.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate (continued)

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Toddlers	Fruit and vegetable juices		2	3	4	1	
	Non-alcoholic beverages (excepting milk based beverages)	2	2	2	3	1	
	Alcoholic beverages	10					
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)				2	8	
	Herbs, spices and condiments	9	1				
	Food for infants and small children	7	3				
	Products for special nutritional use	10					
	Composite food (including frozen products)	6	3	1			
Other children	Grains and grain-based products			9	9		
	Vegetables and vegetable products (including fungi)		5	11	2		
	Starchy roots and tubers	9	9				
	Legumes, nuts and oilseeds	7	7	4			
	Fruit and fruit products		18				
	Milk and dairy products			2	15		1
	Sugar and confectionary	2	16				
	Animal and vegetable fats and oils	11	7				
	Fruit and vegetable juices	1	1	5	11		
	Non-alcoholic beverages (excepting milk based beverages)		3	4	7	4	
	Alcoholic beverages	18					
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)	1		1	6	10	
	Herbs, spices and condiments	14	4				
	Food for infants and small children	18					
	Products for special nutritional use	18					
	Composite food (including frozen products)	9	6	1	2		

Table continued overleaf.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate (continued)

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Adolescents	Grains and grain-based products			6	11		
	Vegetables and vegetable products (including fungi)		4	10	3		
	Starchy roots and tubers	8	9				
	Legumes, nuts and oilseeds	5	6	6			
	Fruit and fruit products	1	16				
	Milk and dairy products			8	9		
	Sugar and confectionary	1	16				
	Animal and vegetable fats and oils	13	4				
	Fruit and vegetable juices	1	1	10	5		
	Non-alcoholic beverages (excepting milk based beverages)			2	9	6	
	Alcoholic beverages	12	5				
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)	1		1	5	10	
	Herbs, spices and condiments	13	4				
	Food for infants and small children	17					
	Products for special nutritional use	17					
	Composite food (including frozen products)	8	5	3	1		
Adults	Grains and grain-based products		3	13	1		
	Vegetables and vegetable products (including fungi)		3	8	5	1	
	Starchy roots and tubers	11	6				
	Legumes, nuts and oilseeds	6	8	3			
	Fruit and fruit products		17				
	Milk and dairy products		1	12	4		
	Sugar and confectionary	4	12	1			

Table continued overleaf.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate (continued)

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Adults	Animal and vegetable fats and oils	12	5				
	Fruit and vegetable juices	2	10	4	1		
	Non-alcoholic beverages (excepting milk based beverages)			3	4	10	
	Alcoholic beverages		11	5	1		
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)			2	2	13	
	Herbs, spices and condiments	11	5	1			
	Food for infants and small children	17					
	Products for special nutritional use	17					
	Composite food (including frozen products)	8	6	1	1	1	
	Grains and grain-based products		4	7	3		
Elderly	Vegetables and vegetable products (including fungi)			7	6	1	
	Starchy roots and tubers	6	8				
	Legumes, nuts and oilseeds	4	8	2			
	Fruit and fruit products		14				
	Milk and dairy products		1	12	1		
	Sugar and confectionary	3	10	1			
	Animal and vegetable fats and oils	8	6				
	Fruit and vegetable juices	1	11	2			
	Non-alcoholic beverages (excepting milk based beverages)			1	4	9	
	Alcoholic beverages	1	8	5			
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)			1	5	8	
	Herbs, spices and condiments	11	2	1			
	Food for infants and small children	14					
	Products for special nutritional use	14					
	Composite food (including frozen products)	7	4	1	2		

Table continued overleaf.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate (continued)

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Very elderly	Grains and grain-based products		3	6	3		
	Vegetables and vegetable products (including fungi)		1	5	5	1	
	Starchy roots and tubers	5	7				
	Legumes, nuts and oilseeds	3	6	3			
	Fruit and fruit products		12				
	Milk and dairy products		1	8	3		
	Sugar and confectionary	4	7	1			
	Animal and vegetable fats and oils	5	7				
	Fruit and vegetable juices	2	9	1			
	Non-alcoholic beverages (excepting milk based beverages)			1	5	6	
	Alcoholic beverages	2	9	1			
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)			1	6	5	
	Herbs, spices and condiments	9	2		1		
	Food for infants and small children	12					
	Products for special nutritional use	12					
	Composite food (including frozen products)	5	4	1	2		
Vulnerable groups Pregnant women	Grains and grain-based products				1		
	Vegetables and vegetable products (including fungi)			1			
	Starchy roots and tubers		1				
	Legumes, nuts and oilseeds		1				
	Fruit and fruit products		1				
	Milk and dairy products				1		
	Sugar and confectionary		1				
	Animal and vegetable fats and oils		1				

Table continued overleaf.

