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To the Minister for Medical Care and Sport and the Inspector General of the Netherlands Food and Consumer Product Safety Authority (NVWA)

Advisory Report of the Director of the Office for Risk Assessment and Research concerning the

Health risks of exceeding the maximum residue level of chlorate in infant formula and baby food

Background

In 2018, the Netherlands Food and Consumer Product Safety Authority (Nederlandse Voedsel- en Warenautoriteit, NVWA) found that the maximum residue level (MRL) of 0.01 mg chlorate/kg was exceeded in infant formula and baby food. This MRL is a generic value, set out in Regulation (EC) No 396/2005[1] of the European Parliament and of the Council on banned pesticides. Regulation (EU) No 2016/1272 of the European Parliament and of the Council similarly establishes this standard for residues of pesticides in infant formula and toddler nutrition. An Amending Regulation[3]was recently adopted establishing (higher) MRLs for foodstuffs other than infant formula and toddler nutrition.

The Association of Dutch Infant and Dietetic Food Industries (Vereniging van Nederlandse Fabrikanten van Kinder-en Dieetvoedingsmiddelen, VNFKD) informed the Enforcement Directorate that it considers the MRL established for chlorate residues to be unrealistic and infeasible and that higher residue concentrations do not lead to health risks. According to the VNFKD, the MRL is exceeded in 65 to 70% of products – despite efforts of the industry. The VNFKD has therefore requested that the NVWA suspend enforcement of this standard.

The Enforcement Directorate of the NVWA has requested that the Office for Risk Assessment & Research (BuRO) provide an opinion regarding the following research questions.

[1]Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.
[2]Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding.
[3] Commission Regulation (EU) 2020/749 of 4 June 2020 amending Annex III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for chlorate in or on certain products.

1. What is the impact of higher concentrations of chlorate on food safety for 1) toddlers aged 1-3 years old and b) infants aged 0-12 months in foodstuffs specifically intended for that target group?

2. At what concentration of chlorate in a) baby foodstuffs and b) infant formula can no adverse effects be expected on the health of this target group?

3. How do other (European) countries deal with this problem?

Approach
BuRO conducted a literature review of the toxicology and health-based guidance value of chlorate and identified existing risk assessments (see Annex I for the search strategy used). In addition, BuRO looked for information on the potential introduction routes of chlorate in the food production process and BuRO consulted with the Ministry of Health, Welfare and Sport (VWS) on the progress and discussions surrounding the Amending Regulation[4] concerning chlorate residues in foodstuffs. Furthermore, NVWA monitoring data in relevant foodstuffs was used to calculate chlorate intake levels based on the dietary patterns of (young) children. Given that this issue is not restricted to the Netherlands, BuRO also made enquiries into the priority, knowledge position and approach to this problem in other European countries through EFSA Focal Points[5]. BuRO obtained additional information on the standards and monitoring activities taking place in countries outside Europe through the Front Office for Food and Product Safety (Front Office Voedsel- en Productveiligheid) at the National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM). Finally, RIVM was asked to use the consumption data of the Dutch National Food Consumption Survey (Voedselconsumptiepeiling, VCP) and the NVWA residue measurements to provide chlorate intake estimates for 1 to 3 year olds. The request also involved an estimate of the chlorate levels in drinking water in the Netherlands.

This opinion was subjected to an independent peer review.

Findings
- Chlorates were previously primarily used in herbicides, but have since been banned as a pesticide within Europe. However, chlorate can also end up in food via other pathways during the production process. Possible introduction pathway include the use of chlorinated (rinsing) water, chlorine-based disinfectants and additives and processing aids with chlorate residues.
- The data shows that single human exposure to doses exceeding 11 to 23 mg/kg body weight can cause methemoglobinaemia (the formation of haemoglobin with oxidised iron that can no longer transport oxygen). This process causes haemolysis (the breakdown of red blood cells) and can potentially lead to kidney failure. Single exposure to chlorate concentrations over 50 mg/kg body weight is considered lethal.
- In the case of prolonged exposure, chlorate will have an impact on the thyroid gland due to competitive inhibition of iodine uptake. Adaptive processes can then cause problems with thyroid function in the long term, particularly in sensitive populations, such as individuals with a (severe) iodine deficiency or impaired thyroid function. Histopathological effects in the thyroid and disruption of the balance of thyroid hormones have been observed in rats and mice. There are no studies available on these effects in humans.

[4] Commission Regulation (EU) 2020/749 of 4 June 2020 amending Annex III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for chlorate in or on certain products.
[5] Focal Points are the points of contact for EFSA and national authorities, research institutes and other stakeholders in the field of food safety.

- Extrapolating the impact on the thyroid gland in a laboratory animal to humans is a complex process. Rodents are believed to be more sensitive to disruption of the thyroid hormone balance than humans. In addition, there are uncertainties regarding the sensitivity of children to the effects of chlorate on the thyroid. Furthermore, there is uncertainty as to the effect of a disturbed thyroid hormone balance on the developing brain of the foetus. Finally, there is general uncertainty as to whether the health-based guidance value provide enough protection for very young children.
- In 2015, EFSA derived a Tolerable Daily Intake (TDI) of 3 µg/kg body weight per day. This value was the result of a read-across from perchlorate for which a study is available on the effects on iodine uptake in humans. The value is conservative compared to the health-based guidance value that are used by other authorities. U.S. EPA and Health Canada use a value of 30 µg/kg body weight per day to assess chronic effects, with BfR (Bundesinstituut für Risikobewerbung) using a limit value of 10 µg/kg body weight per day for both chronic and acute effects.
- BuRO supports the TDI of 3 µg/kg body weight per day established by EFSA and has applied it to the risk assessment: a sub-chronic scenario where the use of the most conservative value is appropriate in view of the age group. In addition, exposure to chlorate from other sources is lifelong, which means that the use of a health-based guidance value for chronic exposure is appropriate.
- The (limited) epidemiological research available into the effects of (per)chlorate exposure from drinking water in pregnant women and neonates does not find a clear link between exposure and effects on the development of the child. BuRO therefore concludes that, given the low (per)chlorate levels in Dutch drinking water and the sufficient supply of iodine for infants fed with infant formula (guaranteed by the statutory limits on iodine addition), the TDI of 3 µg body weight per day can also be applied to infants up to four months old.
- Most drinking water in the Netherlands does not contain chlorate and, as such, chlorate levels are only measured if there is cause to do so. Chlorate may be present in the drinking water in areas where chlorate is present in the surface water or where chlorate is used in the preparation of drinking water. RIVM derived average chlorate levels between 1 and 11 µg/L for these areas. Given that the dataset consists of targeted measurements, BuRO considers the value of 6 µg/L to be realistically conservative for the exposure calculations for the situation in the Netherlands.
- The derived levels in Dutch drinking water based on measured values are well below the proposed European standard of 0.25 mg/L (250 µg/L) in the ongoing review of the European Drinking Water Directive. This proposed standard is likewise higher than the health-based target value of 70 µg/L derived by RIVM in 2018. The proposed European standard may therefore be unnecessarily high for the situation in the Netherlands and the use of this value could lead to unnecessary risks.
- Measurements of chlorate residues in foodstuffs conducted by the NVWA between 2016 and 2019 found concentrations up to 0.41 mg/kg in (follow-on) infant formula and 0.30 mg/kg in ready-made solid baby foodstuffs. In addition, high chlorate levels (up to 0.25 mg/kg) were found in a number of samples of vegetable-based baby food and cereal-based baby food.
- The large degree of variation in chlorate levels within the product groups of infant formula and baby food analysed is striking. The cause of these differences cannot be determined based on the available data.
- The number of residue measurements for fruit-based and cereal-based ready-made solid baby food is limited. This creates uncertainty regarding the actual contribution of these foodstuffs to total exposure to chlorate.
- The exposure calculations, which are based on chlorate levels in drinking water between 0 and 11 µg/L, show that the level in drinking water is a key factor in

overall exposure to chlorate. In the case of infants up to 1 year old, the contribution from drinking water in the average exposure scenarios, which assume chlorate levels of 6 µg/L of drinking water, is approximately 40 to 50% for the various age groups. For toddlers between the age of 1 and 3 years old, exposure from drinking water is 57% with levels of 6 µg/L of drinking water.

- In the case of infants up to 1 year old, exposure to chlorate from infant formula does not exceed the health-based exposure limit of 3 µg/kg body weight per day based on average intake (based on EFSA data and feeding schedules of manufacturers) and median residue levels (P50 of the NVWA residue measurements). This also applies to the scenario in which the contribution from drinking water (with 6 µg chlorate/L) is taken into account. In the case of high consumption quantities (based on EFSA data and feeding schedules of manufacturers) and high residue levels (P95 of the NVWA residue measurements), the TDI is exceeded for all age groups up to 1 year old – this is likewise the case if the contribution from drinking water is not taken into account. As such, health risks cannot be excluded.
- For young children (toddlers), aged 1 to 3 years old, chlorate exposure from the total diet remains below the health-based exposure limit. This applies to all calculated scenarios, including those with the (high) contribution from drinking water. The health risks for this age group are assessed as being negligible.
- If the foodstuffs were to comply with the applicable MRL of 0.01 mg/kg, the TDI of 3 µg/kg of body weight per day would not be exceeded. In the case of the age groups up to 1 year, the TDI is exceeded at chlorate levels over 0.04 mg/kg for (follow-on) infant formula powder and solid baby food. This calculation was based on high consumption quantities and the presence of 6 µg chlorate/L of drinking water. The level of 0.04 mg/kg in powdered milk corresponds to a level of 0.01 mg/kg in prepared (follow-on) infant formula, taking into account the presence of chlorate in the drinking water.
- A number of European countries, including Belgium, Ireland, Austria, Malta, Montenegro, Spain, Turkey and Switzerland, have indicated, through EFSA Focal Points, likewise to be carrying out measurements for chlorate in infant and baby food. These measurements are occasionally incidental in nature or are part of a more extensive monitoring programme. The approach to chlorate in infant and baby food occasionally relates to strict enforcement of the applicable MRL (0.01 mg/kg), to a case-by-case approach on other occasions, or may consist of an open dialogue with the industry aimed at finding solutions to reduce chlorate levels. In an opinion, BfR in Germany writes that occasional intake of drinking water with chlorate levels of 0.07 mg/L will not lead to acute health effects – even if it is occasionally used to prepare infant formula.
- A survey conducted by RIVM shows that outside Europe there are few activities regarding the monitoring of chlorate in infant and baby food, nor have any statutory limits been established.

Reponses to the questions

1. *What is the impact of higher concentrations of chlorate on food safety for 1) toddlers aged 1-3 years old and b) infants aged 0-12 months in foodstuffs specifically intended for that target group?*

Based on the residue levels established by the NVWA, in the case of an average exposure to chlorate (average consumption quantities and the 50th percentile (P50) of the residue levels), the health risks are negligible for infants up to 1 year old. Health risks, however, cannot be excluded in the event of a high level of exposure (high consumption quantities and the 95th percentile (P95) of the residue levels).

The risk of adverse health effects as a result of chlorate intake, based on exposure from the total diet, is assessed as being negligible for toddlers between the age of

1 and 3. These calculations are based on the chlorate levels in foodstuffs and exposure from Dutch drinking water determined by the NVWA.

