Rapport 1 – 2013

Contaminants and minerals in foods for infants and young children

Part 2: Risk and benefit assessment

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Abbreviations

AI Adequate intake, the average observed daily level of intake by a population group of apparently healthy people, used when a population reference intake cannot be determined
Acute RfD Acute reference dose, an estimate of a daily oral exposure for an acute duration (24 hours or less) to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime
As(III) Arsenite (arsenous acid)
As(V) Arsenate(arsenic acid)
ATSDR Agency for Toxic Substances and Disease Registry (USA)
BMD Benchmark dose, the dose of a substance that is expected to result in a predetermined level of an adverse effect (called the benchmark response, BMR)
BMDL Lower confidence limit of the benchmark dose
BW Body Weight
CONTAM Panel EFSA´s Panel on Contaminants in the Food Chain
DMA Dimethylarsinic acid
EC European Commission
EFSA European Food Safety Authority
ESPGHAN The European Society of Paediatric Gastroenterology, Hepatology and Nutrition
EPA Environmental Protection Agency (USA)
EU European Union
FAO Food and Agriculture Organization of the United Nations
FSA Food Standards Agency (United Kingdom)
FSMP Foods for Special Medical Purposes
IARC International Agency for Research on Cancer (France)
IC-PMS Inductively Coupled Mass Spectrometry
ICT Idiopathic Copper Toxicosis
IMM Institute of Environmental Medicine; Karolinska Institutet (Sweden)
IOM Institute of Medicine (USA)
IQ Intelligence Quotient
JECFA Joint FAO/WHO Expert Committee on Food Additives
LBW Low Birth Weight, defined as <2.5 kg
LOAEL Lowest observed adverse effect level, the lowest dose associated with negative health effects/toxic effects
LOQ Limit of Quantification
MMA Methylarsonic acid
MRL Maximum Residue Limit
MOE Margin of exposure, the ratio between a defined point on the dose-response curve for the adverse effect and the human intake
NAG N-acetyl glucosaminidase
NFA National Food Agency (Sweden)

NOAEL No observed adverse effect level - the highest dose not associated with negative health effects/toxic effects
NRC The National Research Council (USA)
NNR Nordic Nutrition Recommendations
PCBF Processed Cereal-based Foods
PTWI Provisional tolerable weekly intake
PKU Phenylketonuria
RI Recommended Intake, expressed as average daily intake over time
RP Reference Point, The NOAEL and/or the LOAEL for the critical effect of a substance, forms the reference point for a risk assessment of a chemical in food. when animal data have to be used.
RR Relative Risk, the ratio of the risk of disease in exposed individuals to the risk of disease in non-exposed individuals
SCF Scientific Committee on Food (EU)
SMR Standardized Mortality Ratio, a ratio between the observed number of deaths in an study population and the number of deaths that would be expected.
SNR Swedish Nutrition Recommendations
TDI Tolerable Daily Intake, an estimate of the amount of a substance in food or drinking water, expressed on a body mass basis (usually mg/kg body weight), which can be ingested daily over a lifetime by humans without appreciable health risk
TWI Tolerable Weekly Intake, an estimate of the amount of a substance in food or drinking water, expressed on a body mass basis (usually mg/kg body weight), which can be ingested weekly over a lifetime by humans without appreciable health risk
WHO World Health Organization
UL Upper Level, according to EFSA (2006) the maximum chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans

Summary and conclusions

Infants and young children are often regarded as two particularly vulnerable groups in terms of food safety. They may be at risk of high exposures to contaminants and minerals at sensitive developmental stages. Also, the requirements for essential nutrients due to their rapid growth and development make them vulnerable to deficiencies of essential minerals.

In the present survey the National Food Agency (NFA) analysed and assessed contaminants and minerals in infant formulae and certain foods for children. The analysed items cover the relevant products from all producers present in the Swedish market in spring 2011. In total 92 different products were analysed for arsenic, cadmium and lead unintentionally present in foods, so-called contaminants, as well as the essential minerals manganese, iron and copper. The result of the project is presented in one report with three parts:

- Contaminants and minerals in foods for infants and young children – analytical results, Rapport 1/2013, Part 1 (1)
- Contaminants and minerals in foods for infants and young children – risk and benefit assessment, Rapport 1/2013, Part 2
- Contaminants and minerals in foods for infants and young children – risk and benefit management, Rapport 1/2013, Part 3 (2)

In the present report, Part 2, intakes of the selected contaminants and minerals from the analysed products were assessed following the principles of risk analysis. Intakes of the contaminants arsenic, cadmium and lead were compared with the available tolerable intakes or reference points. For the essential minerals manganese, iron and copper, intakes were discussed in relation to recommended daily intakes and tolerable upper levels or tolerable daily intakes, when these values were available. The chemical analyses are presented in report Part 1 (1). Risk management and assessment of compliance with legislation were carried out by the NFA in processes parallel to this project and is presented in a separate report, Part 3 (2).

The results from the risk assessment show that rice-based infant food purchased in Sweden could be a significant exposure source of inorganic arsenic. Arsenic levels in rice drinks exceed the EU standard value of 10 µg/L in drinking water. The estimated intakes per portion (1 dl) from rice-based infant food are close to the lower confidence limit on the benchmark dose ($BMDL_{01}$) value identified by European Food Safety Authority (EFSA).

The estimated cadmium intakes were below the tolerable daily intake (TDI) for all products. However, a number of uncertainties exist regarding the level of protection provided to infants and children from the TDI established by EFSA. The rea-

sons are that cadmium uptake is probably higher in children compared to adults, and it may be discussed if the TDI covers all potential health effects associated with cadmium exposure restricted to early-life. Based on this, consideration of an extra margin to the established cadmium TDI in the case of children may be needed.

For lead, EFSA regards that a margin to the reference point (RP) of a factor of 10 or more would ensure that there is no appreciable risk for a clinically significant effect on intelligence quotient (IQ) in children. For foods for special medical purposes (FSMP) used as the sole source of nutrition, the margin to the RP was generally lower than a factor of 10. It should be noted that there is already a potential concern for effects on neurodevelopment at current levels of exposure to lead for infants and children. This suggests that the exposure to lead should be reduced as much as possible.

From a nutritional point of view, the intakes of manganese, iron and copper from the analysed products were found to be adequate. However, some uncertainties exist about the dietary manganese requirements of infants and young children. The exposure assessment also identified potential problems with high manganese intakes from some gruels and porridge products and FSMP products when comparing with the TDI established by the World Health Organization (WHO). However, this TDI for manganese was based on weak scientific evidence and should not be considered as a definite level under which there is no reason for concern. Copper intakes from some FSMP products were high compared to upper level (UL) for children from 1 year of age. Intakes of manganese and copper from infant and follow-on formulae were not of concern compared to the currently available reference values.

During the assessment of intakes of the minerals some shortcomings of existing data were revealed. In order to evaluate if the concentration of a mineral in particular food products is within the acceptable or optimal range, upper and lower levels of intakes must be established. We conclude that a revision of the AI and an establishment of an UL or corresponding values for manganese are urgently needed in order to define an optimal range of manganese concentrations in products intended for infants and young children. Also, an UL for iron for infants and young children and an UL for copper for infants below the age of 1 year must be established. Risk-benefit assessments are needed for manganese, iron and copper in relation to estimated intakes by infants and young children and should be undertaken by researchers or international expert groups. Such assessments are essential for updated legislation and control in order to ensure adequate and safe foods for infants and young children.

It is alarming that products intended for use by infants and young children contain such amounts of contaminants that they potentially could result in adverse health effects. These age groups are particularly vulnerable to exposures of certain contaminants and minerals and effects on development may be irreversible. We call for

action to use presently available methods to reduce concentrations of contaminants such as arsenic and lead in foods intended for infants and young children. Furthermore, we urge that health-based guidance values for children's cadmium exposure and for low and high intakes of essential minerals be updated in order to ensure adequacy and safety of foods for infants and young children.

Sammanfattning och slutsatser

Barn under tre år, i synnerhet spädbarn, kan löpa hög risk att drabbas av negativa hälsoeffekter om de utsätts för kontaminanter och höga halter av mineraler vid vissa viktiga stadier i utvecklingen. I den åldern kan barn också lättare få brist på essentiella mineraler på grund av hög tillväxttakt och stort näringsbehov under utvecklingen.

I den här studien har Livsmedelsverket analyserat kontaminanter och mineraler i modersmjölksersättningar, grötar, vällingar och andra produkter som kan konsumeras av spädbarn och småbarn. De analyserade produkterna kommer från alla producenter som fanns representerade på den svenska marknaden våren 2011. Halterna av kontaminanterna arsenik, kadmium och bly samt de essentiella mineralerna mangan, järn och koppar analyserades i 92 produkter.

Resultatet från Livsmedelsverkets studie presenteras i tre delrapporter:

- Contaminants and minerals in foods for infants and young children – Analytical results, Rapport 1/2013, Part 1(1)
- Contaminants and minerals in foods for infants and young children – risk and benefit assessment, Rapport 1/2013, Part 2
- Contaminants and minerals in foods for infants and young children – risk and benefit management, Rapport 1/2013, Part 3(2). Finns även på svenska – Kontaminater och mineraler i livsmedel för spädbarn och småbarn. Del 3 Hanteringsrapport, Rapport 1/2013.

I denna rapport, dvs delrapport 2, presenteras Livsmedelsverkets värdering av riskerna och nyttan med de funna nivåerna av kontaminanter och mineraler i produkterna enligt riskanalysens principer. I värderingen har det uppskattade intaget från produkterna och risken för hälsoeffekter bedömts när det gäller höga intag av kontaminanter och mineraler samt låga intag av mineraler. I delrapport 1 (1) redovisas halterna från de kemiska analyserna och i delrapport 3 (2) presenteras riskhanteringen, det vill säga vilka åtgärder Livsmedelsverket avser att vidta och de överväganden som ligger till grund för dessa.

Resultaten från riskvärderingen visar att risbaserade produkter köpta i Sverige kan vara en betydande källa till oorganisk arsenik. Denna studie visar att koncentrationen av arsenik i risdrycker kan vara högre än EU:s gränsvärde för dricksvatten, som är 10 mikrogram/liter. Det uppskattade intaget av arsenik från en deciliter av risbaserad dryck ligger nära det referensvärde för negativa hälsoeffekter som identifierats av den europeiska myndigheten för livsmedelssäkerhet, Efsa.