Appendix E: Average contribution of the FoodEx Level 1 category to the total average chronic dietary exposure to chlorate (continued)

Age class	FoodEx Level 1 category	Number of dietary surveys (% average contribution under the Middle Bound scenario)					
		< 1 %	1–5 %	5–10 %	10–25 %	25–50 %	50–75 %
Vulnerable groups Pregnant women	Fruit and vegetable juices		1				
	Non-alcoholic beverages (excepting milk based beverages)				1		
	Alcoholic beverages	1					
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)				1		
	Herbs, spices and condiments		1				
	Food for infants and small children	1					
	Products for special nutritional use	1					
	Composite food (including frozen products)	1					
Vulnerable groups Lactating women	Grains and grain-based products				1		
	Vegetables and vegetable products (including fungi)				1		
	Starchy roots and tubers	1					
	Legumes, nuts and oilseeds		1				
	Fruit and fruit products		1				
	Milk and dairy products				1		
	Sugar and confectionary		1				
	Animal and vegetable fats and oils	1					
	Fruit and vegetable juices				1		
	Non-alcoholic beverages (excepting milk based beverages)				1		
	Alcoholic beverages		1				
	Drinking water (water without any additives except carbon dioxide; includes water ice for consumption)	1					
	Herbs, spices and condiments	1					
	Food for infants and small children	1					
	Products for special nutritional use	1					
	Composite food (including frozen products)			1			

Appendix F. Exposure estimates for chlorate obtained in different dietary surveys

Table F: Mean and 95th percentile (P95) chronic dietary exposure to chlorate (µg/kg b.w. per day) for total population in lower-bound (LB) and upper-bound (UB) scenario

Dietary surveys	Range of dietary exposure (LB–UB) (µg/kg b.w. per day)													
	Infants		Toddlers		Other children		Adolescents		Adults		Elderly		Very elderly	
	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95
ASNS - Adults									1.2–1.5	2.3–2.8	0.88–1.1	1.5–1.7	1.1–1.4	— ^(a)
ASNS – Children					2.1–2.5	3.9–4.3	1.2–1.4	2.3–2.6						
Regional Flanders			2.8–3.3	— ^(a)	2.3–2.7	3.9–4.5								
Diet National 2004							1.2–1.4	2.0–2.3	1.2–1.4	2.0–2.3	0.89–1.1	1.5–1.9	0.82–1.0	1.4–1.8
NUTRICHILD	2.4–3.1	5.0–6.6	2.6–3.2	4.1–5.2	2.3–2.9	4.1–5.0								
Childhealth							0.53–0.62	1.1–1.2						
SISP04					1.9–2.3	3.4–4.2	1.4–1.7	2.6–3.0	1.1–1.4	1.8–2.3				
DANSDA 2005-08					1.9–2.4	3.2–4.0	1.3–1.6	2.2–2.6	1.3–1.6	2.1–2.7	1.1–1.4	1.9–2.5	1.2–1.6	— ^(a)
IAT 2006 07	2.1–2.8	3.6–4.7	2.1–2.8	3.2–4.2										
DIPP 2001 2009	1.7–2.1	3.4–4.2	2.7–3.5	4.1–5.3	2.1–2.6	3.2–3.8								
NWSSP07 08							1.1–1.4	1.7–2.1						
FINDIET2012									1.1–1.4	1.9–2.3	0.86–1.1	1.4–1.8		
INCA2					1.9–2.4	3.2–4.0	1.0–1.3	1.8–2.2	1.0–1.3	1.8–2.2	0.96–1.2	1.6–2.0	0.92–1.2	1.7–2.2
VELS	1.8–2.4	3.3–4.3	2.7–3.2	4.8–5.4	2.3–2.7	3.5–4.0								
EsKiMo					2.0–2.4	3.3–3.8	1.6–1.9	2.6–3.0						
National Nutrition Survey II							1.2–1.5	2.2–2.6	1.3–1.6	2.1–2.6	1.1–1.4	1.7–2.2	1.0–1.3	1.6–2.1
Regional Crete					1.9–2.1	3.7–3.9								
DIET LACTATION GR									0.55–0.65	0.96–1.1				
National Repr Surv									0.66–0.81	1.2–1.4	0.56–0.69	0.97–1.2	0.57–0.69	0.98–1.2
NANS 2012									0.93–1.2	1.7–2.2	0.85–1.1	1.6–2.1	0.75–0.96	1.2–1.6
INRAN SCAI 2005 06	2.9–4.1	— ^(a)	2.6–3.3	— ^(a)	1.9–2.4	3.3–4.2	1.2–1.4	2.0–2.4	0.87–1.1	1.5–1.8	0.77–0.97	1.2–1.6	0.8–1.0	1.2–1.6
EFSA TEST					1.3–1.5	2.5–2.7	0.9–1.1	1.8–2.0	0.69–0.84	1.3–1.5				
FC PREGNANTWOMEN 2011									0.83–1.1	1.4–1.8				
VCP kids			2.3–2.9	4.0–5.0	2.0–2.5	3.9–4.5								
VCPBasis AVL2007 2010					1.8–2.1	3.0–3.3	1.3–1.5	2.2–2.5	1.2–1.4	2.0–2.4	0.95–1.2	1.6–2.0		
VCP-Elderly											0.96–1.2	1.5–1.9	0.91–1.2	1.4–1.9
Dieta Pilot Adults									0.73–0.90	1.4–1.8	0.67–0.83	1.3–1.8	0.71–0.87	— ^(a)
enKid			2.2–2.9	— ^(a)	1.6–2.1	3.2–3.9	0.94–1.2	1.7–2.1						
AESAN									0.78–0.97	1.5–1.9				
NUT INK05					1.7–2.2	2.7–3.4	1.1–1.4	1.8–2.2						
AESAN FIAB							0.81–1.0	1.4–1.8	0.79–0.99	1.6–1.9				
NFA					1.6–1.9	2.8–3.2	1.0–1.2	1.9–2.2						
Riksmaten 2010									0.95–1.2	1.7–2.0	0.8–1.0	1.4–1.8	0.8–1.1	1.4–1.8