2. *At what concentration of chlorate in a) baby foodstuffs and b) infant formula can no adverse effects be expected on the health of this target group?*

Both in the case of infants and toddlers, the applicable MRL of 0.01 mg chlorate/kg of product does not led to the health-based exposure limit being exceeded. The health-based exposure limit (TDI of 3 µg/kg body weight per day) is exceeded for infants up to 1 year old at chlorate levels over 0.04 mg/kg in infant formula powder, follow-on infant formula powder and ready-made commercially available baby food for this age range. Taking into account the contribution of drinking water, a level of 0.04 mg/kg in powdered milk corresponds to a level of 0.01 mg/kg in prepared (follow-on) infant formula. Based on the NVWA measurements, it can be concluded that roughly a quarter of (follow-on) infant formula for infants up the age of 1 year old exceeds this value of 0.04 mg/kg in powdered milk. For ready-made baby food, this percentage is below 10%. A chronic exceedance of the TDI means that health risks cannot be ruled out. This calculation was based on a scenario with high consumption quantities and the presence of 6 µg chlorate/L in drinking water. If 0.04 mg/kg is the maximum level of chlorate in toddler nutrition, the TDI will similarly not be exceeded for the age group of 1 to 3 year olds.

3. *How do other (European) countries deal with this problem?*

Within Europe, there are major differences in terms of the approach to chlorate in infant formula and baby food. Through EFSA Focal Points, a number of European countries indicated that they were familiar with high chlorate levels in infant formulae. A number of countries carry out measurements or have an active programme to monitor or limit levels in infant formula and baby food. These approaches vary from a case-by-case approach to enforcement based on the applicable MRL (0.01 mg/kg) or an open dialogue with the industry with the aim being to find solutions to reduce chlorate levels. In an opinion, BfR in Germany writes that occasional intake of drinking water with chlorate levels of 0.07 mg/L will not lead to acute health effects – even if it is occasionally used to prepare infant formula.

Enquiries made regarding activities in countries outside Europe did not lead to any monitoring activities or specific statutory limits for chlorate in infant formula and baby food emerging.

Advice BuRO

The applicable MRL of 0.01 mg of chlorate/kg of product does not result in exceeding the health-based exposure limit in infants and young children (toddlers). This health-based exposure limit is, however, exceeded for infants up to the age of 1 year old with chlorate levels over 0.04 mg/kg in infant formula powder, follow-on infant formula powder and ready-made commercially available baby food. This is addition to the contribution from other sources, such as from consumption of drinking water. Based on NVWA measurements, roughly a quarter of (follow-on) infant formula for infants up to the age of 1 year old exceeds this value of 0.04 mg/kg in powdered milk. For ready-made baby food, this percentage is below 10%. A chronic exceedance of the TDI means that health risks cannot be ruled out.

I therefore recommend the following

To the Inspector-General of the NVWA

- From a health perspective, a maximum chlorate level should be applied and maintained for (follow-on) infant formula powder (or in the prepared product) and ready-made food intended for infants and young children (toddlers).
- Given the significant differences in chlorate levels between the foodstuffs for infants and toddlers, attempts should be made to engage with the industry to reduce chlorate levels in these foodstuffs and for the relevant developments to be monitored.
- The investigation of chlorate levels in ready-made solid baby foodstuffs based on fruit and cereals should be intensified.

To the Minister for Medical Care and Sport

- Following the Amending Regulation concerning maximum residue levels in certain foodstuffs, putting a review of the MRL for chlorate in solid baby foodstuffs and toddler nutrition on the agenda of the European Commission should be considered. Based on the risk assessment below, the MRL of 0.01 mg/kg for prepared (follow-on) infant formula need not be increased.
- This risk assessment should be shared with your colleague at the Ministry of Infrastructure and Water Management for the benefit of the ongoing review of the Drinking Water Directive. In doing so, it should be indicated that current chlorate levels in Dutch drinking water are (well) below the proposed European standard and that this is vital to the safety of infant formulae prepared using this water.

Yours faithfully,

Prof. Dr. Antoon Opperhuizen
Director of the Office for Risk Assessment & Research

Substantiation

Hazard identification

Chlorate was previously used as a herbicide, however, under Commission Decision 2008/865/EC[6] it may no longer be used as a plant protection product. Despite the ban, chlorate can still end up in food crops, for example, through illegal use as a plant protection product, the spraying of crops with chlorinated water, use of fertilisers containing chlorate and through the uptake of chlorate residues from the soil or groundwater. In addition, chlorate may be introduced during processing and industrial production of foodstuffs. In such cases, chlorate is produced as a by-product of chlorine, chlorine dioxide and hypochlorite for the disinfection, for example, of drinking water, rinsing water, contact surfaces and equipment. If foodstuffs come into contact with these sources during the production process, this may result in chlorate residue in the foodstuffs (EFSA, 2015; Teagasc, 2019). Furthermore, additives and processing aids, such as sodium hydroxide, may also contain chlorate as a contaminant (Kettlitz et al., 2016). According to the European Food Safety Authority (EFSA), it is primarily the industrial processes, and the reuse of process water, that are responsible for the chlorate residues that are found in foodstuffs (EFSA, 2015). In addition, the World Health Organization (WHO) has highlighted the potential introduction of chlorate into foodstuffs through bleaching processes during the production of flour and modified starch and through migration from paper and cardboard food contact materials (WHO, 2016). In 2015, Specialized Nutritions Europe (SNE) identified that the use of raw materials containing chlorate and process water were the principal sources for the presence of chlorate in infant formulae and baby food. Chlorate has the potential to accumulate in foodstuffs during the production process (Kettlitz et al., 2016). Measurements conducted by the Netherlands Food and Consumer Product Safety Authority (Nederlandse Voedsel- en Warenautoriteit, NVWA) (between 2016 and 2019) and measurements conducted by the industry itself show that chlorate residues are regularly found in infant formulae and baby food.

Chlorate (ClO_3^-) is an anion with multiple resonance structures that is able to form salts, for example, with sodium and potassium.

Legal framework

Plant protection product

The use of chlorate as a plant protection product is prohibited (Commission Decision 2008/865/EC). Under Regulation (EC) No 396/2005, Article 18(1)(b), a generic Maximum Residue Level (MRL) of 0.01 mg/kg has been established for non-authorised plant protection products. In practice, this value is equal to the detection limit for most substances and does not take into account substance-specific properties.

Given that introduction pathways other than the use of chlorate as a plant protection product regularly result in detectable chlorate levels in foodstuffs, an Amending Regulation was established[7], which came into force on 28 June 2020.

[6] 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.
[7] Commission Regulation (EU) 2020/749 of 4 June 2020 amending Annex III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for chlorate in or on certain products.

This Amending Regulation sets out temporary MRLs for a number of foodstuffs based on the ALARA principle (As Low As Reasonably Achievable), based on the 95th percentile (P95) of European residue measurements of the relevant product types between 2014 and 2018. The temporary MRLs will be reviewed within a maximum period of five years. This Regulation does not include any MRLs for infant formulae and solid baby foodstuffs: these foodstuffs are subject to the MRL of 0.01 mg/kg under Article 4(2) of the Commission Delegated Regulation (EU) No 2016/127[8]. This Regulation has not been amended and therefore the MRL of 0.01 mg/kg for these foodstuffs included in the Regulation remains in force.

Composition of infant formula and baby food
Regulation (EU) No 609/2013[9] and Commission Delegated Regulation (EU) 2016/127[10] lay down requirements for the composition of foodstuffs intended for infants and young children to ensure that these foodstuffs are safe and healthy for the intended target groups.

Furthermore, under this Regulation, iodine, such as potassium iodide, potassium iodate and sodium iodide, may be added to infant formula, follow-on formula and baby food. Sodium iodate may only be added to baby food.

Commission Delegated Regulation (EU) No 2016/127 establishes a minimum and maximum iodine content for infant formula and follow-on formula. Under this Regulation, both product groups must contain at least 3.6 μg/100 KJ (15 μg/100 kcal) and no more than 6.9 μg/100 kJ (29 μg/100 kcal) of iodine. These requirements were laid down for foodstuffs based on cow's milk protein, goat's milk protein and protein hydrolysates.

Product standards
In 2014, the NVWA established national intervention values (NVWA, 2020) in view of the general MRL of 0.01 mg/kg being regularly exceeded – including in cases where it was unlikely that chlorate was used as a plant protection product. These values applied until 28 June 2020; from which date the Amending Regulation came into force. These intervention values were:

- for all plant products, except vegetables, Annex I of Regulation (EC) No 396/2005: 0.1 mg/kg
- for all vegetables, except carrots, Annex I of Regulation (EC) No 396/2005: 0.25 mg/kg
- for carrots: 0.2 mg/kg
- for other products except baby food and infant formula: 0.1 mg/kg
- baby food and infant formula are assessed according to Commission Regulation (EC) No 125/2006 and Commission Regulation (EC) No 141/2006 0.01 mg/kg. For (follow-on) infant formula, this standard applies to the levels in the prepared product (as consumed).

Drinking water

[8]Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding.
[9]Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control.
[10]Commission Delegated Regulation (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding.

In many countries, drinking water is the principal source of chlorate exposure (EFSA, 2015). Effective disinfection of drinking water using chlorine dioxide and hypochlorite remains vital in the fight against microbial contaminants worldwide – including in large parts of Europe. For that reason, the WHO upheld the existing maximum standard of 0.7 mg of chlorate/L in the reevaluation of its drinking water quality guideline (WHO, 2016;2017a). If health-based guidance value were exclusively relied on to determine the standard, according to the WHO, the standard would be lower, at approximately 0.3 mg/L (WHO, 2016).
In 2018, a proposal for the revision of the Drinking Water Directive[11] was submitted to the European Commission (EC) (EPRS, 2019). The WHO made recommendations to the EC for the review, which included WHO proposals for the use of an annual average standard of 0.35 mg chlorate/L and a maximum standard of 0.7 mg/L for Europe (WHO, 2017b). The EC deviated from this recommendation and proposed a chlorate standard of 0.25 mg chlorate/L. ANSES was instructed to evaluate this standard on behalf of the European Commission (ANSES, 2018). In December 2019, provisional agreement was reached regarding this revision in which the standard was provisionally set at 0.25 mg/L (EC, 2020). This standard was subsequently included in the Council position in October 2020 (de Raad, 2020).

In 2018, the National Institute for Public Health and the Environment (RIVM) derived a health-based exposure limit for chlorate in Dutch drinking water of 0.07 mg/L. This value is not laid down in legislation (ILT, 2019). In the Netherlands, chlorate levels in drinking water is determined solely on the basis of targeted measurements, meaning if there is a specific reason to do so (RIVM, 2020a).

Hazard characterisation (toxicology)

Absorption, distribution, metabolism and elimination

Chlorate is rapidly absorbed into the gastrointestinal tract after oral exposure and spreads with ease throughout the body following ingestion. In the body, chlorate can be converted into chloride and both forms are excreted in urine (EFSA, 2015). Chlorate reduction may lead to the production of chlorite (CIO^{2-}); this compound has been detected in the tissues and urine of rats exposed to chlorate (US EPA, 2006; EFSA, 2015). However, this finding has been called into doubt by EFSA and it may be that excretion as chlorite may not make a significant contribution to the elimination of chlorate (EFSA, 2015).