Det uppskattade intaget av kadmium underskred det så kallade tolerabla dagliga intaget (TDI) för alla analyserade produkter. Det är dock oklart om kadmiumni-

våer under det TDI som fastställts av Efsa innebär att spädbarn och små barn skyddas mot negativa hälsoeffekter av kadmium. Orsakerna till att detta är tveksamt är att kadmiumupptaget sannolikt är högre hos barn än hos vuxna, och att TDI kanske inte inbegriper alla de hälsoeffekter som är associerade med intag av kadmium tidigt i livet. Man bör därför överväga en extra marginal för barns intag av kadmium till det TDI som gäller för vuxna.

Efsa anser att ett intag av bly som ligger tio gånger under ett visst uppskattat hälsomässigt referensvärde innebär att det inte finns någon risk för klinisk relevanta effekter på intelligenskvoten (IQ) hos barn. För vissa livsmedel som kan användas som enda näringskälla och är avsedda för barn med speciella medicinska behov (FSMP), var marginalen till det uppskattade hälsomässiga referensvärdet mindre än en faktor tio. Den blyexponering vi har idag anses bekymmersam när det gäller att risken för effekter på den neurologiska utvecklingen. Exponeringen för bly bör därför minska så mycket som möjligt.

Från nutritionell synpunkt var intagen av mangan, järn och koppar från de analyserade produkterna tillräckliga. Viss osäkerhet finns dock beträffande spädbarns och småbarns behov av mangan. Utvärderingen visade också att det finns potentiella problem med höga manganintag från vissa välling- och grötprodukter samt vissa FSMP-produkter, om man jämför med det TDI som fastställts av WHO. Det vetenskapliga underlaget för detta TDI-värde är dock tveksamt, varför även intag under TDI kan ge anledning till oro. Intaget av koppar från några FSMP-produkter var högt i jämförelse med tolerabelt övre intag (UL) för barn under ett år. Intagen av mangan och koppar från modersmjölksersättningar och tillskottsnäringar gav däremot ingen anledning till oro om man jämför med nu tillgängliga hälsobaserade referensvärden.

I samband med utvärderingen av intaget av de analyserade mineralerna har kunskapsluckor identifierats. För att kunna bedöma om koncentrationen av ett mineral i en speciell livsmedelsprodukt är inom ett acceptabelt eller optimalt intervall, måste det finnas fastställda maximi- och miniminivåer för intaget. Vår uppfattning är att det är nödvändigt att fastställa hur stort manganbehov små barn har och att fastställa ett UL-värde eller motsvarande värde för mangan för att kunna definiera ett optimalt intervall för koncentrationerna av mangan i produkter avsedda för spädbarn och småbarn. Även UL för järn för spädbarn och småbarn samt UL för koppar för barn under ett år måste fastställas. Det behövs risk- och nyttovärderingar av mangan, järn och koppar i relation till uppskattade intag hos spädbarn och småbarn, och dessa utvärderingar bör utföras av forskare eller internationella expertgrupper. Sådana värderingar är viktiga för att uppdatera lagstiftningen och kontrollen för att säkerställa att mat avsedd för spädbarn och småbarn är näringsmässigt lämplig och säker.

Det är alarmerande att produkter avsedda för spädbarn och småbarn innehåller sådana halter av kontaminanter att de potentiellt kan leda till negativa hälsoeffekter. Dessa åldersgrupper är speciellt känsliga för exponering för vissa konta-

minanter och mineraler och effekterna på barns utveckling kan vara irreversibla. Vi vill uppmana berörda aktörer att använda tillgängliga metoder för att reducera koncentrationerna av kontaminanter som arsenik och bly i livsmedel avsedda för spädbarn och småbarn. Det är även angeläget att hälsobaserade riktvärden för kadmiumexponeringen hos barn samt referensvärden för låga och höga intag av essentiella mineraler uppdateras för att säkerställa att livsmedel för spädbarn och småbarn är näringsmässigt lämpliga och säkra.

Introduction

Infants and young children are often regarded as two particularly vulnerable groups in terms of food safety. These groups may be especially vulnerable to high exposures from contaminants and minerals at important stages of development. Furthermore, the requirements for essential nutrients due to rapid growth and development put these groups at risk of deficiencies of essential minerals. It is therefore essential that products intended for use by infants and young children contain minerals in amounts that satisfy their nutritional requirements without leading to adverse effects. In addition, products must not contain contaminants in amounts that could lead to negative health effects.

Concerns about adverse health effects of high concentrations of manganese and possibly also iron in infant formulae were raised in a study by Ljung *et al*, who also found arsenic, cadmium and lead in foods for infants (3). This report as well as other data encouraged the NFA to initate a project to analyse and assess contaminants and minerals in infant formulae and certain foods for children. Because the addition of copper to foods for infants and children has been questioned (4), copper was also included in the project.

Products to be included in the present survey were chosen on the basis of producer and type of products, aiming to cover products from all producers present in the Swedish market in spring 2011. The analysed elements were arsenic, cadmium and lead unintentionally present in foods, so called contaminants, as well as the essential minerals manganese, iron and copper. Ninety two products intended for infants (0-12 months) and young children (1-3 years), including a limited number of products not explicitly intended for consumption by children, were analysed in this survey.

In the present part of the report, the intakes of arsenic, cadmium and lead, were evaluated in relation to guideline values for upper intake levels and risk for development of adverse health effects in infants and young children. The potential adverse effects of low and high intakes of manganese, iron and copper were identified and discussed. Furthermore, the potential benefits (here defined as the absence of risk) and risks considering the requirements and vulnerability of infants and young children to these minerals were evaluated. A possible need for revised risk assessments of the essential minerals manganese, iron and copper was evaluated.

Materials and Methods

This section includes a description of the selection and sampling of products, analyses of contaminants and minerals in the product and the intake assessment of selected products. For further details of product identification, selection, sampling and analyses, the reader is referred to the National Food Agency's report "Concentrations of contaminants and minerals in foods for infants and young children –analytical results"(1).

Food categories included in the project:

- **Foods for Special Medical Purposes (FSMP)** for infants (0-12 months) and young children (1-3 years). In order to facilitate the intake assessment for this product cartegory, FSMP was further divided into FSMP that can be used as the sole source of nutrition and FSMP used as partial nutrition in this report.

- **Infant formulae and follow-on formulae**

- **Processed cereal-based foods for infants and young children (PCBF)** This category includes porridge and gruel products.

- **Breast milk and foodstuffs for normal consumption** include breast milk from a sample of Swedish women and foods that young children might consume which are not explicitly intended for children according to the label.

The project did not include "baby foods" (main dishes and desserts) and so called "growing up milks" (milks intended for young children aged 12 months to 3 years). The reason for this was that products where concentrations of contaminants and manganese were expected to be of concern, such as cereals (including rice) and soy, were prioritised.

Selection and sampling

Products to be included in analysis were chosen on the basis of producer and type of product. A list of analysed food products and labelling information can be found in Appendix I.

Samples were purchased in supermarkets and pharmacies in the counties of Uppsala, Stockholm and Gävleborg, Sweden, as well from web pages marketing the products. In total 253 samples of 92 different products were collected. Sampling was carried out between 4 May 2011 and 13 October 2011. For each product samples from three different batches were included, unless only two batches

(n=21) or one batch (n=5) were available during the period of sampling. Samples were all given a unique number.

In addition, a composite sample of human milk collected week 3 post-partum from 30 volunteers during 2008, 2009 and 2010 (n=90) was analysed. A more detailed description of the selection and sampling of products can be found elsewhere (1).

Determination of concentrations of contaminants and minerals

The samples were analysed by ICP-MS (inductively coupled plasma mass spectrometry) using two different methods. Concentrations of manganese, iron and copper were determined during October and November 2011 at NFA by an accredited method (ISO/IEC 17025 by SWEDAC - Swedish Board for Accreditation and Conformity Assessment). Concentrations of arsenic, cadmium and lead were determined both at the National Food Agency using the above-mentioned accredited method and at ALS Scandinavia AB, Luleå, Sweden, using a method with a higher sensitivity. The method at ALS was the same as the accredited method for routine analysis of these types of samples, with the exception of a lower dilution (5). The results from ALS with the lower reporting limits were used for the risk assessment in this report.

A composite sample from the 3 batches of each product was transferred into 2 tubes, of which one was used for the analysis at the NFA, and the other was sent to be analysed at ALS. All samples were stored either at room temperature or in a refrigerator ('ready for use' samples) until the day of analysis. Products were analysed on an "as purchased" basis, i.e. either as dry powders or in liquid form. In the determination analysis, powders were converted into ready-to-eat products by using dilution factors calculated on a weight to weight basis according to instructions on the package. Only contribution by the specific product is included in the results, which means that the contribution of contaminants in water or milk during dilution was not accounted for. For further details about the method of analysis and the result of the chemical analyses see part 1 of the report.

Intake assessment

In this report, exposure refers to the dietary exposure of contaminants and minerals from the analysed products only, unless otherwise stated.

The results are presented as concentrations of the contaminant or mineral in the ready-to eat-product, in mg or µg per kg product in Appendices II-VII. The product categories (FSMP, infant formulae and follow-on formulae, PCBF and other foods) were further divided in order to make relevant intake estimations. In order to assess whether products fell within established acceptable ranges of

intakes, we calculated intakes per day or per portion of each contaminant or mineral. The assumptions made for estimations of intakes in each category are presented below. For some contaminants and minerals, the contribution (to the total intake) from water to be mixed with the product was also assessed. Details regarding assumed concentrations in water and calculations can be found in each chapter.

Infant formulae
Products in this category are recommended from 0 and 4 months of age, according to the labelling on the packages. For all products, intakes per day or per kg body weight per day were estimated. For infant formula intended from birth, intakes were calculated using a weight of 4.2 kg for a girl at 3 weeks of age (6) and an estimated consumption of 700 ml per day (7, 8). For products recommended from 4 months, a weight of 6.6 kg for a girl (6) and an estimated consumption of 800 ml were used (7).

Follow-on formulae
These products are recommended for infants from 6 months and 8 months respectively and should be consumed as part of an increasingly varied diet. However, because the size of one portion is difficult to estimate, intakes per day or per kg body weight per day were estimated. For products recommended from 6 months of age (7.7 kg), an estimated daily consumption of 900 ml per day was used, assuming energy requirements according to FAO (9) and little intake of complementary foods or breast milk. For the one product recommended from 8 months, a weight of 8.5 kg and consumption of 500 ml per day were assumed based on formula intake in the Euro-growth study (7).