Dietary surveys	Range of dietary exposure (LB–UB) (µg/kg b.w. per day)													
	Infants		Toddlers		Other children		Adolescents		Adults		Elderly		Very elderly	
	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95	Mean	P95
NDNS-RollingProgrammeYears1-3			2.6–3.2	4.3–5.2	2.0–2.4	3.2–3.8	1.1–1.3	2.0–2.4	1.0–1.3	1.8–2.2	0.90–1.1	1.5–1.8	0.9–1.1	1.4–1.8
DNSIYC 2011	1.6–2.0	3.4–4.1	2.3–2.9	4.0–4.8										

b.w.: body weight; LB: lower bound; P95: 95th percentile; UB: upper bound.

(a): 95th percentile calculated over a number of observations lower than 60 require cautious interpretation as the results may not be statistically robust (EFSA, 2011b).

(b): Details on the dietary surveys and the number of subjects are given in Appendix C.

Appendix G. Range of acute exposure estimates for individual food commodities assuming an occurrence value of 0.7 mg/kg

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown.

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Alcoholic beverages	Beer and beer-like beverage	Beer and beer-like beverage	0.75–15.62	7.78–37.38
		Wine, red	0.01–3.93	0.01–8.28
	Wine	Wine	0.09–4.46	1.98–8.24
		Wine, white	0.00–10.61	0.01–8.18
Drinking water	Drinking water	Drinking water	1.15–47.66	3.33–111.31
Fruit and fruit products	Pome fruits	Pear (<i>Pyrus communis</i>)	0.16–7.33	2.08–19.77
		Apple (<i>Malus domestica</i>)	0.90–9.52	1.62–16.20
	Berries and small fruits	Raspberries (<i>Rubus idaeus</i>)	0.01–8.54	0.15–4.58
		Blueberries (<i>Vaccinium corymbosum</i>)	0.06–3.97	1.03–4.02
		Strawberries (<i>Fragaria × ananassa</i>)	0.05–7.09	0.49–10.50
		Table grapes (<i>Vitis euveitis</i>)	0.35–6.29	1.28–10.00
		Bilberry or whortleberry (<i>Vaccinium</i> spp.)	0.25–3.20	0.68–6.86
		Blackberries (<i>Rubus fruticosus</i>)	0.04–4.79	–
		Cranberries (<i>Vaccinium macrocarpon</i>)	0.03–3.25	–
		Cranberry (<i>Vaccinium</i> spp.)	0.14–0.59	–
		Physalis (<i>Physalis peruviana</i>)	0.38–0.65	–
		Currants (red, black and white)	0.00–7.37	0.00–3.32
		Gooseberries (<i>Ribes uva-crispa</i>)	0.08–4.14	1.62–1.62
		Berries and small fruits	0.16–4.94	1.05–1.36
		Rose hips (<i>Rosa canina</i>)	0.02–1.48	3.21–3.70
		Wine grapes (<i>Vitis euveitis</i>)	0.90–2.34	3.27–3.65
		Lingonberry (<i>Vaccinium vitis-idaea</i>)	0.08–0.96	1.67–2.85
	Citrus fruits	Mandarins (<i>Citrus reticulata</i>)	0.21–11.29	1.08–11.57
		Oranges (<i>Citrus sinensis</i>)	0.19–10.63	1.01–9.80
		Citrus fruits	0.77–7.39	3.74–5.83
		Grapefruit (<i>Citrus paradisi</i>)	0.09–10.43	0.19–2.74
		Lemons (<i>Citrus limon</i>)	0.00–1.66	0.00–1.75
		Limes (<i>Citrus aurantifolia</i>)	0.02–1.31	–
		Pomelo (<i>Citrus grandis</i>)	0.75–10.61	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Fruit and fruit products	Stone fruits	Plums (<i>Prunus domestica</i>)	0.18–5.30	0.98–7.00
		Sweet cherry (<i>Prunus avium</i>)	0.02–5.25	1.74–10.08
		Peaches (<i>Prunus persica</i>)	0.15–12.36	1.67–9.38
		Apricots (<i>Prunus armeniaca</i>)	0.05–4.70	0.88–4.67
		Sour cherry (<i>Prunus cerasus</i>)	0.34–6.02	1.43–3.14
		Greengage (<i>Prunus domestica</i> var <i>italica</i>)	0.24–10.77	3.36–3.36
		Mirabelle (<i>Prunus domestica</i> var <i>syriaca</i>)	0.30–7.86	–
		Dried prunes (<i>Prunus domestica</i>)	0.01–1.26	0.20–3.98
	Dried fruits	Dried vine fruits (currants, raisins and sultanas)	0.02–2.10	0.09–3.00
		Dried bananas (<i>Musa</i> \times <i>paradisica</i>)	0.05–3.45	0.28–0.38
		Dried mangoes (<i>Mangifera indica</i>)	0.16–1.28	–
		Dried pears (<i>Pyrus communis</i>)	0.03–0.37	–
		Medlar (<i>Mespilus germanica</i>)	0.50–3.13	–
	Pome fruits	Nashi pear (<i>Pyrus pyrifolia</i>)	2.65–2.65	–