Acute toxicity

Chlorate is fatal to humans in cases of oral exposure of approximately 50 mg/kg body weight and above (EFSA, 2015). The United States Environmental Protection Agency (U.S. EPA) considers a single dose over 100 mg/kg as fatal (US EPA, 2006). Toxic effects following acute exposure will be observed in humans at dosages from 11 to 23 mg/kg body weight. The critical effect with regard to acute toxicity is methemoglobinaemia: the formation of haemoglobin with oxidised iron that can no longer transport oxygen. This process causes haemolysis (the breakdown of red blood cells) and can lead to kidney failure (EFSA, 2015). EFSA concludes that a single high exposure to chlorate will have no effect on thyroid function (EFSA, 2015).

[11] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption.

Toxicity of long-term exposure

Effects on the thyroid

The critical effect with regard to chronic toxicity of chlorate is competitive inhibition of iodine uptake in the thyroid gland. Adaptive processes in the thyroid can subsequently cause problems with thyroid function in the long term, particularly in sensitive populations, such as individuals with an iodine deficiency or impaired thyroid function. Perchlorate is likewise known to have harmful effects on the thyroid in humans. *In vitro* studies that examined the inhibition of iodine transport by the sodium/iodide symporter in rats and humans have shown that chlorate and perchlorate inhibit iodine uptake using the same mechanism. Based on the effects in rats, chlorate is believed to be less potent than perchlorate in this regard (EFSA, 2015).

Animal trials with oral chlorate exposure showed effects on plasma concentrations of thyroid hormones, i.e. a decrease in triiodothyronine (T3) and thyroxine (T4) and an increase in thyroid-stimulating hormone (TSH). Histopathological effects were also observed in the thyroids of rats and mice (non-neoplastic lesions; hypertrophy and hyperplasia of follicles and decrease of colloid[12] in the follicles). An increase in TSH can lead to a higher rate of cell division in and growth of the thyroid gland. Evidence has been found of possible carcinogenic effects on the thyroid of rats and mice; EFSA does not consider these effects to be relevant to humans (EFSA, 2015). The U.S. Environmental Protection Agency has concluded that chlorate is not carcinogenic at exposure levels below the level at which thyroid hormone homeostasis is disrupted (US EPA, 2006). The Joint FAO/WHO Expert Committee on Food Additives (JECFA) likewise has outlined that the tumours observed in the thyroid may result from stimulated cell division due to an increase in TSH production (WHO, 2016). Chlorate is not genotoxic (US EPA, 2006; EFSA, 2015; WHO, 2016).

Due to a number of quantitative differences in the regulation and kinetics of thyroid hormones between humans and rodents, rodents are more sensitive to disruption of the homeostasis of thyroid hormones. As such, humans are likely less sensitive to these effects (EFSA, 2015; WHO, 2016). EFSA cites the fact that infants may be more sensitive to the effects of chlorate on the thyroid, but does not provide any further substantiation in this regard (EFSA, 2015).

Reproductive and developmental toxicity

JECFA has noted that homeostasis of thyroid hormones is highly significant in relation to brain development. For that reason, JECFA has expressed concerns regarding potential neuronal development toxicity due to chlorate. There is insufficient data to assess this effect (JECFA, 2007; WHO, 2016). Reproductive toxicity studies in rats and rabbits have not found any indications of reproductive toxicological properties of chlorate (EFSA, 2015). For that reason, EFSA also cites pregnant women as a vulnerable group for high chlorate exposure (EFSA, 2015).

Haematological effects

In addition to effects on the thyroid, repeated exposure to chlorate will also affect haematological parameters. A number of phenomena have been observed in multiple animal species, including decreases in the number of erythrocytes,

[12] Thyroid follicles contain a supply of thyroglobulin that is stored in vesicles containing protein fluid (colloids). Thyroglobulin is a prohormone that forms the thyroid hormones T3 and T4 through iodination.

haemoglobin concentrations and haematocrit levels. In addition, a number of studies also found non-neoplastic lesions in the bone marrow or spleen (EFSA, 2015).

Studies in healthy adult men with an exposure duration of up to twelve weeks and doses of up to 0.036 mg chlorate/kg body weight per day showed no effects on blood and urine parameters. Nor were any other physiological effects observed (JECFA, 2007; WHO, 2016).

Hazard characterisation (Health-based guidance value)
EFSA
EFSA derived a Tolerable Daily Intake (TDI) for chlorate of 3 μg/kg body weight in its 2015 opinion, based on competitive inhibition of iodine in the thyroid (EFSA, 2015). A TDI is an estimate of the amount of a substance that a person can take in per day for their entire life, without any significant effects on their health. This value was reached by way of a read-across, based on the TDI for perchlorate (0.3 μg/kg body weight per day) that was derived from a study into the effect on iodine uptake in humans. A correction was applied to this value (factor of 10), based on the lower inhibition potential of chlorate, i.e. the difference in dosage at which thyroid follicle hypertrophy was observed in rats.

EFSA has identified groups that may be more sensitive to these effects: foetuses, neonates, persons with a low iodine intake and persons with certain genetic traits.

EFSA has derived an Acute Reference Dose (ARfD) for the acute toxicity of chlorate, which is established at 36 μg/kg body weight based on a No Observed Effect Level (NOEL) from a study with chlorate in humans. The critical effect is methemoglobinaemia.

BfR
The Bundesinstitut für RIsikobewertung (BfR) in Germany has a different perspective from that of EFSA regarding the calculation of the health-based standard for acute effects. BfR believes that an additional safety factor (factor 3) is required in order to calculate the acute health-based exposure limit for foodstuffs that are a large part of the diet due to the potential variations in residue distribution in compound foodstuffs. This difference of views has been described by BfR and EFSA in a joint document (EFSA & BfR, 2015).
In its assessment, BfR recommends the use of the Acceptable Daily Intake (ADI) of 0.01 mg/kg body weight per day (as derived by JECFA) for the assessment of both chronic and acute effects (BfR, 2014;2018).

WHO 2016
In 2007, JECFA derived an Acceptable Daily Intake (ADI) for chlorate of 0 to 0.1 mg/kg (JECFA, 2007). Like a TDI, an ADI is an estimate of the amount of a particular substance that a person can take per day throughout their lives without any significant effects on their health. This ADI was also used in the reassessment of the drinking water quality guidelines by the WHO in 2016 (WHO, 2016).
JECFA assessed histopathological changes (follicle hypertrophy) in the thyroid of male rats in a carcinogenicity study as the most sensitive end point to determine a reference point for the derivation of the health-based exposure limit. An increase in tumour formation was only observed for higher doses. JECFA derived a Bench Mark Dose Level ($BMDL_{10}$[13]) of 1.1 mg/kg body weight per day from this study conducted by the National Toxicology Program (NTP). Because rats are more sensitive to disruption of thyroid hormone homeostasis, JECFA does not use a

[13]$BMDL_{10}$ is the 95% lowest confidence interval of the estimated dose that yields an additional 10% risk.

safety factor for interspecies variability. JECFA does, however, apply a factor 10 for intraspecies variability and a factor 10 for uncertainties in the dataset. These uncertainties primarily relate to neurological developmental toxicity, which may be relevant to pregnant women with a low iodine intake and/or pregnant women who are simultaneously exposed to other substances that inhibit iodine intake in the thyroid such as cyanide from cigarette smoke.

U.S. EPA
In 2006, the U.S. EPA assessed the risk to public health and the environment in the context of the use of chlorate as a plant protection product. The U.S. EPA also chose the histopathological effects in the thyroid gland of male rats from the NTP study as a starting point for the assessment of chronic effects. These data led to the U.S. EPA deriving a BMDL of 0.9 mg/kg body weight per day. An uncertainty factor of 3 is applied to this value for interspecies differences and factor of 10 for intraspecies differences. This has resulted in a health-based exposure limit of 0.03 mg/kg body weight per day. According to the U.S. EPA, this value also protects for effects that have been observed in studies with primates including possible developmental toxicity. The U.S. EPA has stated that the derived health-based exposure limit is protective of all populations, including children, because they are not expected to be more susceptible to chlorate-induced thyroid effects (US EPA, 2006).

The U.S. EPA has analysed several studies but found no substantiation for the derivation of a health-based exposure limit for acute exposure (US EPA, 2006).

Health Canada
In 2008, Health Canada established a Maximum Acceptable Concentration (MAC) for chlorate in drinking water in the Guidelines for Canadian Drinking Water. The MAC follows from a TDI of 0.03 mg/kg body weight per day. This value is based on the No Observed Adverse Effect Level (NOAEL) from a sub-chronic (90-day) study in rats in which thyroid effects were observed (colloid depletion). The derivation of the TDI involved the application of a factor of 1000 as the total safety margin for inter- and intraspecies differences and for the duration of the study (sub-chronic to chronic). The MAC value for chlorate was established by Health Canada at 1.12 mg/L/ drinking water (Health Canada, 2008).

ECHA
The registration dossier for sodium chlorate that was submitted to the European Chemicals Agency (ECHA) established Derived No Effect levels (DNELs) of 0.036 and 0.05 mg/kg body weight per day for the oral exposure of the general population. These values were derived from the NOAEL from the NTP study – in both cases using a total safety factor of 100 (ECHA, 2020).

Selection of the health-based exposure limit by BuRO
For the risk assessment, BuRO has assessed exposure for all age groups to the health-based exposure limit for chronic exposure as established by EFSA at 3 μg/kg body weight per day. This value is conservative compared to the ADIs that are used by the WHO and BfR (10 μg/kg body weight per day) and the health-based exposure limit of the U.S. EPA and Health Canada (30 μg/kg body weight per day). BuRO notes that the various authorities have diverging assessments regarding the uncertainties in the applicability of the TDI or ADI for young children. EFSA cites an uncertainty in the sensitivity of young children to the critical effect (inhibition of iodine uptake in the thyroid) on which the exposure limits are based (EFSA, 2015). The U.S. EPA, however, indicates that children are not more sensitive to this effect (US EPA, 2006). BuRO takes note of this uncertainty, but is not aware of any scientific research that either substantiates or refutes the sensitivity for young children. Due to the addition of iodine to nutrition

for infants, (severe) iodine deficiencies in children in the Netherlands who are bottle fed are unlikely.

For that reason, in this risk assessment, BuRO assumes that the most conservative value (TDI of 3 µg/kg body weight per day as established by EFSA) is also protective for young children. BuRO nevertheless adds the caveat that additional research into the sensitivity of young children to the effects on the thyroid is required.

The decision to use the TDI, which is based on lifelong daily exposure, is conservative in terms of exposure duration due to the fact that the actual intake of infant formula and baby food will only last several months to a few years at most. BuRO considers a health-based exposure limit for acute (24-hour) exposure such as an ARfD to provide insufficient protection due to the fact that exposure to chlorate from infant formula and baby food certainly does not take place solely on a single occasion. In addition, the chlorate intake from other foodstuffs and drinking water, by contrast, is a lifelong scenario.