FSMP used as sole source of nutrition
Foods recommended to children of 0-12 months are included in this product category. These foods are intended for a wide range of conditions, for example prematurity, allergy, malnutrition and phenylketonuria (PKU). Where package information indicated that the product could be used as the sole source of nutrition, the products were put in this category. However, most products in this category may also be used together with other foods. For all products in this category, intakes per day or per kg body weight per day were estimated. For FSMP that could be used as the only source of nutrition from birth, intakes were calculated using a weight of 4.2 kg for a girl at 3 weeks of age (6) and an estimated consumption of 700 ml per day (7, 8). For products intended for use by premature or low birth weight infants, we used the weight 2.5 kg and an estimated daily intake of 400 ml. For FSMP recommended as the sole source of nutrition from 12 months (9.8 kg), a consumption of 900 ml per day based on energy requirements was assumed (9) where no information on recommended intake was found on the package. The energy content of products in the FSMP category was higher than in infant formulae and follow-on formulae.

FSMP as partial nutrition, daily intakes
The package information on some FSMP products indicated that the product should be used together with other foods. For the products Nutramigen 2 lipil, PKU anamix infant lcp+ and XP Maxamaid an intake per day or per kg body weight per day was estimated because the portion sizes were difficult to establish. For Nutramigen 2 lipil, recommended from 6 months of age, an estimated daily consumption of 900 ml per day was used, assuming little complementary food intake and food and energy requirements according to FAO (9). PKU anamix infant lcp+ and XP Maxamaid are intended for children with PKU and daily consumption should be based on protein requirements. For PKU anamix infant lcp+ the FAO protein requirements were used to estimate the daily protein requirement (for an infant weighing 4.2 kg) to 5.5 g protein per day (10). The protein concentration of the product is 2 g/100 ml and daily consumption of PKU anamix infant lcp+ was set at 300 ml/day. A daily protein requirement of 11 g was estimated for a child aged 12 months consuming XP Maxamaid (10). Product protein concentration was 4 g/100 ml and hence a daily consumption of 300 ml/day was used.

FSMP as partial nutrition, intakes per portion
For some FSMP products, package information indicated that the product should be used together with other foods. Intakes of metals were calculated per portion for the following products: Fresubin energy fibre (200 ml), Frebini energy fibre drink (200 ml) and PKU gel (50 g), all recommended for use from 12 months.

Gruel
Cereal-based gruels are common complementary foods in Sweden and belong to the category PCBF. Where recipes were given in number of spoons, the density of the products was calculated to assign portion sizes in grams. Several recipes were often given. Since a child can easily consume a larger amount of gruel than of porridge at one meal, the portion size was set to the recipes on the package that gave a final amount of 200-237 g gruel. The weight of a girl (6) at the lowest age for which the product was recommended (7.7-9.8 kg) was used to calculate the intake per portion. For the contaminants the values in tables are conservative and do not include the potential contributrion from a milk product. However, products to be mixed with a milkproduct were not included in summary tables for iron and copper in order not to present misleadingly low values of these minerals in particular gruels.

Porridge
Porridges belongs to the category PCBF. For all products, an intake per portion was calculated using the same principles as for gruels. We used the weight of a girl (6) at the lowest age for which the product was recommended (6.6-9.8 kg) to calculate the intake per portion. Calculated intakes are based on product mixed

with water, if not stated otherwise. Portion sizes of 50-225 g were used according to instructions for appropriate preparation on the labels.

Foodstuffs for normal consumption
For drinks based on soy or oats, one portion was set at 100 ml. This was assumed to be a reasonable portion size for a 1-year-old child. For Pama 'minute rice', Rolled oats and Oat toasted and milled, a portion size of 130 g was used.

Breast milk
In order to compare breast milk with infant formula, intakes of contaminants and metals were calculated based on a body weight of 4.2 kg for a girl at 3 weeks of age (6) and an estimated consumption of 700 ml per day (7, 8).

Assessment of risks and benefits

This evaluation followed the principles of risk analysis and included hazard identification, hazard characterisation, exposure assessment and risk characterisation (11). Intakes of the contaminants arsenic, cadmium and lead were compared with the available tolerable intakes or reference points. Since contaminants are not essential nutrients, there are no insufficient intakes.

For the essential minerals manganese, iron and copper, intakes were discussed in relation to recommended daily intakes and tolerable upper levels or tolerable daily intakes, when these values were available. While risk refers to health considerations at upper levels of intakes, the benefit of these minerals was described in terms of a reduced risk of adverse health effects such as a state of deficiency. For example, both adverse health effects of insufficient intakes and adverse health effects of excessive intakes of each mineral were discussed under the heading "hazard identification".

The process of comparing risks and benefits of the minerals was based on an EFSA Scientific Opinion (12) However, literature reviews for identification and characterisation of hazard and reduced adverse effects were not as systematic and extensive as may be expected of a full risk benefit assessment.

Arsenic (As)

Hazard identification

Arsenic (As) is ubiquitous in the environment and is usually present in small amounts (1.5-2 mg/kg) in the bedrock. However, concentrations vary considerably, and leakage from naturally occurring arsenic-rich minerals and sediments into groundwater is a growing worldwide public-health problem. In addition, there is increasing concern about elevated concentrations in locally grown food of plant origin, e.g., rice, maize and beans, as well as in root and leafy vegetables (13, 14). Arsenic occurs in the environment in both inorganic and organic forms. People are exposed to arsenic mainly through drinking water and food. In water, arsenic is present mainly in two inorganic forms, as arsenate (As^{V}) and arsenite (As^{III}), which are the most toxic forms to humans. Within the EU there is a limit of 10 µg/L of total arsenic in drinking water (15). Seafood may contain high concentrations of arsenic, in the mg/kg range, but the forms present are mainly organic arsenicals, e.g. arsenobetaine and arsenosugars with low toxicity. In many countries, arsenic-contaminated groundwater is used for irrigation of cereals and root and leafy vegetables. Rice seems to accumulate arsenic more efficiently compared to other commodities (16, 17). Levels up to 160 µg/kg of inorganic arsenic have also been detected in rice even from areas with groundwater not contaminated by arsenic (18). In root and leafy vegetables growing in an arsenic-contaminated area, inorganic arsenic represented 30-100 % and 70-100 % of the total arsenic, respectively (13). Several studies have revealed that inorganic arsenic is the predominant form of arsenic species in raw rice, ranging from 40 to 100 %, irrespective of rice varieties, types of rice, growing seasons or geographical variations (19).

In 2009, EFSA concluded that inorganic arsenic exposures from food and water across 19 European countries have been estimated to range from 0.13 to 0.56 µg/kg bw per day for average consumers, and from 0.37 to 1.22 µg/kg bw per day for 95th percentile consumers. The food categories "fish and seafood" and "cereal and cereal products" were the predominant contributors to overall total arsenic and rice, due to its high content of total arsenic, was the main contributor to the inorganic arsenic forms. High consumers of rice in Europe, such as certain ethnic groups, were estimated to have a daily dietary exposure of inorganic arsenic of about 1 µg/kg bw per day. EFSA also concluded that children under three years of age are the most exposed to inorganic arsenic, with exposure estimates in two different studies showing an inorganic arsenic intake ranging from 0.50 to 2.66 µg/kg bw per day and that the dietary exposure to inorganic arsenic, including from rice-based foods, is in general estimated to be about 2 to 3 times that of adults. Milk intolerant children substituting rice-drink formulae were not included in these estimations (20).

Recently, four studies (3, 21-23) have been published where arsenic has been detected in rice-based infant food. The infant foods were obtained from national supermarket chains and from national pharmacies in Sweden, the United Kingdom and Spain. The Institute of Environmental Medicine (IMM), Karolinska Institutet, Stockholm, Sweden has analysed the levels of essential (iron, manganese, copper) and potentially toxic elements (arsenic, cadmium, lead) in infant formulae, gruels and porridges (3). Total arsenic concentrations of 30 µg/kg were found in the ready-to-eat rice-based gruels and porridges intended for infants from 4 months. Such an amount of arsenic will contribute to an exposure of as much as 1 µg/kg body weight per portion. In a study by Carbonell-Barrachina et al, concentrations of inorganic arsenic between 29 and 121 µg/kg product (mean 69 µg/kg), representing 64 % (range 36-89 %) of the total amount of arsenic, were found in thirteen samples of gluten-free infant rice intended for consumption from 4 months of age (21). In 17 different "baby rice" products studied by Meharg et al, the concentrations of inorganic arsenic ranged from 60 to 160 µg/kg product (mean 117 µg/kg) (22) and in 15 different rice drinks the concentrations of inorganic arsenic ranged from 7.1 to 21 µg/L (mean concentration 13 µg/L) (23). In these studies the concentration of inorganic arsenic was on average 53 % (range 33-69 %) and 67 % (range 55-86 %) of the total amount of arsenic, respectively.

Rice-based gruels, porridges and drinks are often recommended for children who are lactose intolerant or have a diagnosis of cow's milk protein allergy. A survey of total and inorganic arsenic in rice drinks was carried out by the Food Standards Agency (FSA) in the UK in 2008. The results of the FSA survey were in accordance with the results obtained by Meharg *et al* (23). The concentrations of inorganic arsenic ranged from 5 to 20 µg/L (mean concentration 13 µg/kg) and represented 56 % of the total arsenic concentration. Twelve of the 17 analysed rice drinks exceeded the EU total arsenic limit of 10 µg/L in drinking water. Because of a concern for high exposure to arsenic, the FSA advises parents not to give rice drinks to children younger than 4.5 years (24) and in Denmark the advice is not to give rice drinks to children younger than 3 years of age, especially to children below 10 kg in weight (25).

Arsenic is not included in the Swedish National Monitoring Programme, but in 2001 the NFA conducted a survey of arsenic, cadmium and lead in different types of rice available on the Swedish retail market. An average of 64 % (range 17-100 %) of the total arsenic in rice in this survey consisted of inorganic arsenic. The concentrations of inorganic arsenic ranged from 40 to 190 µg/kg product "as sold" (mean concentration 111 µg/kg) (26).