		Quince (<i>Cydonia oblonga</i>)	0.02–1.42	–
	Miscellaneous fruits	Bananas (<i>Musa</i> \times <i>paradisica</i>)	0.82–7.33	1.36–13.53
		Avocados (<i>Persea americana</i>)	0.11–5.56	1.34–9.02
		Kiwi (<i>Actinidia deliciosa</i> syn. <i>A. chinensis</i>)	0.31–5.79	1.18–9.01
		Pineapples (<i>Ananas comosus</i>)	0.09–6.15	1.63–8.95
		Mangoes (<i>Mangifera indica</i>)	0.51–5.20	2.11–8.10
		Persimmon (Sharon fruit) (<i>Diospyros kaki</i>)	0.27–6.28	0.70–3.25
		Papaya (<i>Carica papaya</i>)	0.01–6.28	0.24–0.24
		American persimmon (<i>Virginia kaki</i>) -	0.35–0.35	–
		Carambola (<i>Averrhoa carambola</i>)	0.55–2.92	–
		Cherimoya (<i>Annona cherimola</i>)	1.13–1.56	–
		Dates (<i>Phoenix dactylifera</i>)	0.09–1.42	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Fruit and fruit products	Miscellaneous fruits	Figs (<i>Ficus carica</i>)	0.08–3.89	–
		Longan fruit (<i>Dimocarpus longan</i>)	2.13–2.13	–
		Lychee (Litchi) (<i>Litchi chinensis</i>)	0.14–5.08	–
		Miscellaneous fruits	0.56–3.60	–
		Passion fruit (<i>Passiflora edulis</i>)	0.12–1.20	–
		Pomegranate (<i>Punica granatum</i>)	0.14–5.17	–
		Prickly pear (cactus fruit)	0.71–5.00	–
	Jam, marmalade and other fruit spreads	Jam	0.17–2.32	0.43–6.43
	Other fruit products (excluding beverages)	Fruit, purée	0.63–8.39	3.25–12.86
		Fruit compote	0.09–7.27	2.40–18.85
		Fruit, canned	0.23–4.91	1.31–14.15
		Other fruit products (excluding beverages)	0.00–7.88	0.04–0.06
Fruit and vegetable juices	Fruit juice	Juice, Apple	0.80–14.12	3.14–28.50
		Juice, Orange	0.80–13.92	2.36–25.67
		Juice, Grape	0.08–30.56	5.25–18.04
		Juice, Passion fruit	0.03–3.30	0.72–0.72
		Juice, Pear	0.07–7.27	–
		Juice, Prune	0.26–7.52	–
	Mixed fruit juice	Juice, Strawberry-Cherry	1.72–1.72	–
		Mixed fruit juice	1.41–6.10	–
	Concentrated fruit juice	Concentrated fruit juice	0.00–6.16	0.52–24.82
	Fruit nectar	Nectar, Apple	1.70–11.64	20.00–20.00
		Fruit nectar	0.45–12.89	7.09–18.10
		Nectar, Banana	1.07–10.45	–
		Nectar, Mango	0.71–5.15	–
		Nectar, Pear	1.90–13.37	–
		Nectar, Pineapple	2.31–6.78	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Grains and grain-based products	Grains for human consumption	Rice	0.16–13.13	0.57–12.18
		Corn grain	0.08–10.37	0.25–6.03
		Wheat grain	0.00–3.19	0.01–5.83
		Millet grain	0.12–3.17	1.31–1.31
		Barley grain	0.05–2.93	0.39–0.91
		Buckwheat grain	0.02–2.69	–
		Oats, grain	0.01–1.93	–
		Spelt grain	0.36–1.20	–
		Corn milling products	0.01–2.68	0.08–3.46
	Grain milling products	Rye milling products	0.02–2.50	0.06–1.75
		Other milling products	0.03–4.55	0.51–1.50
		Oat milling products	0.06–1.94	0.72–0.72
		Spelt milling products	0.07–0.35	–
		Wheat milling products	0.05–2.94	0.10–6.09
	Pasta (Raw)	Pasta (Raw)	0.05–4.67	0.65–11.41
		Pasta, wheat flour, without eggs	0.32–5.26	0.75–9.00
	Fine bakery wares	Pastries and cakes	0.53–5.14	1.35–9.10
	Breakfast cereals	Cereal flakes	0.10–2.40	0.39–4.94
		Mixed breakfast cereals	0.13–2.54	0.65–4.50
Herbs, spices and condiments	Spices	Pepper, black and white (<i>Piper nigrum</i>)	0.00–2.62	0.00–2.60
		Ginger (<i>Zingiber officinale</i>)	0.00–0.52	0.11–0.23
		Cloves (<i>Syzygium aromaticum</i>)	0.00–0.07	–
		Spices	0.00–0.27	0.00–0.09
		Paprika powder	0.00–0.39	0.01–0.07
		Turmeric (Curcuma)	0.00–0.03	0.02–0.07
		Chervil, herb (<i>Anthriscus cerefolium</i>)	0.00–0.51	–
	Herbs	Chives, herb (<i>Allium schoenoprasum</i>)	0.00–0.52	0.02–0.92
		Herbs	0.00–0.32	0.00–0.50
		Parsley, herb (<i>Petroselinum crispum</i>)	0.00–0.23	0.01–0.38
		Dill, herb (<i>Anethum graveolens</i>)	0.00–0.20	0.02–0.18