Use of the TDI for the risk assessment for infants under 4 months
There is general uncertainty as to whether health-based guidance value provide protection for infants up to 4 months. BuRO therefore consulted the literature for the effects of (per)chlorate on the development of unborn and newborn children. Little information is available regarding the long-term effects of exposure to (per)chlorate of these infants. Interference with iodine uptake by the thyroid gland is particularly a critical effect for foetuses and infants, given that neuronal development is dependent on thyroid hormones (Leung et al., 2010).

The available research primarily focuses on the effects of perchlorate exposure of pregnant women via drinking water and the effect on thyroid hormone concentrations in the mother and newborn. A US study identified a link between exposure of the mother to perchlorate via drinking water and an increase of TSH concentrations in the newborn within 24 hours after the birth. These association was less pronounced in measurements taken 24 hours after the birth (Steinmaus et al., 2010). A Chilean study found no relationship between perchlorate exposure from drinking water and TSH, thyroglobulin or T4 concentrations in the mother and child (Téllez et al., 2005). This study was based on a comparison between three cities with perchlorate levels of 114.6 and 0.5 µg/L drinking water. The study similarly did not find any effects on various growth parameters in the neonates. This population had a good iodine status.

A US review of epidemiological studies into the effects of perchlorate exposure from the environment on the functioning of the thyroid in neonates found no conclusive association (Tarone et al., 2010). The review included studies in which perchlorate exposure was high: levels in drinking water up to 340 µg/L and the medical application of perchlorate in pregnant women with therapeutic doses up to 1 gram per day.

Kirk et al. (2005) examined samples of breast milk and cow's milk from Texas. Perchlorate was detectable in 81 of the 82 samples (Kirk et al., 2005). The average concentrations in cow's milk and breast milk were 2.0 and 10.5 µg/L respectively with maximum concentrations of 11 and 92 µg/L respectively. For breast milk samples with a perchlorate concentration of more than 10 µg/L, iodine concentration appeared to have a linear correlation to the inverse of the perchlorate concentration (r^2 >0.9, n=6). The presence of perchlorate in milk reduced the iodine concentration.

Based on the information described above, BuRO has concluded that, given the low (per)chlorate levels in the drinking water in the Netherland and the sufficient supply of iodine for infants who are fed with infant formula (guaranteed by statutory limits), the TDI can also be used for infants up to 4 months old for the present risk assessment.

Exposure

Sampling data

Between 2016 and 2019, the Enforcement Directorate of the NVWA analysed chlorate levels in infant formula, follow-on formula, cereal-based baby food and other foodstuffs for babies and young children. The first two categories include the bottle formula for infants aged 0 to 6 months and 6 to 12 months old respectively. Foodstuffs intended for babies and young children (toddlers) include ready-made solid food (including vegetable meals and fruit pouches for children between 4 months and 3 years old). The category of cereal-based baby food includes cereal-based foodstuffs such as porridges, bars, cereals and biscuits for children between 4 months and 3 years old. Based on the product descriptions in the NVWA database, BuRO classified the foodstuffs into the various age groups for the purposes of the risk assessment.

The samples were analysed at the NVWA laboratory using UPLC-MS/MS with a limit of detection (LOD) of 5 or 0.5 µg chlorate/kg and a limit of quantification (LOQ) of 10 or 1 µg chlorate/kg. In total, 166 foodstuffs intended for infants up to 1 year old were analysed. The results of the samples are summarised in Table 1.

In total, samples were taken from 78 foodstuffs intended for young children between the ages of 1 and 3. These foodstuffs relate specifically to foodstuffs intended for this age group and does not include homemade dishes and snacks. The results of these sample are shown in Table 2. Table 2 also shows the data of fruit, vegetables and potatoes given that these foodstuffs are also part of the diet of 1 to 3 year olds.

Table 1 Overview of the NVWA monitoring data of chlorate levels in foodstuffs for infants up to 1 year over the period from 2016 to 2019.

Category	Number of samples (N)	Range (mg/kg)	P50[1] (mg/kg)	P95[1] (mg/kg)
Age: 0–6 months				
Infant formulae	26	0.01–0.138	0.02	0.104
Age: 4–6 months				
Cereal-based baby food porridges	9	0.001–0.010	0.005	0.010
Cereal-based baby food: biscuits	1	0.225	0.225	0.225
Baby food: fruit	2	0.005	0.005	0.005
Age: 6–12 months				
Follow-on infant formula	29	0.01—0.41	0.02	0.16
Cereal-based baby food: porridges	27	0.001–0.15	0.01	0.02
Cereal-based baby food biscuits	6	0.01	0.01	0.01
Baby and toddler food: fruit	4	0.01	0.01	0.01
Baby and toddler food: vegetables	15	0.01–0.30	0.01	0.25
Baby food: meal	47	0.01–0.11	0.01	0.06

[1] The P50 and P95 are based on an upper-bound calculation where values below the limit of detection (LOD) are equal to the LOD and values between the LOD and LOQ (limit of quantification) are equal to the LOQ. Depending on the analytical method, the LOD is 0.5 or 5 μg/kg and the LOQ is 1 or 10 μg/kg.

The Enforcement Directorate furthermore indicates that measurements conducted by the industry itself purport to show that 65 to 70% of infant formula does not meet the standard of 0.01 mg chlorate/kg. However, BuRO does not have access to these data and, as such, cannot include it in the analysis.

In its opinion of 2015, EFSA also reports a single result of infant formula with high chlorate levels (2.5 mg/kg dry weight). At the time, EFSA had insufficient data to include this infant formula in the exposure estimate and risk assessment, but in substantiation of the levels identified referred to a Japanese study from 2013 in which levels in the order of milligrams of chlorate per kg were similarly found in infant formula (EFSA, 2015).

Table 2 Overview of the NVWA monitoring data of chlorate levels inf foodstuffs (specially intended) for young children between 1 and 3 years olds between 2016 and 2019.

Food category for 1 to 3 years olds	**Number of samples (N)**	**Range (mg/kg)**	**P50[1] (mg/kg)**	**P95[1] (mg/kg)**
Follow-on infant formula: 12+ months	10	0.01–0.291	0.044	0.21
Jar meals	45	0.005—0.106	0.01	0.06
Fruit snacks	4	0.005—0.01	0.008	0.01
Cereal-based toddler food: biscuits	4	0.01	0.01	0.01
Cereal-based toddler food: porridge[2]	27	0.001–0.15	0.01	0.02
Other product groups				
Fruit	25	0.01	0.01	0.01
Vegetables	78	0.001–0.32	0.003	0.12
Potato	6	0.01	0.01	0.01

[1] The P50 and P95 are based on an upper-bound calculation where values below the limit of detection (LOD) are equal to the LOD and values between the LOD and LOQ (limit of quantification) are equal to the LOQ. Depending on the analytical method, the LOD is 0.5 or 5 µg/kg and the LOQ is 1 or 10 µg/kg.
[2] These data is equal to the values for the age group of 6 to 12 months in Table 1. For this product group, the foodstuffs for children from 6 months old were also used for 1 to 3 year olds.

<u>Chlorate levels in Dutch drinking water</u>
Most drinking water in the Netherlands does not contain chlorate. In the Netherlands, chlorate levels are only established by way of targeted measurements, if there are reasons to conduct such measurements, such as detection of chlorate in extracted surface water or if chlorate is added to water during purification (this only takes places in a number of regions) (RIVM, 2020a). The measurements available are therefore limited in number but are likely to be the worst case for the Dutch situation.

Measurements regarding drinking water in the Netherlands are kept in the REWAB (Registratie opgaven van Drinkwaterbedrijven) database – an information system for the quality reports of drinking water companies. The REWAB database is used by the Human Environment and Transport Inspectorate (Inspectie Leefomgeving en Transport, ILT) for the preparation of annual reports on Dutch drinking water quality (RIVM, 2020a).

In the 2018 report on drinking water quality, ILT states that chlorate levels over the signalling value[14] of 1 µg/L were found in 11 of the 122 measurements of surface water for drinking water extraction (ILT, 2019). Drinking water companies

[14] The signalling value is the concentration for which, if exceeded, an investigation is launched into any environmental and health risks, origin and possibilities to dispose of the chemical compound.

use exemption values for surface water intake between 20 and 50 µg/L. There is no statutory maximum for chlorate levels in drinking water. However, RIVM has derived a health-based target value of 70 µg/L. The reported exceedances in surface water are below that standard (maximum of 66 µg/L). Of the exceedances of the drinking water standard reported, only 0.5% (1 report) related to chlorate (ILT, 2019).

Based on the chlorate measurements from the REWAB database between 2015 and 2019, RIVM estimated the chlorate levels in drinking water for regions where chlorate could be present in the drinking water (RIVM, 2020a). The database contains 569 chlorate measurements from four drinking water companies and a limited number of extraction locations. The dataset contains minimum, maximum and mean concentrations per drinking water production station and the total number of measurements per station. Based on these data, RIVM was able to derive a mean lower-bound concentration of 1 µg/L. This value is equal to half of the lowest report LOD. The mean upper-bound concentration was determined by RIVM at 11 µg/L: this was calculated based on the mean concentrations reported by drinking water production stations where chlorate was detected at levels above the LOD. The medium-bound scenario was set by RIVM at 6 µg/L, the mean of the upper-bound and lower-bound concentrations. Given that the dataset consists of targeted measurements and applies to areas where chlorate may be present in the drinking water, BuRO considers the value of 6 µg/L to be realistically conservative for the exposure calculations of the Dutch situation.

Chlorate levels in processing aids and additives
Processing aids and additives may contain chlorate as a contaminant. These substances may be added to the foodstuff directly or may be used during the production process. A study conducted by Kettlitz *et al.* showed that sodium hydroxide in particular regularly contains high levels of chlorate (Kettlitz et al., 2016). In this study, chlorate was found in 80% of the samples at concentrations up to 32 mg chlorate/kg sodium hydroxide. In this study, chlorate was also found in other calcium and potassium salts and other additives such as carrageenan (E407). Sodium hydroxide is produced through the electrolysis of brine. Electrolysis can be carried out using mercury cells, diaphragm cells or membrane cells. The mercury cell method is known to work efficiently and leaves relatively little chlorate in the product (< 5 mg/kg) compared to other techniques. This method has the disadvantage that mercury residue may be left behind in the reaction product and that this may result in a negative environmental impact from the mercury (Kettlitz et al., 2016). In addition, under Regulation (EU) 2017/852[15], the use of mercury electrodes for chlor-alkali processes (such as the production of sodium hydroxide) is no longer permitted as of 11 December 2017. As a result of this ban, the other methods, resulting in more chlorate being left behind in the reaction product, will be used.

Monitoring activities and approach in other European countries
EFSA Focal Points
In order to assess how this problem is being dealt with in other European countries, BuRO made enquiries along EFSA Focal Points[16] regarding the priority, knowledge position and approach in 37 other European countries, of which twelve provided a response. Three countries indicated that they either are not actively engaged with chlorate in infant formula and baby food or that they intend to get

[15] Regulation (EU) 2017/852 of the European Parliament and of the Council of 17 May 2017 on mercury, and repealing Regulation (EC) No 1102/2008.
[16] Focal Points are the interface between EFSA and the national authorities in the area of knowledge exchange on food safety, research institutes and other stakeholders.

started on the issue soon. Six countries stated that they have an active programme.