Hazard characterisation

Inorganic arsenic is highly toxic and is classified as a human carcinogen (Group 1) on the basis of sufficient epidemiological evidence for carcinogenicity in humans. Inorganic arsenic causes cancer in the urinary bladder, lung, skin and possibly also in the kidney and liver (27). Chronic exposure to inorganic arsenic is

also associated with a variety of non-cancerous effects in humans, such as peripheral vascular insufficiency, liver- and neurotoxicity, diabetes mellitus and hypertension (28, 29). However, all these effects have been studied in adults only.

Arsenic readily passes through the placenta in humans (30) and recent studies indicate adverse effects on pregnancy outcomes, reduced birth weights and increased morbidity in infectious diseases during infancy (31-33).

Very little arsenic is excreted in breast milk. Fängström *et al* (34) reported low concentrations of arsenic, at about 1 µg/L, in breast milk, despite high arsenic exposures via drinking water (up to 1,000 µg/L). Most of the arsenic in breast milk was in the inorganic arsenite form (As^{III}). Low concentrations of arsenic have also been reported in Swedish breast milk (median 0.55 µg/L) (35).

Recently published epidemiological studies show that children may be susceptible to inorganic arsenic. Early-life exposure to low levels of inorganic arsenic in drinking water (<50 µg/L) has been associated with increased infant mortality and morbidity, mainly due to impaired immune function (31-33).

During foetal development and early childhood, the brain is particularly vulnerable to arsenic. Experimental and epidemiological studies have shown associations between foetal exposure to arsenic and neurotoxicity and behavioural changes. Prenatal exposure of mice to lower doses of arsenic (50 µg/L) has been shown to result in learning deficits (36).

Exposure to arsenic through drinking water has been associated with impaired cognitive function in school-aged children in a few cross-sectional studies (37, 38). In those studies children's intellectual function was reduced in relation to exposure to arsenic in drinking water, after adjustment for socio-demographic covariates and water manganese. Children with water arsenic levels above 50 µg/L achieved significantly lower performance and full-scale scores than children with water arsenic levels below 5 µg/L. Adverse effects of arsenic exposure on the IQ in pre-school girls have also been found in a longitudinal study (39).

Data suggests that exposure to arsenic during early life or *in utero* may result in an increase in liver and lung cancer mortality as well as an increase in respiratory disease in later life (40, 41). The long-term mortality impact of early-life exposure has been investigated in the city of Antofagasta in Northern Chile. This city has had a distinct period of very high arsenic exposure that began in 1958 and lasted until 1971, when an arsenic removal plant was installed. The investigators compared cancer mortality rates under the age of 20 years with those of an unexposed region, focusing on children that were born during (1958-1970; ~ 870 µg/L), shortly before (1950-1957; ~ 90 µg/L) or after (1971-1981; < 100 µg/L) the high exposure period. The investigators found that those exposed to high arsenic concentrations, such as young children, had an increased liver cancer mortality with a relative risk (RR) of 10.6 (95 % CI, RR=2.9–39.2) while mortality from the most common childhood cancers, leukemia and brain cancer, was not increased in the

exposed population (40). Mortality from lung cancer and bronchiectasis diseases among adults 30-49 years old in Antofagasta in relation to early-life exposure has also been investigated. The results showed a significantly increased standardised mortality ratio (SMR) for lung cancer (SMR = 7.0, 95 % CI, 5.4-8.9) and bronchiectasis (SMR = 12.4, 95 % CI, 3.3-31.7) for those born just before the high-exposure period (1950-1957) and exposed in early childhood. For those born during the high-exposure period (1958-1970) with probable exposure *in utero* and early childhood, the SMR for lung cancer was 6.1 (95 % CI, 3.5-9.9) and the SMR for bronchiectasis was 46.2 (95 % CI, 21.1-87.7) (41).

Humans metabolise inorganic arsenic via methylation to methylarsonic acid (MMA) and dimethylarsinic (DMA), which are both excreted in the urine. The formation of DMA metabolite can be considered a detoxification mechanism, whereas the MMA fraction is associated with an increased risk of adverse health effects (42-44).

Exposure assessment

Estimated intakes for all individual products are detailed in Appendix II. Median arsenic concentrations in the different ready-to-eat products are summarised in Table 1. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 2) or a single portion (Table 3).

In the exposure assessment, it is assumed that all arsenic in the different products is in the inorganic form. As shown in Table 1, the highest arsenic concentrations in the investigated ready-to-eat products were found in the rice-based gruels and in the rice-based porridges, and ranged from 8.4 to 19 µg/kg (median 17 µg/kg) and from 4 to 41 µg/kg (median 23 µg/kg), respectively. The arsenic concentrations were much lower in the gruels and porridges based on oat, wheat, rye, spelt or corn and ranged from 0.65 to 6.5 µg/kg.

The arsenic concentrations in the ready-to-eat infant formulae and follow-on formulae ranged from 0.54 to 4.6 µg/kg (Table 1). Arsenic concentrations in rice drinks were 18 and 30 µg/kg while in oat and soya drinks, arsenic concentrations were ≤ 2 µg/kg.

The estimated daily median intakes ranged between 0.05 and 0.12 µg/kg bw while the estimated daily intakes for individual products ranged between 0.02 and 0.86 µg/kg bw (Table 2). The highest estimated daily intake of 0.86 µg/kg bw was from the FSMP product Minimax enteral formula for children, which contained 11 µg/kg arsenic (see Appendix II). According to the labeling, this product contains 11.8 g carbohydrate per 100 mL, including rice flour, maltodextrin and lactose. The estimated intake, as a reference, from breast milk was 0.09 µg/kg bw (Table 2). For the product categories in Table 3, the estimated intakes *per portion*

range between 0.01 and 0.49 µg/kg bw, and the estimated intakes *per portion* for individual products range between 0.007 and 0.89 µg/kg bw. The estimated intakes *per portion* for FSMP products when used as partial feeding (range between 0.02 and 0.05 µg/kg bw) were lower compared to the other product categories. The estimated intake from rice drinks, assuming a consumption of 100 ml, was 0.19 and 0.31 µg/kg bw (Table 3) while the estimated intake of arsenic from the soya and oat drinks was ≤ 0.02 µg/kg bw.

Table 1. Summary of median concentrations and (range) of total arsenic in ready-to-eat* baby food.

Product category		**No. of products**	**Arsenic concentration µg/kg**
Infant formula		9	0.77 (0.54-0.90)
Follow-on formula		4	0.88 (0.71-4.6)
FSMP as sole source of nutrition		21	0.90 (0.49-11)
FSMP as partial feeding		6	1.7 (0.68-3.7)
Gruel	oat-, wheat-, rye- or corn-based	10	0.67 (0.54-1.5)
	rice-based	4	17 (8.4-19)
Porridge	oat-, wheat- or spelt-based	16	1.7 (0.86-6.5)
	rice-based	10	23 (4.0-41)
Foodstuffs for normal consumption			
Soya drink		4	0.96 (0.81-1.7)
Oat drink		3	0.88, 1.0, 2.0
Rice drink		2	18, 30
Porridge/gruel	oat-based	2	0.53, 0.61
	rice-based	1	32

*Products were analysed on an "as sold basis" and the results for powders are converted into ready-to-eat products by using dilution factors.

Table 2. Summary of estimated daily intakes of arsenic expressed as µg/day and µg/kg bw/day from infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial nutrition.

Product category	**Age (months)**	**No. of products**	**Median intake and (range)**	
			µg/day	**µg/kg bw/day**
Infant formula	0-4	9	0.55 (0.38-0.63)	0.12 (0.08-0.15)
Follow-on formula	6-8	4	0.80 (0.64-2.3)	0.10 (0.08-0.27)
FSMP as sole source of nutrition	0-12	21	0.57 (0.23-6.7)	0.12 (0.06-0.86)
FSMP as partial feeding[a]	0-12	3	0.20, 0.21, 1.3	0.02, 0.05, 0.17
Breast milk[b]	3 weeks	-	0.38	0.09

[a]The intake of these products was calculated as daily intakes in accordance with calculations for intakes of follow-on formulae. [b]Arsenic concentration (median=0.55 µg/L (SD=0.15)) in 64 samples of human milk collected in Sweden (35). An infant 3 weeks old, weighing 4.2 kg and consuming of 700 ml breast milk per day was assumed.

Table 3. Summary of estimated median intakes of arsenic expressed as µg/portion and as µg/kg bw *per consumed portion* from gruel, porridge, FSMP as partial feeding (51 - 237g) and from soya, oat and rice drinks (100 ml)

Product category		Age (months)	No. of products	Median intake and (range)	
				µg/portion	µg/kg bw/portion
Gruel	oat-, wheat-, rye- or corn-based	6 – 12	10	0.16 (0.12-0.35)	0.02 (0.02-0.05)
	rice-based		4	4.0 (2.0-4.5)	0.49 (0.26-0.58)
Porridge	oat-, wheat- or spelt-based	4 – 12	16	0.28 (0.12-0.77)	0.04 (0.02-0.09)
	rice-based		10	2.6 (0.66-5.9)	0.37 (0.10-0.89)
FSMP as partial feeding		12	3	0.18, 0.40, 0.47	0.02, 0.04, 0.05
Foodstuffs for normal consumption					
Soya drink		12	4	0.10 (0.08-0.17)	0.01 (0.01-0.02)
Oat drink		12	3	0.09, 0.10, 0.20	0.01, 0.01, 0.02
Rice drink		12	2	1.8, 3.0	0.19, 0.31
Porridge/ gruel	oat-based	12	2	0.07, 0.08	0.007, 0.008
	rice-based	12	1	4.2	0.43

Risk characterisation

The World Health Organization (WHO) has classified arsenic as a human carcinogen (27, 45). The US National Research Council (NRC) has performed a risk assessment of arsenic in drinking water and estimated that the lifetime cancer risks for lung and bladder cancer is 3 to 4 cases per 1,000 individuals at a drinking water concentration of 10 µg/L (1L/day), which is the permissible level in drinking water within the EU. This estimation greatly exceeds the tolerable limit of one extra case of cancer per 100,000 individuals (29).

The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) modelled the dose-response data from key epidemiological studies and estimated benchmark doses (BMDs) corresponding to a benchmark response of 1 % extra risk (BMD_{01}). Resulting $BMDL_{01}$ (the lower 95th confidence limit of the $BMDL_{01}$) values varied between 0.3 and 8 µg/kg body weight per day for cancers of the lung, skin and bladder, as well as skin lesions (20).