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Herbs, spices and condiments	Herbs	Basil, herb (<i>Ocimum basilicum</i>)	0.00–0.11	0.03–0.15
		Thyme, herb (<i>Thymus</i> spp.)	0.00–0.06	0.01–0.04
		Sage, herb (<i>Salvia officinalis</i>)	0.00–0.22	0.01–0.01
		Rosemary, herb (<i>Rosmarinus officinalis</i>)	0.00–0.05	–
		Tarragon, herb (<i>Artemisia dracunculus</i>)	0.00–0.09	–
	Seasoning or extracts	Salt	0.00–0.16	0.01–0.35
	Herb and spice mixtures	Mixed herbs	0.03–1.28	0.05–0.14
Legumes, nuts and oilseeds	Flavourings or essences	Vanilla pods	0.00–0.03	0.04–0.06
	Legumes, beans, dried	Beans (<i>Phaseolus vulgaris</i>)	0.21–4.84	0.56–13.13
		Lentils (<i>Lens culinaris</i> syn. <i>L. esculenta</i>)	0.08–8.71	0.77–8.24
		Broad bean (<i>Vicia faba</i>)	0.07–3.54	4.73–4.73
		Mung bean (<i>Phaseolus aureus</i>)	0.20–1.76	0.77–4.52
		Black eye bean (<i>Vigna unguiculata</i>)	2.59–5.07	4.29–4.29
		Chick pea (<i>Cicer arietinum</i>)	0.05–4.37	1.27–4.16
		Peas (<i>Pisum sativum</i>)	0.04–4.47	0.15–3.30
		Peanut (<i>Arachis hypogea</i>)	0.05–4.32	0.50–2.06
		Soya beans (<i>Glycine max</i>)	0.05–3.78	0.61–1.36
		Legumes, beans, dried	0.35–6.98	–
	Legumes, beans, green, without pods	Peas, green, without pods (<i>Pisum sativum</i>)	0.08–5.95	0.18–9.44
		Beans, green, without pods (<i>Phaseolus vulgaris</i>)	0.04–4.31	2.06–4.60
		Legumes, beans, green, without pods	0.31–3.97	–
		Lentils, green (<i>Lens culinaris</i> syn. <i>L. esculenta</i>)	0.09–1.95	–
	Tree nuts	Chestnuts (<i>Castanea sativa</i>)	0.05–2.31	2.01–2.01
		Walnuts (<i>Juglans regia</i>)	0.02–1.45	0.34–1.71
		Hazelnuts (<i>Corylus avellana</i>)	0.00–2.50	0.26–1.49
		Cashew nuts (<i>Anacardium occidentale</i>)	0.03–2.06	0.52–1.25
		Pistachios (<i>Pistachia vera</i>)	0.02–5.60	0.67–0.67
		Coconuts (<i>Cocos nucifera</i>)	0.00–1.62	0.10–0.45
		Almond, bitter (<i>Prunus amygdalus amara</i>)	0.01–0.56	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure (µg/kg b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Milk and dairy products	Liquid milk	Cow milk	0.91–25.42	3.07–55.95
		Liquid milk	0.15–17.35	4.59–43.08
	Milk based beverages	Flavoured milk	0.17–11.90	4.67–30.27
	Milk derivatives	Lactose	0.00–0.44	0.01–1.33
	Fermented milk products	Fermented milk products	0.83–14.20	1.62–32.40
	Cheese	Cheese	0.08–4.53	0.24–7.78
	Cream and cream products	Cream	0.07–1.82	0.32–3.13
		Cream and cream products	0.10–0.78	0.00–0.00
	Concentrated milk	Dried milk	0.02–10.05	0.08–1.84
	Whey and whey products (excluding whey cheese)	Whey dried	0.00–0.72	0.00–1.78
Whey and whey products (exc. whey cheese)		0.28–6.37	1.27–1.27	
Non-alcoholic beverages (excepting milk-based beverages)	Tea (Infusion)	Tea (Infusion)	0.80–13.84	3.65–26.73
	Coffee (Beverage)	Coffee (Beverage)	0.06–14.48	2.34–14.08
	Soft drinks	Soft drinks	0.21–12.28	2.87–26.25
		Cola beverages, caffeinic	0.88–9.66	4.70–19.94
Starchy roots and tubers	Potatoes and potatoes products	Main-crop potatoes	0.09–7.29	1.48–14.51
		New potatoes	0.36–7.78	1.19–7.00
		Potatoes and potatoes products	0.44–5.89	1.52–12.21
		Potato boiled	1.21–7.76	2.19–11.50
	Other starchy roots and tubers	Sweet potatoes (<i>Ipomoea batatas</i>)	0.28–5.65	4.92–7.32
		Jerusalem artichokes tubers	0.44–4.01	–
		Other starchy roots and tubers	1.34–1.34	–
Sugar and confectionary	Sugars	White sugar	0.07–1.70	0.23–4.39
	Chocolate (Cocoa) products	Chocolate (Cocoa) products	0.07–1.28	0.40–3.16
		Chocolate bar	0.22–3.14	0.93–2.35
		Bitter chocolate	0.06–1.39	0.36–2.33
		White chocolate	0.05–1.94	1.90–1.93
	Sugars	Sugars	0.10–0.59	0.30–2.19
	Honey	Honey	0.02–0.94	0.06–1.31