- Belgium is following the European discussion but does not currently have an active monitoring programme itself. Risk assessments are carried out if chlorate is detected in baby and toddler food by the authorities. Belgium uses the standard of 0.01 mg/kg in accordance with the European legislation that applies to infant formula and baby food.
- Ireland is currently working on a comprehensive programme to reduce the use of chlorinated agents in the food industry as a whole. Ireland has monitoring data that shows that this is necessary. Ireland has not prepared a specific risk assessment for chlorate in formulae for infants and young children due to the fact that there are no concerns about iodine deficiencies in the relevant populations as a result of the composition of infant formula and follow-on formula. Neither do studies into the iodine status of the Irish population show any deficiencies.
- Latvia has indicated that it does not have a monitoring programme or approach to the risk assessments in place.
- Austria launched a monitoring programme in 2015, under which approximately 200 samples have now been analysed. Austria does not have a dedicated risk assessment for chlorate in baby food, but uses its own MRL of 0.02 mg/kg alongside the applicable standard for perchlorate.
- Malta has a monitoring programme for chlorate but has not provided any further details.
- In 2019, Montenegro conducted a small-scale monitoring programme for chlorate in formulae for infants and young children, in which 11 samples were analysed.
- In Spain, the national food safety authority (AESAN) is currently in a dialogue with the industry, where the sector has expressed concerns through the industry organisation Manufacturers of Child Dietary Products (ANDI) regarding the lack of feasibility of the applicable MRL. Spain has introduced the industry's position into the discussions on the Amending Regulation at European level. The Commission has indicated that baby food will not be included in establishing new (realistic) MRLs under Regulation (EC) No 396/2005. In Spain, the risks of the relevant foodstuffs are assessed in the event that chlorate residues are detected in baby food.
- In 2018 and 2019, Switzerland carried out an enforcement project for imported foodstuffs, which was characterised by 13 positive samples out of a total of 66 and in which chlorate levels varied between 0.0026 and 0.032 mg/kg. Switzerland applies the MRL of 0.01 mg/kg.
- Turkey currently applies the MRL of 0.01 mg/kg for the assessment of residues of plant protection products in formulae for infants and young children – except for a number of exceptions. This limit is also used for chlorate, which often does not enter the product as a plant protection product. Turkey is following the ongoing discussion on the revision of chlorate standards in the context of the review of Regulation (EC) No 396/2005 and has noted that formulae for infants and young children falls outside of this scope. For that reason, Turkey believes that this issue should also involve examination of the options available within Commission Delegated Regulation (EU) No 2016/127 and Commission Directive 2006/125/EC – if no options are available, the MRL of 0.01 mg/kg will be upheld.

<u>Literature review on the approach of other European authorities</u>
The Irish Agriculture and Food Development Authority (Teagasc) has published a strategy on the reduction of the amount of chlorate in milk products, with a specific focus on infant formula (Teagasc, 2019). The current recommendations focus mainly on the optimal use of chlorinated cleaning agents in practice, both in

dairy farming and in the processing industry. At present, Teagasc is conducting research into the use of alternative cleaning protocols and their effectiveness against microbial contaminants. The project will also focus on identifying concentrations of chlorate in milk products, the possible accumulation of chlorate in the production chain, the efficacy and safety of chlorine-free alternatives and the evaluation of various water disinfection technologies. Teagasc has also studied the potential application of nanofiltration for the removal of chlorate residue from milk by applying this technique in a concentration step during the production process. This method allows chlorate levels in milk products to be reduced by approximately 60% (Dairy reporter, 2019; W. McCarthy, 2019).

In an update of the opinion on the health risks of chlorate, BfR in Germany has stated that the level of chlorate residues in foodstuffs must be reduced (BfR, 2018). In the update, BfR specifically refers to the fact that infants who are exclusively bottle fed are the most sensitive population. According to BfR, it is critical to this group that the water that is used to prepare the infant formula contains very little chlorate given that otherwise this would lead to the TDI of 10 µg/kg body weight per day being exceeded; this is unlikely for the ARfD. BfR states that the occasional intake of drinking water with chlorate levels of 0.07 mg/L is therefore unlikely to lead to health risks – even if such drinking water is occasionally used to prepare infant formula (BfR, 2018).

Monitoring activities and approach in third countries
At BuRO's request, RIVM made enquiries with authorities in countries outside Europe on the subject of monitoring programmes and limit values specifically targeted at chlorate in infant formula and food for young children (RIVM, 2020a). Four authorities (the U.S. Food and Drug Administration, Health Canada, Food Standards Australia New Zealand and the Ministry of Health, Labour and Welfare of Japan) and the Codex Committee on Contaminants responded to these enquiries. None of the queried countries has established a specific monitoring programme or established product limits. Neither does the Codex Alimentarius Commission have any product limits for chlorate in these foodstuffs.

Exposure calculations
For the purposes of the exposure calculations, BuRO differentiated between four key age groups. The classification of these groups was based on differences in consumption patterns and body weight of the children. This classification is similar to the age ranges used by EFSA when assessing the exposure of young children to pesticides (EFSA, 2018). For the purposes of the exposure calculations, five scenarios were subsequently developed for the age groups up to 1 year old:

A. an average exposure estimate based on common consumption quantities, based on various data sources and median (P50) chlorate levels based on the NVWA data. This calculation assumes that there is usually no chlorate present in the drinking water.
B. an average exposure estimate based on common consumption quantities, based on various sources and median (P50) chlorate levels based on the NVWA data. This calculation assumes that chlorate is present in the drinking water (medium-bound average of targeted measurements; 6 µg/L);
C. a high exposure estimate based on high consumption quantities and the P95 of the residue levels identified. This calculation assumes that there is usually no chlorate present in the drinking water.
D. a high exposure estimate based on high consumption quantities and the P95 of the residue levels identified. This calculation assumes that chlorate is present in the drinking water (medium-bound average of targeted measurements; 6 µg/L); and

E. a worst-case exposure estimate in which, in addition to high consumption quantities and the P95 of the residue levels identified, a very high concentration of chlorate is also present in the drinking water (upper-bound average of targeted measurements; 11 µg/L).

Exposure for the total diet was calculated by RIVM for 1 to 3 year olds (RIVM, 2020a). This calculation was made on the basis of the Dutch National Food Consumption Survey (VCP) 2012-2016 for this age group and the chlorate levels as determined in the NVWA monitoring programme. In addition to foodstuffs specifically intended for young children (toddlers), this calculation also took into account exposure from other foodstuffs, such as vegetables, fruit, potatoes, and drinking water.

Please refer to Annex III for a detailed description of the exposure calculations of the four age groups and the five scenarios.

Risk characterisation
A key aspect in the risk assessment of the thyroid effects of chlorate is the iodine status of the exposed population. Given that Commission Delegated Regulation (EU) No 2016/127[17] sets out legal requirements for iodine levels for infant formula and follow-on formula, it is unlikely that this population has an iodine deficiency.

For the risk assessment, BuRO has assessed exposure at the health-based exposure limit for chronic exposure as established by EFSA at 3 µg/kg body weight per day for all age groups. Table 3 compares exposure calculated for the various age groups and scenarios up to 1 year old with this health-based exposure limit.

Table 3 Overview of the exposure from (follow-on) infant formula and ready-made solid baby food and comparison with the health-based exposure limit (3 µg/kg body weight per day) for infants up to 1 year old.

Age (months)	**Exposure in µg/kg body weight/day *(TDI exceedance factor)***				
	No chlorate in drinking water		6 µg/L drinking water		11 µg/L drinking water
	average	**high**	**average**	**high**	**worst-case**
0 - 4	0.6 (*0.2*)	3.7 (*1.2*)	1.1 (*0.4*)	5.1 (*1.7*)	6.3 (*2.1*)
4 - 6	0.6 (*0.2*)	6.3 (*2.1*)	1.2 (*0.4*)	7.0 (*2.3*)	7.5 (*2.5*)
6 - 12	0.7 (*0.2*)	8.3 (*2.8*)	1.1 (*0.4*)	8.8 (*2.9*)	9.2 (*3.1*)

The comparison of the calculated exposure with the health-based exposure limit shows that mean exposure and median residue concentrations for all age groups studied do not exceed the TDI. This also applies for the scenarios in which chlorate is present in the drinking water. The health risks in all of these scenarios is assessed as being negligible.

The high exposure estimates, based on high consumption quantities (P95 and feeding schedules) and P95 residue concentrations, exceed the TDI for all age

[17]COMMISION DELEGATED REGULATION (EU) 2016/127 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding.

groups – even if chlorate is not present in the drinking water. In these scenarios, health risks cannot be ruled out.

In accordance with the exposure calculations, Table 3 shows that the contribution from drinking water accounts for approximately 40 to 50% of total exposure for all age groups up to 1 year old, at mean exposure and chlorate levels of 6 µg/L. At higher consumption quantities and residue levels in infant formulae, the relative contribution from drinking water decreases.

RIVM calculated exposure from the total diet for 1 to 3 year olds (Annex III). In the most conservative scenario (based on the 95th percentile of the consumption distribution and upper-bound chlorate levels in the food and drinking water), exposure is 1.3 µg/kg body weight per day. This exposure is over a factor of 2 below the TDI. The health risks to this age group are therefore considered negligible.

Determination maximum chlorate levels in infant formula without TDI exceedance

Infants up to 1 year old
The exposure calculations for infants up to 1 year old were carried out based on the assumption that the foodstuffs contain a concentration of chlorate equivalent to the MRL of 0.01 mg/kg at high consumption quantities. As such, it is assumed that (follow-on) infant formula contains levels of 0.01 mg chlorate/kg in the prepared product (MRL is based on the levels in the product as it is consumed). The chlorate in the prepared formula originates both from the drinking water and powdered milk. These calculations show that the TDI of 3 µg/kg body weight/day is not exceeded for any of the age groups up to 1 year old. As such the current MRL provides sufficient protection (Table 4).

Table 4 Results of the exposure calculation for the age groups up to 1 year old if all foodstuffs contain chlorate levels equal to the MRL, TDI = 3 µg/kg bw/day.

Aged (months)	Exposure (µg/kg bw/day)[1]
0 - 4	2.9
4 - 6	1.6
6 - 12	1.5

[1] The exposure calculation assumed high consumption quantities, chlorate levels of 0.01 mg/kg in all foodstuffs; for (follow-on) infant formula these levels apply in the prepared food.

Subsequently, based on the same exposure calculations (high consumption quantities), it was assessed from which chlorate levels the TDI would be exceeded. This appears to be the case for all age groups at chlorate levels, in infant formula powder, follow-on infant formula powder and ready-made solid baby food, over **0.04 mg/kg** (please see Annex II for the underlying calculations). This was determined by fixing the concentration of all foodstuffs to this value in the exposure calculations and comparing the total intake with the TDI. This also involved the assumption that the drinking water contains chlorate levels of 0.006 mg/L. Levels of 0.04 mg/kg in powdered milk and levels of 0.006 mg/L in drinking water correspond to levels of 0.01 mg/kg in prepared (follow-on) infant formula (see Annex II). If drinking water does contain chlorate levels of 0.011 mg/L, the TDI will be exceeded at these levels in powder. However, BuRO considers this upper-bound value, based on targeted measurements, to be overly conservative for this determination, particularly given that chlorate will occasionally be present in Dutch drinking water.