In the seventy-second meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 2010, a BMDL of 3.0 µg/kg body weight per day (range: 2-

7 µg/kg body weight per day) was proposed for inorganic arsenic. This BMDL corresponded to a 0.5 % increased incidence of lung cancer determined from epidemiological studies (46). The JECFA: s provisional tolerable weekly intake (PTWI) for inorganic arsenic of 15 µg/kg body weight/week (equivalent to 2.1 µg/kg body weight/day) from 1988 is in a region comparable to the BMDL values identified by EFSA and JECFA, respectively. Thus, EFSA and JECFA considered that a PTWI of 15 µg/kg body weight was no longer appropriate as protection against adverse health effects. Consequently, JECFA withdrew its previous PTWI (46). It should be noted, however, that all risk assessments mentioned above are based on chronic effects, especially cancer, in adults with long-term exposure to arsenic.

In the present investigation, arsenic concentrations in the ready-to-eat baby food ranged from 0.5 to 41 µg/kg. The highest arsenic concentrations were found in the porridge products based on wholegrain rice (100 %), (31 and 41 µg/kg) and in porridge products based on rice flour (28 and 29 µg/kg). However, in the porridges based on rice or oats/wheat flour with added fruits or vegetables the arsenic concentrations ranged from 4.6 to 23 µg/kg (Appendix II). In two gruel products based on 89 % and 84 % rice flour, the arsenic concentrations were 17.6 and 16.5 µg/kg, respectively. The lowest arsenic concentrations were found in corn-based gruels (range 0.5-1.5 µg/kg).

The estimated intake of arsenic *per portion* from the investigated rice-based gruels, which are intended for infants from 6 months of age, was 0.49 µg/kg body weight, while for rice-based porridges intended for infants from 4 months of age was 0.37 g/kg body weight *per portion*. This estimated intake is higher than the intake by adults consuming 1 L drinking water containing arsenic at the EU standard value of 10 µg/L (0.17 µg/kg body weight per day). It should be emphasised that even this relatively low level of exposure is associated with an increased risk of cancer. The lifetime cancer risks of lung and bladder cancer were estimated to be 3 to 4 cases per 1000 individuals at a drinking water concentration of 10 µg/L (29).

Among the FSMP used as a sole source of nutrition, an enteral formula (Minimax enteral formula for children) for infants from 6 months of age for dietary management of disease-related malnutrition contained the highest concentration of arsenic (11 µg/kg). The estimated daily intake of arsenic for infants consuming this formula is 0.86 µg/kg body weight.

The concentrations of arsenic in the two investigated rice drinks were 18 and 30 µg/L. Both values exceeded the EU standard value of 10 µg/L in drinking water. The estimated intake of arsenic from the rice-based drinks, assuming a consumption of 100 ml, was 0.19 and 0.31 µg/kg body weight (Table 3). If, however, the intake is based on the NFA recommendation for children of 500 ml milk/day, the intake of arsenic would amount to 1.6 µg/kg body weight.

Discussion

Several studies have shown that rice contains elevated concentrations of arsenic. This is due to its efficiency in accumulating arsenic into the grains compared to other cereal crops. Inorganic arsenic is the predominant form of arsenic in rice. (19). In the present investigation the highest arsenic concentrations in the ready-to-eat products were found in the porridges based on wholegrain rice (up to 41 µg/kg) and on rice flour (up to 29 µg/kg) as well as in rice drinks (up to 30 µg/kg). Similar results have previously been reported for infant foods purchased in Sweden, the United Kingdom and Spain.

The estimated intake of arsenic from a single portion of 51 g of rice-based porridge intended for infants from 4 months of age is 2.1 µg arsenic, i.e. 0.32 µg/kg body weight. The estimated intake of arsenic from 100 ml of the rice-based drinks is 3.0 µg arsenic, i.e. 0.31 µg/kg body weight. These estimated intakes, assumed from a single portion of 51 g or 100 ml consumption per day, are higher than the intake by adults consuming 1 L drinking water containing inorganic arsenic at the EU parametric value (limit value) of 10 µg/L (0.17 µg/kg body weight per day). Even this relatively low level of exposure via drinking water is associated with an increased risk of lung and bladder cancer (29).

Rice drinks are an alternative for children who are lactose intolerant or who have a diagnosis of cow´s milk protein allergy. Formulas based on rice protein have also become available for infants with cow´s milk protein allergy (47). In the present investigation, however, no rice-based formulae or follow-on formulae were analysed, but in a recent study inorganic arsenic levels of 12 µg/kg were found in rice-based formula (48).

Levels of arsenic were much lower in the gruels and porridges based on oat, wheat, rye, spelt or corn. It should be noted, however, that the contribution from water to the total daily dietary intake of arsenic could be even higher. In Sweden, arsenic concentrations up to 260 µg/L have been detected in private drinking wells with a 95th percentile of 10.14 µg/L (49).

The estimated dietary exposures to arsenic of infants from single portions of rice-based food were within the range of $BMDL_{01}$ values (0.3 to 8 µg/kg bw per day). Cancerous and non-cancerous effects in adults have been identified in this range due to long-term exposures (20), but in infants there are no reference points at present. Children, however, seem to be very susceptible to toxic effects of inorganic arsenic. Early-life exposure to low levels of inorganic arsenic in drinking water has been associated with increased infant morbidity and mortality, as well as impaired child development (31, 37-39, 50). Moreover, data suggests that exposure to arsenic during early-life or *in utero* may produce an increase in liver and lung cancer mortality as well as an increase in respiratory disease in later life (40, 41). More research on the association between arsenic exposure during early childhood and subsequent adverse health effects later in life, including development of cancer, is needed.

Conclusion

The present investigation shows that rice-based infant food purchased in Sweden could be a significant exposure source of inorganic arsenic. The estimated intakes *per portion* from those products are close to the $BMDL_{01}$ value identified by EFSA.The arsenic intake can be even higher if rice-based infant food is prepared with water containing arsenic. The investigation also shows that arsenic levels exceeding the EU standard value of 10 µg/L in drinking water can be found in rice-based drinks. The low content of arsenic in breast milk is an important argument for recommending breast-feeding.

Cadmium (Cd)

Hazard identification

Cadmium (Cd) is a heavy metal that occurs naturally and as an environmental contaminant. Non-ferrous metal mining and refining, manufacture and application of phosphate fertilizers, fossil fuel combustion, and waste incineration (e.g. sewage sludge) and disposal are the main anthropogenic sources of cadmium in the environment (51).

For non-smokers, food is the major source of cadmium exposure (52). The highest cadmium concentrations can be found in offal products, such as liver and kidney, certain wild mushrooms, and shellfish (53, 54). Foods from plants generally contain higher concentrations of cadmium than meat, egg, milk and dairy products, and fish muscle (55). He and Singh (56) reported that, for plants grown in the same soil, accumulation of cadmium decreased in the order: leafy vegetables > root vegetables > grain crops. Cereal products and potatoes contribute most to the dietary cadmium exposure of the general Swedish population (57).

Kinetics

Generally speaking, the absorption of cadmium following oral exposure depends on physiologic status (age; body stores of iron, calcium, and zinc; pregnancy history etc) and on the presence and levels of ions and other dietary components ingested together with cadmium. Individuals with low body stores of iron may have a higher absorption than those with adequate iron stores (51). This is probably due to up-regulation of divalent metal transporter 1, which has a high affinity for cadmium (58). The absorption of cadmium from the diet is about 1-10 % for adults (men and individuals with adequate iron status are probably in the lower range of this interval while individuals with low iron stores and iron deficencies are in the higer range) (51, 59). Absorption appears to be higher in newborns and infants, and in contrast to adults, independent of iron status (59, 60). The type of diet may also influence cadmium uptake: for example it has been observed that the bioavailability of cadmium is lower for a diet that includes shellfish once a week or more, compared to a diet low in shellfish (61).

The highest concentrations of cadmium can be found in the liver and kidney. For chronic dietary exposure, the kidney constitutes the target organ where cadmium accumulates, with a biological half-life of around 10-30 years (55). The cadmium concentration in the kidney is proportional to the concentration in urine. Because of this, the urinary cadmium concentration can be used as a marker of long-term exposure (62). Cadmium is also excreted in the faeces (51).

Health effects
The sensitive target organs of chronic cadmium toxicity are the kidneys and bones following oral exposure, and the kidneys and lungs following inhalation exposure. Other effects that have been observed in humans and/or animals include reproductive toxicity, hepatic effects, haematological effects, and immunological effects (51). There are also studies that suggest a role for dietary cadmium in cancer development, and an association between cadmium and increased mortality (55, 63-65). The International Agency for Research on Cancer (IARC) has classified cadmium as a human carcinogen (group I) on the basis of sufficient evidence for carcinogenicity in both humans and experimental animals (66). According to the IARC: "Cadmium and cadmium compounds cause cancer of the lung. Also, positive associations have been observed between exposure to cadmium and cadmium compounds and cancer of the kidney and of the prostate" (67).

In humans, the effects of cadmium have mostly been studied in adults. Cadmium-induced renal damage is characterised by proximal tubular reabsorptive dysfunction. The earliest signs of tubular toxicity are increased excretion of low-molecular weight proteins, such as β2-microglobulin (β2-M) and α1-microglobulin (α1-M), also called protein HC, and retinol-binding protein (RBP). The increased excretion of such low-molecular weight proteins is an accepted indicator of kidney damage and regarded as an adverse effect in adults (55). After prolonged and/or high exposure the tubular injury may progress to glomerular damage with decreased glomerular filtration rate, and eventually to renal failure.

Cadmium can also cause bone damage, either via a direct effect on bone tissue or indirectly as a result of renal dysfunction. While it is well known that high cadmium exposure can cause bone damage, the relationship between low cadmium exposure and increased risk of osteoporosis and fractures in adults is now more frequently discussed (68-70).

Information regarding potential effects of cadmium exposure that are relevant in an early human life context are quite limited. Environmental exposure to cadmium is known to induce oxidative stress in adults, and recent studies suggest that early-life exposure to cadmium via breast milk may also induce oxidative stress (71). A few small cross-sectional epidemiological studies indicate an adverse effect of cadmium exposure on child development, supported by experimental studies showing cadmium-induced neurotoxicity (59). A number of quite small cross-sectional studies have also indicated that cadmium exposure may have a negative effect on foetal growth (59). Recently, in a large, population-based, longitudinal mother-child cohort in Bangladesh (n = 1,616) an association between maternal cadmium exposure and and birth size in girls (but not in boys) was observed (72). Even more recently, based on data from the same cohort (n = 1,305), an association between early-life cadmium exposure and lower child intelligence scores is argued (73).