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Vegetables and vegetable products (including fungi)	Brassica vegetables	Head cabbage	0.44–4.99	1.04–9.31
		Kohlrabi	0.13–4.47	0.78–7.78
		Cauliflower (<i>Brassica oleracea</i> var. <i>botrytis</i>)	0.06–8.48	0.58–6.60
		Broccoli (<i>Brassica oleracea</i> var. <i>italica</i>)	0.36–7.29	1.07–6.21
		Brussels sprouts	0.12–5.37	0.25–3.21
		Kale (<i>Brassica oleracea</i> convar. <i>Acephalea</i>)	0.04–3.24	0.04–3.11
		Brassica vegetables	0.41–1.48	1.72–1.77
		Chinese cabbage (<i>Brassica pekinensis</i>)	0.09–4.18	0.80–1.56
	Bulb vegetables	Onions, bulb (<i>Allium cepa</i>)	0.10–1.33	0.33–3.50
		Spring onions, bulb (<i>Allium cepa</i>)	0.03–2.43	0.07–1.78
		Garlic, bulb (<i>Allium sativum</i>)	0.00–0.58	0.02–0.90
		Shallots, bulb	0.04–0.40	0.17–0.23
	Cocoa beans and cocoa products	Cocoa powder	0.02–1.08	0.03–1.73
		Cocoa beans and cocoa products	0.63–0.74	–
	Fruiting vegetables	Melons (<i>Cucumis melo</i>)	0.20–11.74	2.85–13.48
		Watermelons (<i>Citrullus lanatus</i>)	0.62–11.86	1.58–12.00
		Cucumbers (<i>Cucumis sativus</i>)	0.17–3.13	0.42–9.21
		Tomatoes (<i>Lycopersicon esculentum</i>)	0.26–3.77	0.88–8.97
		Courgettes (Zucchini)	0.14–4.07	0.92–6.92
		Sweet corn (<i>Zea mays</i> var. <i>saccharata</i>)	0.10–6.13	0.27–6.79
		Gherkins (<i>Cucumis sativus</i>)	0.06–3.80	0.27–5.59
		Peppers, paprika (<i>Capsicum annuum</i> , var. <i>grossum</i> and var. <i>longum</i>)	0.09–1.35	0.30–4.22
		Pumpkins (<i>Cucurbita maxima</i>)	0.00–8.26	0.03–3.47
		Aubergines (egg plants) (<i>Solanum melongena</i>)	0.09–5.64	0.46–3.39
		Chilli pepper (<i>Capsicum frutescens</i>)	0.01–0.45	0.11–0.91
		Okra, lady's fingers (<i>Hibiscus esculentus</i>)	0.10–4.01	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Vegetables and vegetable products (including fungi)	Fungi, cultivated	Cultivated mushroom (syn. Button mushroom)	0.16–3.73	0.52–3.50
		Fungi, cultivated	0.05–4.00	0.99–2.80
		Oyster mushroom (<i>Pleurotus ostreatus</i>)	0.20–1.09	–
		Shiitake mushroom (<i>Lentinus edodes</i>)	0.20–1.14	–
	Fungi, wild, edible	Boletus (<i>Boletus</i> (and other) spp.)	0.39–4.94	2.50–2.50
		Fungi, wild, edible	0.04–1.75	1.07–2.07
		Cantharelle (<i>Cantharellus cibarius</i>)	0.05–1.41	–
	Leaf vegetables	Spinach (fresh) (<i>Spinacia oleracea</i>)	0.10–7.40	0.73–6.75
		Leaf vegetables	0.01–3.32	0.48–6.73
		Spinach (<i>Spinacia oleracea</i>), preserved, deep-frozen or frozen	0.22–3.94	1.53–6.67
		Endive, scarole (broad-leaf endive)	0.01–4.40	0.70–5.38
		Beet leaves (<i>Beta vulgaris</i>)	0.09–3.22	1.57–4.02
		Witloof (<i>Cichorium intybus</i> var. <i>foliosum</i>)	0.39–2.54	1.50–3.72
		Lettuce, excluding Iceberg-type lettuce	0.14–11.31	0.35–3.57
		Iceberg-type lettuce	0.00–2.42	0.24–2.61
		Lamb's lettuce (<i>Valerianella locusta</i>)	0.08–1.14	0.71–1.00
		Rocket, Rucola (<i>Eruca sativa</i> , <i>Diplotaxis spec.</i>)	0.04–1.02	0.36–0.77
		Water cress (<i>Nasturtium officinale</i>)	0.01–0.79	0.38–0.38
		Cress (<i>Lepidium sativum</i>)	0.02–1.26	–
		Dandelion leaf (<i>Taraxacum officinalis</i>)	0.00–3.75	–
		Land cress (<i>Barbarea verna</i>)	0.05–0.13	–
		Sorrel (<i>Rumex</i> spp.)	0.00–9.33	–
		Vine leaves (grape leaves) (<i>Vitis euvitis</i>)	0.01–0.53	–

Table continued overleaf.