Based on the NVWA dataset, it can be concluded that roughly a quarter of (follow-on) infant formula for children up to 1 year old contains chlorate levels of more than 0.04 mg/kg (6 of the 26 samples of infant formula and 8 of the 29 samples of follow-on formula). For ready-made solid baby food this is below 10%.

Young children between 12 and 36 months old
BuRO assessed whether the foregoing chlorate concentration of 0.04 mg/kg in commercially available foodstuffs intended for infants and young children may have an impact on young children (toddlers).

RIVM calculated that in upper-bound concentrations of chlorate in drinking water and the other foodstuffs, the P95 chlorate intake of toddlers aged 12 to 36 months old is equal to 1.3 (1.1–1.8) µg/kg body weight per day (RIVM, 2020a). By far the majority of this intake (65%) comes from drinking water, followed by 10% from follow-on milk (powder), 9% from fruit, 6% from cereals, 6% from vegetables, 3% from jars of solid food and 1% jars of fruit puree. These figures are based on the consumption data of the Dutch National Food Consumption Survey (VCP). If a toddler were to be fed with primarily commercially available foodstuffs, intake could be based on a manufacturer's feeding schedule. Based on feeding schedules and method, BuRO assumes that a toddler will eat one jar meal (250 grams), a fruit puree jar (200 grams) and drink 300 mL of follow-on milk (Nutrica, 2020a). Follow-on milk for toddlers contains 11.6 to 14.9 grams of powder per 100 mL (Nutrica, 2020b; Nutricia, 2020a). According to the VCP, toddlers between 12 and 36 months old eat roughly 10 grams of cereal-based products such as breakfast cereals, crackers and rusk (RIVM, 2020b). A toddler between 12 and 36 months old will have a body weight of 12 kg (EFSA, 2012). If the maximum chlorate concentration is 0.04 mg/kg, chlorate intake will be 0.023 mg/day (1.0 µg/kg body weight per day). Intake of chlorate from other foodstuffs will not result in exceedance of the TDI.

The TDI for toddlers may be exceeded if they join the family meal time routine and the chlorate concentration of the vegetables is high (e.g. 112 g spinach with a chlorate concentration of 0.32 mg/kg). The risk assessment of this aspect falls beyond the scope of this advice.

Uncertainties in the risk assessment
The health-based exposure limit is characterised by two major uncertainties. Based on the available data, it is unclear whether young children are more sensitive than adults to the effects of competitive inhibition of iodine uptake in the thyroid caused by chlorate. Secondly, in a general sense, the health-based guidance value do not always provide protection for children up to 4 months old. Based on the available literature, BuRO concludes that the TDI for the current risk assessment of this age group can be applied, however, given the sensitivity of this group, caution should continue to be exercised and more research into the long-term effects is required.

In addition, there are other uncertainties:

- For the age groups up to 1 year old, there are only six samples of ready-made solid fruit-based baby food and all these measurements are below the limit of detection (Table 1). Given that EFSA previously concluded that chlorate residues have been detected on (processed) fruit, this limited dataset may not provide an accurate representation of the chlorate levels in this product group (EFSA, 2015). No levels exceeding the LOQ were found on fruit in the available measurements conducted by the NVWA. More measurements in this product group should lead to a more reliable estimate.

- The contribution to exposure from cereal-based baby foodstuffs (porridges and biscuits) is limited for the age groups of 4 to 6 months and 6 to 12 months old, based on the current calculations. In relation to this product group, BuRO does not that the datasets are small and that a number of (very) high chlorate levels were measured in these foodstuffs. Additional measurements will help expand the dataset and allow the maximum chlorate concentrations to be ascertained better.

- The limited size of the dataset for fruit jars and biscuits also applies to the intake calculations for 1 to 3 year olds by RIVM (n=4).

- Regional differences apply to chlorate levels in Dutch drinking water. These differences are related to the application of chlorate (or absence thereof) in the disinfection of drinking water and the presence of chlorate in extracted surface water. In order to include these regional differences in the assessment of Dutch circumstances, BuRO has included the contribution of chlorate intake from drinking water in overall exposure.

Conclusions
Prolonged exposure to chlorate may lead to problems with thyroid function, particularly in sensitive groups, such as individuals with an iodine deficiency. Chlorate may be introduced into food by a variety of pathways and may accumulate during the production of food. Based on the NVWA dataset it can be concluded that formula and food for infants and toddlers regularly contains high levels of chlorate, making this a substantial source of exposure for young children.

For the risk assessment, BuRO has assessed exposure at the health-based exposure limit for chronic exposure as established by EFSA at 3 µg/kg body weight per day. In this risk assessment, BuRO assumes that this health-based standard provides protection for infants and toddlers in part due to the fact that iodine deficiency is unlikely due to the addition of iodine to infant formula. Targeted research into the long-term effects of chlorate exposure of young children, however, is not available.

The health-based exposure limit is not exceeded, in the case of exposure from foodstuffs with chlorate levels equal to the P50 of NVWA measurements, for all age groups up to 1 year old – even if the contribution of chlorate from drinking water is included. The risk of negative health effects in these scenarios is negligible in these scenarios. The health-based exposure limit is, however, exceeded, in the case of high consumption of foodstuffs with chlorate levels equal to the P95 of the NVWA measurements, for all age groups up to 1 year old – even without the contribution from drinking water. As such, health risks cannot be ruled out for prolonged consumption of these foodstuffs. For toddlers aged between 1 and 3, chlorate exposure from the total diet remains (well) below the health-based exposure limit. Chlorate levels in drinking water has a significant impact on overall exposure for all age groups studied.

Given the small size of the dataset, more measurement data is required from fruit-based baby food and cereal-based baby food. The contribution of the latter category to total exposure appears to be low based on the current calculations, but a number of (very) high chlorate levels have been measured in this product group.

If all foodstuffs were to comply with the applicable MRL of 0.01 mg/kg, the health-based exposure limit would not be exceeded in any of the age groups studied. Based on a relatively low chlorate concentration in the drinking water of the Netherlands of 6 µg/L, a chlorate concentration of 0.04 mg/kg for (follow-on) infant formula powder and solid baby and toddler food would not lead to the TDI being exceeded. For (follow-on) infant formula, this corresponds to a level of 0.01 mg/kg in the prepared product.

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Annex I. Literature review search strategy

Two searches were conducted for general information about chlorate in foodstuffs and specifically infant formula and toddler nutrition. A search for public scientific literature was carried out in the appropriate databases and a search for grey literature was carried out by way of a Google search.

1. The databases Pubmed and Scopus were used for the public literature. A search was carried out based on the following keywords in titles and/or abstract: chlorate AND residue; chlorate AND food; chlorate AND food (supply) chain; chlorate AND infant formula; chlorate AND toddler; chlorate AND milk; chlorate AND toxicology; chlorate AND iodine uptake; chlorate AND thyroid; chlorate AND health risk; chlorate AND risk assessment; chlorate AND food production; chlorate AND toxicology; chlorate AND breast milk.

2. The search functions of Google were used for the grey literature as well as the specific websites of authorities such as EFSA, ANSES, BfR, FDA and Health Canada.

For information on the effects of chlorate on the thyroid and the development of infants, a search was carried out on PubMed using ((thyroid[Title/Abstract]) AND (hormone[Title/Abstract])) AND (chlorate[Title/Abstract]) and Google scholar (thyroid hormone chlorate newborns).

Annex II. Calculation of maximum chlorate levels were the TDI is not exceeded

<u>Infants up to 4 months</u>
Body weight: 4.8 kg
Intake per day from drinking water: 1128 mL x 0.006 µg/ml = 6.768 µg/day
TDI: 3 µg/kg bw/day x 4.8 kg= 14.4 µg/day
Quantity of powdered milk 3.59 g powdered milk/kg bw per day x 4.8 kg = 172.32 g powder/day.

14.4 µg/day - 6.768 µg/day from drinking water = 172.32 g powder/day x Y (maximum concentration in powder). Y = 0.044 mg/kg in powder.

<u>Conclusion: maximum of 0.04 mg/kg in powder. This value will be used for further calculations.</u>

The corresponding level in the prepared product is therefore 14.4 µg / 1128 mL = 0.013 µg/mL ~0.013 mg/kg.

<u>Infants from 4 to 6 months</u>
Body weight: 6.95 kg
Intake per day from drinking water: 720 mL x 0.006 µg/ml = 4.32 µg/day
Intake per day from powder: 110.4 g powder x 0.04 µg/g = 4.416 µg/day
Total intake from infant formula: 8.736 µg/day
The corresponding level in prepared infant formula is therefore is 8.736 µg/ 720 mL= 0.012 µg/mL ~0.012 mg/kg

Consumption of solid baby food: 125 g vegetables and 125 g fruit= 250 g/ day total
TDI: 3 µg/kg bw/day x 6.95 kg= 20.85 µg/day.

Flexibility in TDI excluding infant formula: 20.85 – 8.736 = 12.114 µg/day
Maximum level in solid baby food = 12.114 µg/ 0.250 kg = 48.5 µg/kg = 0.048 mg/kg.

<u>Infants from 6 to 12 months</u>
Body weight: 8.4 kg
Intake from (follow-on) infant formula equal to previous group: 8.736 µg/day

TDI: 3 µg/kg bw/day x 8.4 kg= 25.2 µg/day.

Consumption of solid baby food: 200 g vegetables, 200 g fruit and 10 g cereals = 410 g/day total.

Flexibility in TDI excluding infant formula: 25.2 – 8.736 = 16.464 µg/day
Maximum level in solid baby food = 16.464 µg/ 0.410 kg= 40 µg/kg = 0.040 mg/kg.

Annex III. Exposure calculations

For the purposes of the exposure calculations, BuRO differentiated between four key age groups. The classification of these groups was based on differences in consumption patterns and body weight of the children. This classification is similar to the age ranges used by EFSA when assessing the exposure of young children to pesticides (EFSA, 2018). For the purposes of the exposure calculations, five scenarios were subsequently developed for the age groups up to 1 year old:

A. an average exposure estimate based on common consumption quantities, based on various data sources and median (P50) chlorate levels based on the NVWA data. This calculation assumes that there is usually no chlorate present in the drinking water.
B. an average exposure estimate based on common consumption quantities, based on various sources and median (P50) chlorate levels based on the NVWA data. This calculation assumes that chlorate is present in the drinking water (medium-bound average of targeted measurements; 6 µg/L);
C. a high exposure estimate based on high consumption quantities and the P95 of the residue levels identified. This calculation assumes that there is usually no chlorate present in the drinking water.
D. a high exposure estimate based on high consumption quantities and the P95 of the residue levels identified. This calculation assumes that chlorate is present in the drinking water (medium-bound average of targeted measurements; 6 µg/L); and
E. a worst-case exposure estimate in which, in addition to high consumption quantities and the P95 of the residue levels identified, a very high concentration of chlorate is also present in the drinking water (upper-bound average of targeted measurements; 11 µg/L).