Hazard characterisation

As discussed above, some data exists regarding the potential effects of cadmium exposure in an early-life context, for example observed effects on foetal growth, which may be considered as critical effects in assessments that focus on infants and children. However, reliable dose-response relationships needed for a quantitative health risk assessment are not available. Early markers of kidney damage are instead used as the critical endpoint in the present assessment, which is in line with traditional cadmium risk assessments. It should be noted, however, that the use of such critical endpoints implies a long-term exposure context, and does not account for the potential health effects that might be relevant for early-life exposure.

Dose-response assessment using a variety of early markers of kidney damage has identified urinary cadmium reference points for early kidney effects in adults, as a result of long-term exposure, between 0.5 and 3 µg Cd/g creatinine (55).

In 2009, EFSA performed a risk assessment of cadmium (58) and established a tolerable weekly intake (TWI) of 2.5 micrograms cadmium per kilo body weight. Increased excretion of the kidney marker β2-M was used as the critical endpoint in this assessment. A meta-analysis of epidemiological data was performed using the benchmark dose (BMD) method. Lower confidence bounds on the BMD (BMDLs) in the range of 4-6 µg Cd/g creatinine were obtained, depending on choices made in dose-response modelling. The lowest BMDL value of 4 µg Cd/g creatinine was selected as the reference point (RP): it is the dose resulting in a 5 % increased risk of adverse levels of β2-M, where "adverse levels" are defined as β2-M values above the 95th percentile. To account for the fact that data on group means were used instead of individual observations an uncertainty factor of 4 was applied to the RP (4 µg Cd/g creatinine), which resulted in a critical concentration in urine of 1 µg Cd/g creatinine.

The TWI is developed by toxicokinetic modelling using data on 680 Swedish never-smoking women (56-70 years of age) living in the town of Uppsala and part of the Swedish Mammography Cohort (74). The urinary cadmium concentration resulting from a long-term dietary cadmium intake of 2.5 µg/kg bw per week (the TWI) was estimated to be lower than the critical concentration of 1 µg Cd/g creatinine for 95 % of the studied population. EFSA considered the risk of adverse effects on the kidney function at an individual level, associated with the dietary exposures across Europe, to be very low, but concluded that the current exposure to cadmium at the population level should be reduced (58).

Using the same epidemiological dataset, the JECFA established a provisional tolerable monthly intake of 25 µg Cd/kg bw (75). If expressed on a weekly basis, this value is about twice as high as the EFSA TWI. As a consequence, EFSA was asked by the European Commission to confirm their TWI. A number of methodological differences in the derivation of the respective guidance values were identified. Following this evaluation, EFSA concluded that the approach they had

adopted was appropriate, and their TWI (2.5 µg/kg bw/week) was maintained in order to ensure a high level of consumer protection (76).

Investigations indicate that a critical cadmium concentration in urine in the same range as that established by EFSA (1 µg Cd/g creatinine) also appears to be relevant with respect to an increased risk of osteoporosis and fractures (0.5-1 µg Cd/g creatinine) (59, 77). The TWI of 2.5 µg Cd/kg bw/week (corresponding to 1 µg Cd/g creatinine) expressed on daily basis, i.e. 0.36 µg Cd/kg bw/day (TDI equivialent), was used as a reference in this assessment, and as pointed out before, this accounts for the long-term exposure, but it does not account for potential effects relevant in a early-life context. This introduces an uncertainty that needs to be considered.

Exposure assessment

Estimated intakes for all individual products are presented in Appendix III. Summary results for different product categories are presented in Tables 4 and 5. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 4) or a single portion (Table 5).

For product categories in Table 4, estimated cadmium intakes for individual products range between 0.01 and 0.20 µg/kg bw/day. One FSMP product used as the sole source of nutrition is associated with a cadmium intake higher than 0.1 µg/kg bw/day (see Appendix III). An estimate of the intake from breast milk is given as a reference in Table 4.

In Table 5, estimated cadmium intakes for individual products range between 0.001 and 0.19 µg/kg bw/day. Two gruel products, three porridge products, and one product in the category foodstuffs for normal consumption are associated with intakes higher than 0.1 µg/kg bw/day (see Appendix II).

Table 4. Summary of estimated intakes of cadmium (µg/kg bw/day).

Product category	Age (months)	N	Intake[a]
Infant formula	0-4	9	0.04 (0.01-0.08)
Follow-on formula	6-8	4	0.03 (0.01-0.04)
FSMP as sole source of nutrition	0-12	21	0.03 (0.01-0.2)
FSMP as partial feeding	0-12	3	0.01, 0.02, 0.04
Breast milk	3 weeks	90	0.02[b]

[a]Median (range).

[b]A cadmium concentration in breast milk of 0.1µg/kg was used (a composite sample of human milk collected w 3 post-partum from 30 volunteers during 2008, 2009 and 2010; n = 90 samples were pooled in the analysis). An infant weighing 4.2 kg (weight used for infants 0-4 months) and consuming 700 ml breast milk per day was assumed.

Table 5. Summary of estimated intakes of cadmium (µg/kg bw/portion).

Product category	Age (months)	N	Intake[a]
Gruel	6-12	14	0.03 (0.003-0.19)
Porridge	4-12	26	0.05 (0.002-0.16)
FSMP as partial feeding	12	3	0.01, 0.02, 0.04
Foodstuffs for normal consumption	12	12	0.03 (0.001-0.14)

[a]Median (range).

Contribution from drinking water

The median cadmium concentration in municipal drinking water in Sweden is below 0.01 µg/l based on analyses from approximately 1,500 water purification plants between 2008 and 2011 (4,002 analyses in total). Combining a value of 0.01 µg/l with a consumption of 630 ml water (used for preparing 700 ml infant formula) by a child with a body weight of 4.2 kg (about 3 weeks old) results in a cadmium intake of 0.0015 µg /kg bw/day.

Risk characterisation

Summary results of estimated cadmium intakes expressed in terms of a percentage of the TDI (2.5 µg/kg bw/week/7 ≈ 0.36 µg/kg bw/day) are given Table 6, and summary results of estimated intakes expressed in terms of the number of portions required to reach the TDI are given in Table 7. Product-specific information is given in Appendix II.

For product categories in Table 6, the estimated median exposure to cadmium is about 10 % of the TDI. Exposures higher than 20 % of TDI are observed for one infant formula and three FSMP products used as the sole source of nutrition. The highest estimated cadmium exposure was around 50 % of the TDI (FSMP product used as the sole source of nutrition).

For product categories in Table 7, the estimated median number of portions to reach the TDI for cadmium is around 10. The number of portions to reach the TDI is less than 6 for three gruel products, seven porridge products, and three food-stuffs for normal consumption.

Table 6. Summary of estimated intakes of cadmium expressed in terms of a percentage of the TDI of 0.36 µg/kg bw/day.

Product category	Age (months)	N	% of TDI[a]	More than 20 % of TDI[b]
Infant formula	0-4	9	11 (3-21)	1
Follow-on formula	6-8	4	8 (3-11)	0
FSMP as sole source of nutrition	0-12	21	9 (4-55)	3
FSMP as partial feeding	0-12	3	4, 7, 12	0

[a]Median (range).
[b]The number of products associated with exposure that are higher than 20 % of the TDI.

Table 7. Summary of estimated intakes of cadmium expressed in terms of the number of portions required to reach the TDI of 0.36 µg/kg bw/day.

Product category	Age (months)	N	No. of portions to reach TDI[a]	Less than 6 portions to reach TDI[b]
Gruel products	6-12	14	12 (2-105)	3
Porridge	4-12	26	7 (2-175)	7
FSMP as partial feeding	12	3	9, 16, 67	0
Foodstuffs for normal consumption	12	12	12 (3-442)	3

[a]Median (range).
[b]The number of products for which the no. of portions to reach the TDI is less than 6.

Discussion

For cadmium, there is a margin to the TDI for all products. For most products the estimated exposure is a factor 5 below the TDI, or 6 portions or more are required to reach the TDI. For a few gruel products, porridge products and other products, however, the number of portions needed to reach the TDI can be regarded to be too low if consumed on a long-term basis (i.e. 2-3).

Cadmium uptake may be higher in infants and children than in adults, and the TDI only considers the life-long exposure context. It may be debated if and how such uncertainties should be accounted for, i.e. the relevance of considering an extra uncertainty factor and in that case its size, when using the present TDI. The identification of products (Tables 6 and 7) that contribute with more than 20 % of the TDI, or products for which the number of portions to reach the TDI is less than 6, is not used to indicate a health concern. However, it highlights that for some investigated products, the estimated exposure may potentially be higher than

desired if account is taken of possible limitations in the TDI with respect to the early-life context that this assessment concerns.

Conclusion

In general, estimated intakes of cadmium appear not to be of high concern with respect to long-term exposure and the health context the TDI is based on. However, a number of uncertainties exist regarding the level of protection when using the EFSA-derived TDI for infants and children, which may require the consideration of an extra margin to the TDI.

Lead (Pb)

Hazard identification

Lead (Pb) is a heavy metal that occurs naturally and, to a greater extent, as an environmental contaminant. Anthropogenic sources of lead include the mining and smelting of ore, manufacture of products containing lead, combustion of coal and oil, and waste incineration. Many anthropogenic sources of lead, most notably leaded gasoline, lead-based paint, lead solder in food cans, lead-arsenate pesticides, and shot and sinkers, have been eliminated or strictly regulated due to lead's persistence and toxicity (78).

Human exposure to lead can occur via food, water, air, soil and dust or dirt. Food is the major source of exposure to lead (79). The highest lead concentrations can be found in liver, kidney and meat from game, certain wild mushrooms, and shellfish (53, 54, 79). Basic food products such as fish, meat, cereals, vegetables and dairy products generally have low levels. EFSA concluded that cereal products contributed most to the dietary lead exposure of the general European population (79). Non-dietary exposure to lead is likely to be of minor importance for the general adult population in the EU, while for children, house dust and soil can be an important source of exposure to lead.