Table G: Range of estimates of acute exposure to chlorate food by food across dietary surveys ($\mu\text{g/kg}$ b.w. per day, only consumers) assuming an occurrence value of 0.7 mg/kg in all food commodities. Mean and 95th percentile acute exposures are shown. (continued)

FoodEx Level 1	FoodEx Level 2	FoodEx Level 3	Range of acute exposure ($\mu\text{g/kg}$ b.w. per day) ^(a)	
			Mean exposure	P95 dietary exposure ^(b)
Vegetables and vegetable products (including fungi)	Legume vegetables	Beans, with pods (<i>Phaseolus vulgaris</i>)	0.03–7.10	0.31–5.65
		Peas, with pods (<i>Pisum sativum</i>)	0.28–2.21	0.67–2.41
		Legume vegetables	0.03–1.23	0.09–0.64
	Root vegetables	Carrots (<i>Daucus carota</i>)	0.10–4.69	0.27–10.35
		Parsnips (<i>Pastinaca sativa</i>)	0.03–8.43	0.35–4.13
		Beetroot (<i>Beta vulgaris</i> subsp. <i>vulgaris</i>)	0.06–3.28	0.43–3.89
		Salsify (<i>Tragopogon porrifolius</i>)	0.22–2.25	2.23–3.72
		Turnips (<i>Brassica rapa</i>)	0.07–4.38	0.20–3.46
		Radishes (<i>Raphanus sativus</i> var. <i>sativus</i>)	0.01–2.10	0.43–2.06
		Celeriac (<i>Apium graveolens</i> var. <i>rapaceum</i>)	0.01–9.38	0.01–1.84
		Parsley root (<i>Petroselinum crispum</i>)	0.02–1.12	0.03–1.20
	Stem vegetables (Fresh)	Leek (<i>Allium porrum</i>)	0.03–2.88	0.16–4.36
		Asparagus (<i>Asparagus officinalis</i>)	0.08–3.40	0.40–4.30
		Celery (<i>Apium graveolens</i> var. <i>dulce</i>)	0.02–3.85	0.15–3.64
		Fennel (<i>Foeniculum vulgare</i>)	0.02–4.76	0.07–3.24
		Globe artichokes (<i>Cynara scolymus</i>)	0.08–2.30	1.67–3.09
		Rhubarb (<i>Rheum</i> \times <i>hybridum</i>)	0.08–6.19	0.13–0.87
		Chicory roots (<i>Cichorium intybus</i>)	0.88–2.96	2.80–3.28
	Sugar plants	Peppermint (<i>Mentha</i> \times <i>piperita</i>)	0.00–0.09	–
	Tea and herbs for infusions (Solid)	Sauerkraut	0.45–2.28	1.17–5.83
		Tomato purée	0.02–1.19	0.08–4.27
		Sun-dried tomatoes	0.07–0.87	–

b.w.: body weight; P95: 95th percentile.

(a): Range of acute exposure food by food across dietary surveys and age classes.

(b): The 95th percentile estimates obtained on dietary surveys/age classes with less than 60 observations may not be statistically robust (EFSA, 2011b). Those estimates were not included in this table.

(c): In specific dietary surveys the consumption of drinking water is missing ('Regional Crete' and 'Childhealth') or underreported ('National Dietary Survey' and 'National Repr Surv').

GLOSSARY

Acidophilic cells of the pituitary gland	Summary term for the two different types of cells of the anterior pituitary gland, somatotrophes (which generate somatropin, i.e. growth hormone) and mammotrophs (which generate prolactin).
Hofmeister or lyotropic series	Classification of ions in their ability to decrease or increase the solubility of nonpolar molecules.
Anuria	(Complete) absence of urinary output.
Ataxia	Lack of coordination of the voluntary muscles, resulting in irregular movements of the body.
Blood osmotic fragility	Degree/proportion of haemolysis of red blood cells under osmotic stress (placement in hypotonic solution).
Chaotropic	Ability to destabilize hydrogen bonding and hydrophobic interactions.
Chromophobic cells of the pituitary gland	One of three cell types (basophiles and acidophiles being the others) of the pituitary gland.
Codocytes (leptocytes)	Red blood cells, characterized by a disproportional increase in the surface membrane area to volume ratio and decreased osmotic fragility.
Echinocytes	Red blood cells which have become crenated/have an abnormal cell membrane.
Extramedullary haematopoiesis	Refers to haematopoiesis occurring outside of the medulla of the bone.
Haematuria	Presence of blood or red blood cells in the urine.
Haemoglobinaemia	Presence of excessive free haemoglobin in the blood plasma.
Haemoglobinuria	The presence of haemoglobin in the urine.
Haemolysis	Disintegration of red blood cells, with the release of haemoglobin, occurring in the living organism or in a blood sample.
Hyperthyroidism	Overproduction of the thyroid hormone by excessive activity of the thyroid gland; characterized by increased basal metabolism.
Hypothalamic-pituitary-thyroid (HPT) feedback pathway	Part of the endocrine system responsible for the regulation of metabolism; it depends upon the hypothalamus, pituitary gland and thyroid gland.
Hypothyroidism	Insufficient production of thyroid hormones by insufficient functioning of the thyroid gland.
Intravascular coagulation	Formation of blood clots within one or more blood vessels.