Exposure for the total diet was calculated by RIVM for 1 to 3 year olds (RIVM, 2020a). This calculation was made on the basis of the Dutch National Food Consumption Survey (VCP) 2012-2016 for this age group and the chlorate levels as determined in the NVWA monitoring programme. In addition to foodstuffs specifically intended for young children (toddlers), this calculation also took into account exposure from other foodstuffs, such as vegetables, fruit, potatoes, and drinking water.

Age group 1: infants from 0 to 4 months who exclusively consume infant formula
EFSA has determined that for the risk assessment for infants up to 4 months, a consumption of 200 to 260 mL/kg body weight per day can be used as a conservative mean and for high consumption quantities for non-accumulating substances in infant formula (EFSA, 2017). EFSA derived the highest consumption quantity from the P95 intake of infants between 14 and 27 days old (the group with the highest intake per kg body weight). Based on an analysis conducted by BuRO of the method for the preparation of infant formula, it is estimated that a dry weight of 13.8 grams of formula is used per 100 mL of infant formula for this age group (Nutricia, 2020b). According to the instructions for the preparation of infant formula, tap water must be boiled. Given the chemical properties of chlorate, it is assumed that boiling will not affect chlorate levels.

Furthermore, this exposure estimate assumes that the amount of chlorate in Dutch drinking water is usually negligible. The mean upper-bound concentration in conjunction with the presence of chlorate in Dutch drinking water during targeted measurements was established by RIVM at 11 µg/L (RIVM, 2020a). This concentration was chosen as the conservative upper bound for chlorate levels in drinking water. The medium-bound mean of 6 µg/L determined by RIVM is included in the mean intake calculation. The variables for the exposure calculation are listed in Table III.1.

Table III.1 Variables as used in the exposure estimate for infants up to 4 months old

	Average intake	**High intake**
Intake of infant formula	200 mL/kg bw/day	260 mL/kg bw/day
Intake of drinking water [1]	180 mL/kg bw/day	235 mL/kg bw/day
Amount of powder [1]	27.6 grams/kg bw/day	35.9 grams/kg bw/day
Chlorate levels of infant formula	0.02 mg/kg[2]	0.104 mg/kg[3]
Chlorate levels of drinking water	absent and 0.006 mg/L[4]	absent, 0.006mg/L[4] and 0.011 mg/L [5]

[1] The method for the preparation of infant formula is based on instructions issued by producers. This assumes that one level measured scoop of solid product is equal to 4.6 grams (Nutricia, 2020b).
[2] P50 of the chlorate residues found in this product group by the NVWA.
[3] P95 of the chlorate residues found in this product group by the NVWA.
[4] Medium-bound scenario of the mean chlorate levels detected in targeted measurements of Dutch drinking water.
[5] Upper-bound scenario of the mean chlorate levels detected in targeted measurements of Dutch drinking water.

Scenario A
Mean exposure per kg body weight is: (0 µg/ML x 180 mL) chlorate from drinking water + (0.02 µg/g x 27.6 g) from infant formula with average levels of chlorate of = **0.6 µg chlorate/kg body weight/day**.

Scenario B
Mean exposure per kg body weight is: (0.006 µg/ML x 180 mL) chlorate from drinking water + (0.02 µg/g x 27.6 g) from infant formula with average levels of chlorate of = **1.1 µg chlorate/kg body weight/day**.

Scenario C
High exposure per kg body weight is: (0 µg/ML x 235 mL) chlorate from drinking water + (0.104 µg/g x 35.9 g) from infant formula with high levels of chlorate of = **3.7 µg chlorate/kg body weight/day**.

Scenario D
High exposure per kg body weight is: (0,006 µg/ML x 235 mL) chlorate from drinking water + (0.104 µg/g x 35.9 g) from infant formula with high levels of chlorate of = **5.1 µg chlorate/kg body weight/day**.

Scenario E
Worst-case exposure per kg body weight is: (0,011 µg/ML x 235 mL) chlorate from drinking water + (0.104 µg/g x 35.9 g) from infant formula with high levels of chlorate of = **6.3 µg chlorate/kg body weight/day**.

Assuming a TDI of 3 µg/kg body weight per day, this TDI is reached in the event of a chlorate concentration of 0.04 mg/kg in infant formula (high level of intake) if the drinking water used has a chlorate concentration of 6 µg/L and 0.01 mg/kg if the concentration of chlorate in the drinking water used is 11 µg/L.

Age group 2: infants between 4 to 6 months old, infant formula and solid baby food

For this age group it is assumed that children between the ages of 4 to 6 months will start eating ready-made solid food in addition to infant formula. According to the feeding schedules of manufacturers, an infant of this age will consume four servings of 200 mL of infant formula and 125 grams of vegetables and 125 grams of fruit per day – possibly in the form of jars of solid baby food (Nutrica, 2020a). Based on an analysis conducted by BuRO of the recipe for the preparation of infant formula, it is estimated that a dry weight of 13.8 grams of formula is used per 100 mL of infant formula for this age group (Nutricia, 2020b). The variables for the exposure calculation are listed in Table III.2.

BuRO notes that the small dataset for fruit-based baby food (fruit pouches) may not provide an accurate or complete picture of chlorate levels in this product group. There are only six measurements available in total, of which two are for foodstuffs for this age group. None of the foodstuffs revealed chlorate levels exceeding the LOD. The contribution of these foodstuffs to overall chlorate exposure may be underestimated, in particular because chlorate is also found on (processed) fruit (EFSA, 2015), although the 25 samples from the NVWA database all were below the LOQ. In the present calculations, the concentration in these foodstuffs is set at the value of the LOQ (high level of intake) and LOD (average intake) of the analytical method.

No samples were taken from vegetable snacks for the age group of 4 to 6 months, which is why this exposure calculation is based on the assumption that the residue measurements in the vegetable snacks intended for infants aged 6 to 12 months are also representative of this age group.

For this age group, chlorate intake from cereal-based baby food has not been taken into account. For biscuits, there is only 1 measurement available with a very high concentration (0.225 chlorate mg/kg), which is unlikely to be a representative level, particularly given that measurements in biscuits for the age group of 6 to 12 months are all below the LOD (Table 1). As such, more measurements are required for this food group. As regards the porridges, all measurements of foodstuffs for this age group are below the limit of detection and the intake of these foodstuffs is expected to be low, resulting in the contribution to total exposure being considered low. However, this assumption is based on a small dataset.

Table III.2 Variables as applied in the exposure estimate for infants between 4 to 6 months old. The chlorate levels in the foodstuffs have been based on the P50 of the NVWA residue measurements for the mean intake calculation; the P95 was used for the high intake calculations.

	Average intake	**High intake**
Body weight	6.95 kg	6.95 kg
Intake of infant formula	800 mL/day	800 mL/day
Intake of drinking water [1]	720 mL/day	720 mL/day
Amount of powder [1]	110.4 grams/day	110.4 grams/day
Chlorate levels of infant formula	0.02 mg/kg	0.104 mg/kg
Chlorate levels of drinking water	absent and 0.006 mg/L4	absent, 0.006 mg/L and 0.011 mg/L
Portion size of solid baby food	125 grams/day	125 grams/day
Chlorate levels jars of vegetable puree[2]	0.01 mg/kg	0.25 mg/kg
Chlorate levels jars of fruit puree[3]	0.005 mg/ kg (LOQ)	0.01 mg/kg (LOD)

[1] The method for the preparation of infant formula is based on instructions issued by producers. This assumes that one level measured scoop of solid product is equal to 4.6 grams (Nutricia, 2020b).
[2] Based on the measurements of vegetable puree snacks intended for the age group of 6 to 12 months old.
[3] Based on six measurements of foodstuffs intended for infants between 4 and 12 months old.

Scenario A:
Mean exposure: (0 µg/mL x 720 mL) from drinking water + (0.02 µg/g x 110.4 g) from infant formula = 2.2 µg chlorate/day from infant formula.
Mean exposure from ready-made solid baby food (vegetable) is µg/kg vegetable snack x 0.125 kg = 1.25 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 5 µg/kg x 0.125 kg = 0.6 µg chlorate/day.
Total mean exposure is then 2.2 + 1.25 + 0.6 = 4.1 µg chlorate/day.

According to the standard values used by EFSA in a risk assessment, an infant between 0 and 12 months old will have a body weight of 5 kg (EFSA, 2012). EFSA makes no further distinction in terms of smaller age groups as is envisaged in these exposure calculations. For that reason, BuRO has used the average Dutch body weights as reported by Ouders van nu (Ouders van nu, 2020). According to this source, the average body weight for infants aged 4 to 6 months is 6.95 kg.

As such, mean exposure is 4.1 µg chlorate/6.95 kg body weight = 0.6 µg chlorate/kg body weight/day.

Scenario B
Mean exposure is: (0,006 µg/mL x 720 mL) from drinking water + (0.02 µg/g x 110.4 g) from infant formula = 6.5 µg chlorate/day from infant formula.
Mean exposure from ready-made solid baby food (vegetable) is µg/kg vegetable snack x 0.125 kg = 1.25 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 5 µg/kg x 0.125 kg = 0.6 µg chlorate/day.
Total mean exposure is then 6.5 + 1.25 + 0.6 = 8.4 µg chlorate/day.

As such, mean exposure is 8.4 µg chlorate/6.95 kg body weight = 1.2 µg chlorate/kg body weight/day.

Scenario C
High exposure is: (0 µg/mL x 720 mL) from drinking water + (0.104 µg/g x 110.4 g) from infant formula = 11.5 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.125 kg = 31.3 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.125 kg = 1.3 µg chlorate/day.
Total exposure is then 11.5 + 31.3 + 1.3 = 44.1 µg chlorate/day.

The high level of exposure is then 44.1 µg chlorate/6.95 kg body weight = 6.3 µg chlorate/kg body weight/day.

Scenario D
High exposure is: (0,006 µg/mL x 720 mL) from drinking water + (0.104 µg/g x 110.4 g) from infant formula = 15.8 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.125 kg = 31.3 µg chlorate/day.
High exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.125 kg = 1.3 µg chlorate/day.
Total, high level of exposure is then 15.8 + 31.3 + 1.3 = 48.4 µg chlorate/day.

The high level of exposure is then 48.4 µg chlorate/6.95 kg body weight = 7.0 µg chlorate/kg body weight/day.

The intake of 125 grams of vegetables from a jar that contains 0.25 mg chlorate/kg therefore exceeds the TDI.

Scenario E
Exposure is: (0,011 µg/mL x 720 mL) from drinking water + (0.104 µg/g x 110.4 g) from infant formula = 19.4 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.125 kg = 31.3 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.125 kg = 1.3 µg chlorate/day.
Total exposure is then 19.4 + 31.3 + 1.3 = 52 µg chlorate/day.

The worst case exposure is the 52 µg chlorate/6.95 kg body weight = 7.5 µg chlorate/kg body weight/day.

The TDI is exceeded for infants aged 4 to 6 months in the case of a high level of intake. Based on a maximum concentration of chlorate of 0.01 mg/kg in jars of vegetable and fruit puree, the maximum chlorate concentration in milk powder would be allowed to be 0.10 and 0.07 mg/kg respectively for drinking water concentrations of 6 and 11 µg/L. In the event that jars of vegetable and fruit puree contain up to 0.04 mg/kg of chlorate, this is 0.04 and 0.004 mg/kg.