Kinetics

The extent and rate of absorption of lead through the gastrointestinal tract depend on characteristics of the individual (e.g. age, fasting state, nutritional calcium and iron status and pregnancy etc.), the amount of lead ingested and on physicochemical characteristics of the ingested lead (e.g. particle size, mineralogy, solubility, and lead species) (78). The toxicokinetics of lead in children appear to be similar to those in adults, with the exception of a higher absorption of ingested lead in children. Children can absorb 40-50 % of an oral dose of water-soluble lead compared to 3-10 % for adults. Children who are iron or calcium deficient have higher blood lead concentrations than children who are iron or calcium replete. Absorption of lead may increase during pregnancy (78).

The distribution of lead in the body is route independent (78). The principal vehicle for the transport of lead from the intestine to the various body tissues is the red blood cells, in which lead is bound primarily to haemoglobin (80). Lead in blood is considered to be the best indicator of the concentration of lead in soft tissues, reflecting recent and, to some extent, past exposure. The half-life of lead in blood and soft tissues is about 20-40 days, whereas in the skeletal pool the half-life of lead is approximately 10-30 years (78-80). In adults, about 80-95 % of the total body burden of lead is found in the bones, compared with about 73 % in children (78, 80). Lead is excreted primarily in urine and faeces regardless of the route of exposure (78).

Lead can be transferred from the mother to the foetus. The maternal/foetal blood lead concentration ratio, indicated from cord blood lead measurements, is approximately 0.9. Maternal lead can also be transferred to infants during breastfeeding. Studies have reported lead concentrations in maternal blood and breast milk. In general, these studies indicate that breast milk/maternal blood concentration ratios are < 0.1, although values of 0.9 have been reported (78).

Health effects

The most sensitive targets for lead toxicity are the developing nervous system, the haematological and cardiovascular systems, and the kidneys. However, due to the multi-modes of action of lead in biological systems, lead could potentially affect any system or organs in the body (78). IARC classified inorganic lead as probably carcinogenic to humans (Group 2A, evidence inadequate in humans, sufficient in animals) (81). According to EFSA: "Overall, extensive experimental evidence shows that various water-soluble and water-insoluble lead compounds can induce kidney tumours in rodents. In addition, one study showed that renal tumours can occur in the absence of lead-induced nephropathy. It is also noteworthy that the induction of brain gliomas, which are rarely spontaneous, occurred after oral exposure to lead in rats. Lead proved to be an effective renal tumour carcinogen/ promoter in rats and mice exposed to various organic renal carcinogens." (78).

Signs of acute lead intoxication include dullness, restlessness, irritability, poor attention span, headaches, muscle tremor, abdominal cramps, kidney damage, hallucinations, loss of memory, encephalopathy. Signs of chronic lead toxicity include tiredness, sleeplessness, irritability, headaches, joint pain, and gastrointestinal symptoms (80).

Lead interferes with the activity of several of the enzymes involved in the biosynthesis of haem. The anaemia induced by lead is primarily the result of both inhibition of haem synthesis and shortening of erythrocyte lifespan (78). According to WHO (80) anaemia occurs at blood lead levels in excess of 40 µg/100 ml in children and 50 µg/100 ml in adults.

In humans, the central nervous system is the main target organ for lead toxicity. One of the major concerns regarding lead toxicity is the cognitive and neurobehavioural deficits that are observed in children exposed to lead. There is considerable evidence demonstrating that the developing brain is more vulnerable to the neurotoxicity of lead than the mature brain. In children, elevated blood lead levels are associated with a reduced IQ score and reduced cognitive functions up to at least seven years of age. There is some evidence that this subsequently in adults leads to a reduced grey matter volume in the brain, especially in the prefrontal cortex. In a number of studies in adults an association between blood lead concentration, elevated systolic blood pressure and chronic kidney disease has been identified at relatively low blood lead levels (79).

Hazard characterisation

In 2010, EFSA performed a risk assessment of lead (79). Neurotoxicity, cardiovascular effects and renal toxicity were identified as the critical effects. The developing brain was identified as the most vulnerable organ for lead exposure. Epidemiological data on the three endpoints was analysed using the benchmark dose (BMD) method.

EFSA (79) did not regard it to be appropriate to derive health-based guidance values for lead (e.g. tolerable weekly intake), since the epidemiological data provided little or no evidence for the existence of thresholds for the critical endpoints. Because of this EFSA derived reference points and calculated approximate margins of exposure. The arguments behind the statements of EFSA (79) and FAO/WHO (75) regarding the non-existence of thresholds for lead toxicity are not fully clear. However, EFSA recommendations include that further efforts should be made to increase the understanding of the lead dose-response relationship.

Developmental neurotoxicity

Lanphear *et al* (82) conducted a detailed analysis of pooled data from seven international cohort studies and reported an inverse relationship between the blood lead concentration and the concomitant IQ score after adjustment for confounders. This was based on data on children of ages between 4 years and 10 months, and 7 years, in six cohorts, and at ages between 5 years and 10 years in one cohort. EFSA used the same data on 1,333 children in their analysis (79). EFSA performed the BMD calculations based on standard multiple regression models (83). As the dependent variable the full IQ score was used. Covariates included study site, birth weight, HOME score, maternal education and maternal IQ, as these variables were found to be statistically significant in the original analysis (82). The BMD analysis was done using each of the four blood lead exposure variables available: concurrent lead, peak lead, life time average lead and early childhood lead.The BMDL (the lower 95th confidence limit on the BMD) corresponding to a 1% change in full scale IQ score (i.e. a decrease in IQ by 1 point on the full scale IQ score) was estimated from the data. The benchmark response of 1 % was selected because such a change was within the range of observable values and could have significant consequences for human health on a population basis (79, 84). Besides the consideration of different dose measures, different dose-response models (a linear, logarithmic, and piecewise linear model) were also considered in the BMD analysis, resulting in a range of BMDL values. EFSA concluded that concurrent blood lead was the most reliable dose measure for assessing effects on developmental neurotoxicity: this measure is suggested to best reflect steady state concentrations of lead in the body of children (79, 82). Based on concurrent blood lead levels, the BMDL resulting from the piecewise linear model was selected. EFSA regarded that uncertainties when using this model, relative to the others, were of least importance. The reference point (BMDL) for developmental neurotoxicity was determined to 12 µg/l (blood lead). Using the Integrated Exposure Uptake Biokinetic Model for Lead in children, this corresponds to a dietary lead

exposure in infants and children of 0.5 µg lead/kg bw per day. This assumes negligible exposure from air, and from soil and dust (79). EFSA concluded that a margin of exposure of 10 or greater (an exposure of 10% of the RP or lower) should be sufficient to ensure that there was no appreciable risk of a clinically significant effect on IQ. At lower margins of exposure, but greater than 1 (exposures between 10 % and 100 % of the RP), the risk is likely to be low, but not such that it could be dismissed as of no potential concern (79).

Other effects
EFSA (79) also established reference points for renal and cardiovascular effects for adults. The reference point (BMDL) for kidney effects in adults was determined to 15 µg/l (blood lead). Using the equation of Carlisle and Wade (85), this corresponds to a dietary lead exposure of 0.63 µg/kg bw per day when assuming negligible exposure from air and soil. The reference point (BMDL) for effects on systolic blood pressure in adults was determined to 36 µg/l (blood lead) and 8.1 µg/g (tibia bone mineral lead). Using the equation of Carlisle and Wade (85), the BMDL of 36 µg/L, based on blood lead, corresponds to a dietary lead exposure of 1.50 µg/kg bw per day. This assumes negligible exposure from air and soil.

Exposure assessment

Estimated intakes for all individual food products are presented in Appendix IV. Summary results for different product categories are presented in Tables 8 and 9. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 8) or a single portion (Table 9).

For product categories in Table 8, estimated intakes for individual products range between 0.02 and 0.14 µg/kg bw/day. One follow-on formula, and five FSMP products used as the sole source of nutrition are associated with intakes higher than 0.1 µg/kg bw/day (see Appendix IV). An estimate of the intake from breast milk is given as a reference in Table 8; this intake (0.35 µg/kg bw/day) is at the upper end of the intake interval estimated for the analysed products, but below the RP of 0.5 µg/kg bw/day.

In Table 9, estimated intakes for individual food products range between 0.001 and 0.26 µg/kg bw/portion. One gruel product, one porridge product, and one FSMP product used as partial feeding are associated with intakes higher than 0.1 µg/kg bw/day (see Appendix IV).

Table 8. Summary of estimated intakes of lead (µg/kg bw/day).

Product category	Age (months)	N	Intake[a]
Infant formula	0-4	9	0.04 (0.04-0.08)
Follow-on formula	6-8	4	0.05 (0.03-0.14)
FSMP as sole source of nutrition	0-12	21	0.07 (0.03-0.14)
FSMP as partial feeding	0-12	3	0.02 (0.04-0.10)
Breast milk	3 weeks	90	0.35[b]

[a]Median (range).
[b]A lead concentration in breast milk of 2.1 µg/kg was used (a composite sample of human milk collected w 3 post-partum from 30 volunteers during 2008, 2009 and 2010; n = 90 samples were pooled in the analysis). An infant weighing 4.2 kg (weight used for infants 0-4 months) and consuming 700 ml breast milk per day was assumed.

Table 9. Summary of estimated intakes of lead (µg/kg bw/portion).

Product category	Age (months)	N	Intake[a]
Gruel	6-12	14	0.01 (0.01-0.21)
Porridge	4-12	26	0.01 (0.004-0.26)
FSMP as partial feeding	12	3	0.04, 0.04, 0.12
Foodstuffs for normal consumption	12	12	0.003 (0.001-0.01)

[a]Median (range).

Contribution from drinking water

The median lead concentration in municipal drinking water in Sweden is 0.11 µg/l based on analyses from approximately 1,500 water purification plants between 2008 and 2011 (4,518 analyses in total). Combining this median value with a consumption of 630 ml water (used for preparing 700 ml infant formula) by a child with a body weight of 4.2 kg (about 3 weeks old) results in a lead intake of 0.017 µg/kg bw/day.

Risk characterisation

For developmental neurotoxicity, the reference point (RP) for lead is 0.5 µg/kg bw/day. Summary results of estimated intakes expressed in terms of a percentage of the RP are given in Table 10, and summary results of estimated intakes expressed in terms of the number of portions required to reach the RP are given in Table 11. Product-specific information is given in Appendix IV.

For product categories in Table 10, the estimated median exposure is in the range of 8-14 % of the RP. Exposures higher than 10% of the RP are observed for three infant formulae, two follow-on formulae, 16 FSMP products used as the sole source of nutrition, and one FSMP product used as partial feeding.