Methaemoglobin	Is a form of the oxygen-carrying metalloprotein haemoglobin, in which the iron in the haem group is in the Fe^{3+} (ferric) state and not the Fe^{2+} (ferrous) state of normal haemoglobin.
Multinodular toxic goitre	A thyroid gland that contains autonomously functioning thyroid nodules, with resulting hyperthyroidism.
Reticulocyte	Immature red blood cells
Segmented neutrophils	Subdivision of neutrophil granulocytes/neutrophils; 2nd subdivision banded neutrophils.

ABBREVIATIONS

2-AA	2-aminoanthracene
4-NQO	4-nitroquinoline-N-oxide
ADI	Acceptable Daily Intake
AFC Panel	EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
ALT	Alanine aminotransferase
AOEL	Acceptable Operator Exposure Level
ARfD	Acute Reference Dose
ASC	Acidified Sodium Chlorite
AST	Aspartate aminotransferase
B(a)P	Benzo(a)pyrene
BE	Belgium
BfR	Bundesamt für Risikobewertung (Germany)
BMDL ₁₀	Benchmark dose lower confidence limit
BMD	Benchmark dose
b.w.	Body weight
CHO	Chinese Hamster Ovary
CI	Confidence interval
ClO ₃ ⁻	Chlorate
ClO ₂ ⁻	Chlorite
Cl ⁻	Chloride
CONTAM Panel	EFSA Panel on Contaminants in the Food Chain
CP	Chlorambucil
CVUA	Chemisches und Veterinaeruntersuchungsamt Stuttgart
CZ	The Czech Republic
DAR	Draft Assessment Report (EU)
DATA Unit	EFSA Evidence Management Unit
DBPs	Disinfection by-products
DE	Germany
DIPP	Dietary survey
DMBA	7, 12-dimethylbenzanthracene
DNEL	Derived no effect level
EC	European Commission
EC ₅₀	Half maximal effective concentration
ECD	Electrical conductivity detection
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals

ECHA	European Chemicals Agency
EMS	Ethylmethanesulfonate
ES	Spain
FAO	Food and Agriculture Organization of the United Nations
FoodEx	EFSA Food classification and description system for exposure assessment
Freshfel	European Fresh Produce Association
GSH	Glutathione
GSSG	Oxidised glutathione
HeLa	Human Epitheloid Cervix Carcinoma Cell Line
HepG2	Human Hepatocyte Carcinoma Cell Line
HPLC	High Performance Liquid Chromatography
HPT	Hypothalamic-Pituitary-Thyroid (feedback pathway)
I	Iodine
IC ₅₀	Half maximal inhibitory concentration
JECFA	Joint FAO/WHO Expert Committee on Food Additives
KClO ₃	Potassium chlorate
LB	Lower Bound
LC ₅₀	Medium lethal concentration
LC	Left-censored (data)
LC-MS	Liquid Chromatography-Mass Spectrometry
LC-MS/MS	Liquid Chromatography-tandem Mass Spectrometry
LD ₅₀	Medium lethal dose
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of Detection
LOQ	Limit of Quantification
MMC	Mitomycin C
MRL	Maximum Residue Limit
MS	Mass Spectrometry
MS/MS	Tandem Mass Spectrometry
n.a.	not applicable
NaCl	Sodium chloride
NaClO ₃	Sodium chlorate
n.d.	not derived
NADPH	Nicotinamide Adenine Dinucleotid Phosphate
NCE	Normochromatic erythrocytes
NIS	Sodium-Iodine Symporter
NOAEL	No Observed Adverse Effect Level

NOEL	No Observed Effect Level
NRC	National Research Council of the National Academics (U.S.)
n.t.	not tested
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
O ₂	Oxygen
OR	Odds ratio
PCE	Polychromatic erythrocytes
pp	<i>Post partum</i>
PRIMo	Pesticide Residue Intake Model
PROFEL	European Association of Fruit and Vegetable Processors
QuPpe	Quick Polar Pesticide Method
RASFF	Rapid Alert System for Food and Feed
RBC	Red blood cell
RED	Reregistration Eligibility Decision
RfD	Chronic Reference Dose
RP	Reference Point
S9	Supernatant fraction obtained from an organ (usually liver) homogenate by centrifuging at 9 000 g for 20 minutes in a suitable medium; this fraction contains cytosol and microsomes
SCOFAH	Standing Committee on the Food Chain and Animal Health (UK)
T3	Triiodothyronine
T4	Thyroxine
TBG	Thyroxine-Binding Globulin
TDI	Tolerable Daily Intake
TEM	Triethylenemelamine
TRR	Total Radioactive Residues
TSH	Thyroid Stimulating Hormone
UB	Upper Bound
UDS	Unscheduled DNA Synthesis
USA	United States of America
US EPA	United States Environmental Protection Agency
WHO	World Health Organization
WHO/IPCS	World Health Organization/International Program on Chemical Safety