Age group 3: infants aged 6 to 12 months, follow-on formula and solid baby food
In this scenario, children between 6 and 12 months old are expected to consume follow-on infant formula and ready-made solid baby food. According to the feeding schedule of manufacturers, an infant of this age consumes two to three feeds of 200 mL of follow-on formula and 200 grams of vegetables and 200 grams of fruit per day, depending on their age, possibly in the form of jars of solid baby food (Table III.3). In addition, one serving of 5 to 10 grams of cereals (porridges

prepared with the follow-on formula) is part of the feeding schedule (Nutrica, 2020a). Based on an analysis conducted by BuRO of the method for the preparation of infant formula, it is estimated that a dry weight of 13.8 grams of formula is used per 100 mL of infant formula for this age group (Nutricia, 2020b). The variables for the exposure calculation are listed in Table III.3.

The limitations of the small dataset for fruit-based baby food (fruit puree snacks) similarly applies to this age group. In total only six samples were available, of which four for foodstuffs intended for this age group. No chlorate levels over the LOD were found in any of the products. The contribution of these foodstuffs to overall chlorate exposure may be underestimated, particularly because chlorate has also been detected on (processed) fruit. In the present calculations, the concentration in these foodstuffs is equated to the LOQ of the analytical method.

In this exposure calculation, no distinction is made for vegetable puree snacks between vegetable puree snacks and meals (containing meat of fish). The measurement results in these product groups (Table 1) have been combined for the exposure calculation.

The limited dataset for chlorate residues in baby biscuits does not contain any measurements exceeding the limit of detection. Given that the intake amounts are also considered to be small, it is estimated that the contribution of this product to total chlorate exposure will be minor. Nevertheless, additional measurements in this product group are required in order to get a more accurate picture of the chlorate levels in these foodstuffs.

Scenario A
Mean exposure is: (0 µg/mL x 540 mL) from drinking water + (0.02 µg/g x 82.2 g) from infant formula = 1.6 µg chlorate/day from infant formula.
Mean exposure from ready-made solid baby food (vegetable) is 10 µg/kg vegetable snack x 0.200 kg = 2 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.200 kg = 2 µg chlorate/day.
Mean exposure from cereals (porridge) is 10 µg/kg x 0.005 kg = 0.05 µg chlorate/day.
Total mean exposure is then 1.6 + 2 + 2 + 0.05 = 5.7 µg chlorate/day.

According to the standard values used by EFSA in a risk assessment, an infant between 0 and 12 months old will have a body weight of 5 kg (EFSA, 2012). EFSA makes no further distinction in terms of smaller age groups as is envisaged in these exposure calculations. For that reason, BuRO has used the average Dutch body weights as reported by Ouders van nu (Ouders van nu, 2020). According to this source, the average body weight for infants aged 6 to 12 months is 8.4 kg.

As such, mean exposure is 5.7 µg chlorate/8.4 kg body weight = **0.7 µg chlorate/kg body weight/day.**

Table III.3 Variables as applied in the exposure estimate for infants between 6 to 12 months old. The chlorate levels in the foodstuffs have been based on the P50 of the NVWA residue measurements for the mean intake calculation; the P95 was used for the high intake calculations.

	Average intake	**High intake**
Body weight	8.4 kg	8.4 kg
Intake of follow-on formula	600 mL/day (3 servings of 200 mL)	800 mL/day (4 servings of 200 mL)
Intake of drinking water [1]	540 mL/day	720 mL/day
Amount of powder [1]	82,2 grams/day	110.4 grams/day
Chlorate levels in follow-on formula	0.02 mg/kg	0.16 mg/kg
Chlorate levels of drinking water	absent and 0.006 mg/L	absent, 0.006 mg/L and 0.011 mg/L
Portion size solid baby food	200 grams/day	200 grams/day
Chlorate levels in jars of vegetable puree or meal[2]	0.01 mg/kg	0.25 mg/kg
Chlorate levels jars of fruit puree[3]	0.01 mg/kg (LOD)	0.01 mg/kg (LOD)
Serving size cereal porridge	5 grams/day	10 grams/day
Chlorate levels in cereals (porridge)	0.01 mg/kg	0.02 mg/kg

[1] The method for the preparation of infant formula is based on instructions issued by producers. This assumes that one level measured scoop of solid product is equal to 4.6 grams (Nutricia, 2020b).
[2] Based on the 62 measurements in jars of vegetable puree and meals combined (Table 1).
[3] Based on six measurements of foodstuffs intended for infants between 4 and 12 months old.

Scenario B
Mean exposure is: (0,006 µg/mL x 540 mL) from drinking water + (0.02 µg/g x 82.2 g) from infant formula = 4.8 µg chlorate/day from infant formula.
Mean exposure from ready-made solid baby food (vegetable) is 10 µg/kg vegetable snack x 0.200 kg = 2 µg chlorate/day.
Mean exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.200 kg = 2 µg chlorate/day.
Mean exposure from cereals (porridge) is 10 µg/kg x 0.005 kg = 0.05 µg chlorate/day.
Total mean exposure is then 4.8 + 2 + 2 + 0.05 = 8.9 µg chlorate/day.

As such, mean exposure is 8.9 µg chlorate/8.4 kg body weight = **1.1 µg chlorate/kg body weight/day.**

Scenario C
High exposure is: (0 µg/mL x 720 mL) from drinking water + (0.16 µg/g x 110.4 g) from infant formula = 17.7 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.200 kg = 50 µg chlorate/day.
High exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.200 kg = 2 µg chlorate/day.
High exposure from cereals (porridge) is 20 µg/kg x 0.010 kg = 0.2 µg/kg chlorate/day.
Total exposure is then 17.7 + 50 + 2 + 0.2 = 69.9 µg chlorate/day.

The high level of exposure is then 69.9 µg chlorate/8.4 kg body weight = 8.3 µg chlorate/kg body weight/day.

Scenario D
High exposure is: (0,006 µg/mL x 720 mL) from drinking water + (0.16 µg/g x 110.4 g) from infant formula = 22 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.200 kg = 50 µg chlorate/day.
High exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.200 kg = 2 µg chlorate/day.
High exposure from cereals (porridge) is 20 µg/kg x 0.010 kg = 0.2 µg/kg chlorate/day.
Total exposure is then 22 + 50 + 2 + 0.2 = 74.2 µg chlorate/day.

The high level of exposure is then 74.2 µg chlorate/8.4 kg body weight = 8.8 µg chlorate/kg body weight/day.

Scenario E
Exposure is: (0,011 µg/mL x 720 mL) from drinking water + (0.16 µg/g x 110.4 g) from infant formula = 25,6 µg chlorate/day from infant formula.
High exposure from ready-made solid baby food (vegetable) is 250 µg/kg vegetable puree snack x 0.200 kg = 50 µg chlorate/day.
High exposure from ready-made solid baby food (fruit) is 10 µg/kg x 0.200 kg = 2 µg chlorate/day.
High exposure from cereals (porridge) is 20 µg/kg x 0.010 kg = 0.2 µg/kg chlorate/day.
Total exposure is then 25.6 + 50 + 2 + 0.2 = 77.8 µg chlorate/day.

The worst case exposure is the 77,8 µg chlorate/8.4 kg body weight = **9.2 µg chlorate/kg body weight/day.**

These calculations show that the contribution of cereal-based baby food (porridge) is relatively small. BuRO does, however, note that occasionally (very) high levels have been measured in this product category. As such, more measurements in this product group are required in order to gain a more accurate picture.

If the chlorate concentration in (jars) of vegetable and fruit puree were 0.01 mg/kg, the maximum concentration in powdered milk would be allowed to be 0.15 and 0.12 mg/kg at 6 and 11 µg/L chlorate in the water respectively. For a chlorate concentration in (jars) of vegetable and fruit puree of 0.04 mg/kg, the maximum concentration in powdered milk would be allowed to be 0.04 and 0.01 mg/kg for 6 and 11 µg/L chlorate in the water respectively.

Age group 4: young children (toddlers) 1 to 3 years old, exposure from total diet
RIVM calculated exposure to chlorate from the total diet for 1 to 3 year olds (toddlers from 12 to 36 months old) based on the Dutch National Food Consumption Survey (VCP) 2012-2016 (RIVM, 2020a). This approach also includes exposure from foodstuffs such as vegetables, fruit, potatoes and drinking water in addition to chlorate exposure from foodstuffs specifically intended for toddlers.
The VCP contains information on the dietary intake of 440 children for this age group, measured over two non-consecutive days in the 2012-2016 period. Chlorate levels in the various foodstuffs come from the NVWA monitoring data for the period of 2016 up to and including 2019.

FO conducted upper-bound, medium-bound and lower-bound calculations for both the scenario in which chlorate is not present in the drinking water and for the scenario in which chlorate is present in the drinking water (RIVM, 2020a). The exposure estimate in the various scenarios is summarised in Table III.4. The lower-bound calculation assumes that for all samples in which chlorate levels are below the limit of quantification (LOQ), the concentration is equal to the limit of detection (LOD) and levels below the LOD are equated to 0 mg/kg. The upper-bound calculation assumes that chlorate levels below the limit of detection (LOD) are equal to the LOD, and levels between the LOD and LOW are equal to the LOQ, whereas the medium-bound calculation uses ½ LOD and ½ LOQ respectively for these samples. The calculations used chlorate levels in the drinking water to the amount of 1 µg/L in the lower-bound, 6 µg/L in the medium-bound and 11 µg/L in the upper-bound scenario. Detailed information regarding these figures was previously outlined in the section on chlorate levels in Dutch drinking water.

Table III.4 Exposure to chlorate for toddlers between 12 and 36 months old from total diet.

Percentile of consumption distribution	**Exposure in µg/kg bw/day** ***(95% confidence interval)***		
	lower-bound	**medium-bound**	**upper-bound**
No chlorate present in drinking water			
P50	0.05 *(0.01—0.10)*	0.08 (0.05—0.13)	0.13 (0.10—0.17)
P95	0.60 *(0.25—0.98)*	0.60 (0.30—1.0)	0.68 (0.40—1.1)
Chlorate present in drinking water			
P50	0.08 (0.06—0.13)	0.30 (0.27—0.34)	0.52 (0.49—0.57)
P95	0.65 (0.29—1.0)	0.95 (0.64—1.4)	1.3 (1.1—1.8)

RIVM's calculations show that follow-on infant formula, drinking water and foodstuffs based on cereals (porridge) make the highest contribution to the overall chlorate exposure of 1 to 3 year olds in the scenario where chlorate is present in drinking water. Although all measurements conducted by the NVWA in fruit were below the LOD and LOQ, this product group appears likewise to make a significant contribution in the medium-bound and upper-bound calculations – this is potentially due to the high levels of intake of the product group. In the scenario in which chlorate is present in the drinking water, the contribution of drinking water to the total exposure is 22% at a level of 1 µg/L, 57% at a level of 6 µg/L and 65% at a level of 11 µg/L. For the situation in the Netherlands, these calculations are conservative given that most drinking water does not contain chlorate.