In Table 11, the number of portions to reach the RP varies between and within the different product categories, but is generally larger than 10. The number of portions to reach the TDI is less than 10 for two gruel products, two porridge products, and one FSMP product used as partial feeding.

Table 10. Summary of estimated intakes of lead expressed in terms of a percentage of the RP of 0.5 µg/kg bw/day.

Product category	Age (months)	N	% of RP[a]	More than 10 % of RP[b]
Infant formula	0-4	9	8 (7-16)	3
Follow-on formula	6-8	4	10 (6-27)	2
FSMP as sole source of nutrition	0-12	21	14 (6-27)	16
FSMP as partial feeding	0-12	3	5, 8, 20	1

[a]Median (range).
[b]The number of products associated with exposure that are higher than 10 % of the RP.

Table 11. Summary of estimated intakes of lead expressed in terms of the number of portions required to reach the RP of 0.5 µg/kg bw/day.

Product category	Age (months)	N	No. of portions to reach RP[a]	Less than 10 portions to reach RP[b]
Gruel products	6-12	14	50 (2-86)	2
Porridge	4-12	26	49 (2-119)	2
FSMP as partial feeding	12	3	4, 11, 13	1
Other	12	12	162 (36 - 454)	0

[a]Median (range).
[b]The number of products for which the no. of portions to reach the RP is less than 10.

Discussion

For several products the margin to the RP is greater than a factor of 10 (an estimated daily intake less than 10 % of the RP, or more than 10 portions required to reach the RP). EFSA regards that a margin to the RP equal to a factor of 10 would ensure that there is no appreciable risk of clinically significant effects on IQ. For exposures higher than this (10-100 % of the RP) EFSA states that the risk is likely to be low, but not such that it could be dismissed as of no potential concern. In

this context, some concerns can be identified with individual products in this assessment, in particular for the FSMP products used as the sole source of nutriation, for which 16 out of 21 individual products are associated with exposures higher than 10 % of the RP.

Conclusion

The present assessment supports the conclusions made by EFSA in its risk assessment that there is a potential concern for effects on neurodevelopment at current levels of exposure to lead for infants and children. Also, other studies indicate that the current blood lead levels in Swedish children are in the range of the RP of 12 µg/l (86). This suggests that exposure to lead should be reduced as much as possible.

Manganese (Mn)

Nutritional background

Physiological function of manganese

Manganese is an essential nutrient, necessary as a cofactor for several enzymes and important for the normal development of the foetus. Manganese is utilised by superoxide dismutase – an antioxidant enzyme – and plays a role in the activation of glycosyltransferase, which is necessary for mucopolysaccharides found in cartilage, bone and other connective tissues (87).

Dietary sources of manganese

Manganese is found in a variety of foods and concentrations vary considerably. The highest concentrations (exceeding 10 mg per kg) have been detected in grains, nuts and rice (88). Other sources of manganese in foods are, for example, vegetables, legumes, fruits and tea (89). In a Swedish study of market baskets (90) the highest average percentage contribution to the total daily supply of manganese came from cereal products (61 %), followed by fruit (18 %), sugar and sweets (8 %), vegetables (6 %) and potatoes (4 %) (91). Moreover, manganese may be found in drinking water. Currently there is, to our knowledge, no nation-wide compilation of detected concentrations of manganese in drinking water from Swedish municipalities, but according to unpublished data the average concentration in groundwater used as drinking water in Sweden is 150 ± 510 µg/L, median 60 µg/L (92).

Recommendations and intakes

When data is judged to be insufficient to set a population reference intake such as a RI, an adequate intake (AI) may be used to estimate adequacy of intakes. According to the American Institute of Medicine (IOM) (93) the AI for children 0-6 months of age is set at 3 µg/ day based on the intake from breast milk. For children 7-12 months of age AI was set at 600 µg/day based on an estimated intake from food. For children 1-3 years old and 4-8 years old, AI was set at 1.2 mg/day and 1.5 mg/day respectively. Breast milk may contain concentrations of manganese in a range of 3.1-7.5 µg/L, although maternal intake via drinking water and foods varies considerably. According to Ljung & Vahter (3) infant formulae have been found to contain manganese in a concentration range of 25-499 µg/L - not including additional manganese from drinking water. Many infant formulae contain about hundred times higher concentrations than those found in breast milk. Concentrations of manganese in the product ready for consumption could be even higher, as the water used for preparation may also contain manganese. Analysis of market baskets representing a typical Swedish diet (exluding drinking water) showed an average daily exposure of 4.0 mg in adults (91), indicating that

intakes in the adult population are well above the AI set by IOM (currently 1.8 mg/day for women and 2.3 mg/day for men). According to the Swedish market basket study, cereal-based products contributed to more than 60 % of manganese intake in adults. Because cereal is a part of the diet for most infants and young children, a substantial contribution of natural manganese from complementary foods can be assumed.

Hazard identification

Adverse effects of insufficient manganese intake
Manganese deficiency in humans can result in impaired growth, poor bone formation and skeletal defects, reduced fertility and birth defects, abnormal glucose tolerance, and altered lipid and carbohydrate metabolism (88). The development of an erythaematous rash on the torsos of young men placed on a manganese-depleted diet has been observed (94). In experimental animals a variety of adverse effects has been described, for example impaired growth, skeletal abnormalities, reproductive deficits, ataxia of the newborn, and defects in lipid and carbohydrate metabolism (88). Consequently, deficiency seems to cause comparable effects in experimental animals and humans.

Some data suggest that a suboptimal manganese status may occur in humans with epilepsy, osteoporosis, or exocrine pancreatic insufficiency, in individuals undergoing chronic haemodialysis, and in children with Perthes' disease or phenylketonuria (88). It is, however, not clear whether manganese deficiency has a role in the development of these diseases (89).

Adverse effects of excessive manganese exposure
Subtle neurobehavioural effects have been identified as the most critical endpoint in studies of manganese in experimental animals and manganese in high doses is regarded as a neurotoxic substance. The mechanisms by which manganese exerts neurotoxicity have not been clearly explained, though it is known that manganese is a cellular toxicant that can impair transport systems, enzyme activities, and receptor functions (95, 96). Neurotoxic effects in humans have mainly been shown in occupational studies of inhalation of high doses of manganese by workers (97). Furthermore, neurobehavioural and neurotoxic effects in several species of experimental animals (mice, rats, guinea pigs and monkeys) have been demonstrated following both inhalation and oral intake of manganese.

The studies in rats are probably of limited value as absorption is not regulated in a similar way in humans. Moreover, it has been demonstrated that distribution of manganese in the brain in rats compared to nonhuman primates (in this case the marmoset) is different (98). Studies in monkey may be more relevant since the

postnatal development of the brain in primates is likely to be more similar to that of humans.

Many epidemiologic studies including children have been carried out in order to investigate potential associations between intake of manganese from drinking water and/or levels of manganese in blood/hair on the one hand and results of a variety of tests regarding behaviour, hyperactivity, learning ability and intelligence on the other (99-101). In conclusion, these studies indicate that relatively low intakes of manganese by children may affect the nervous system in a negative way, which has been demonstrated predominantly in disturbances of the behaveour (92) and/or in intellectual impairments (100). In addition, an association between manganese exposure from water and neurological effects in elderly individuals has been indicated in an epidemiological study (102).

Hazard characterisation

Adverse effects of insufficient manganese intake
Manganese deficiency seems to be extremely rare in humans. This is probably due to the ubiquitous presence of manganese in foods. At present no published data regarding the prevalence of manganese deficiency have been found. According to Aschner & Aschner (103) naturally occurring deficiency states of manganese have not been recognised and Hardy *et al* (104) states that there is very little evidence of manganese deficiency being clinically relevant in humans.

Adverse effects of excessive manganese exposure
It has been estimated that approximately 1-5 % of ingested manganese is absorbed from the gastrointestinal tract. The absorption of manganese is regulated in adults, as it is subject to homeostatic control, which means that the absorption is reduced when intake of manganese is high. However, in infants this regulation is not yet fully developed, which may result in considerably higher exposure in infants in comparison with adults (103). In addition, infants have a low bile flow, which may result in lower excretion of manganese via bile. The retention of manganese in infants is thus higher than in adults (103).

Manganese in human milk appears in the trivalent oxidation state bound to lactoferrin. Lactoferrin is the major iron-binding protein in milk. In infant formula, manganese is in the divalent oxidation state and different mechanisms from those operating in the absorption of manganese from human breast milk are likely to be involved (87). Since individuals with low iron stores have been found to absorb more manganese than individuals with normal iron stores, interaction between the absorption of manganese and iron clearly exists, i.e. iron status affects the uptake of manganese (105).

Experimental animals

Studies on experimental animals like the mouse, rat, guinea pig, and monkey have demonstrated that oral intake of manganese may be associated with neurotoxic effects. However, neither an no observed adverse effect level (NOAEL) nor a dose-response regarding neurotoxicity could be demonstrated in the studies in experimental animals assessed by the Scientific Committee on Food (SCF) according to the latest opinion expressed in 2000 (88). In young growing rats the lowest dose level associated with neurotoxic effects (neuronal degeneration in cortical and cerebellar sections of the brain) has been found at an oral dosage of 0.28 mg/kg body weight (106), which may be suggested as an lowest observed adverse effect level (LOAEL) for this kind of effect. Effects of this kind at this dose level have, however, not consistently been observed in growing rats. Some investigators report effects at considerably higher dose levels. For example Dorman *et al* (107) did not observe any adverse histological changes in the brain region of growing rats exposed to 11 or 22 mg of manganese per kg body weight. Generally, the sensitivity seems to decrease with age as several studies on rats indicate that higher doses are generally needed to induce neurotoxic effects in adult rats, but also in this case results are not entirely consistent. The lowest dose associated with neurobehavioural effects (in this case learning ability) in adult rats (females) has been reported to be 0.36 mg/ kg body weight (108). In infant rhesus monkeys the lowest found dose levels associated with neurotoxic effects have been found at 300 µg/kg body weight (109). In this study neurobehavioural effects of manganese in daily dosages of 100 and 300 µg/kg body weight, administered in soy-based infant formula, were investigated. The results of this study indicate that components (including manganese) in soy formula may influence brain development as reflected in behavioural measures. In this context, it should be noted that soy-based infant formulae also contain other substances, for example phytoestrogens, phytates and aluminium, which potentially can result in negative health effects. In adult monkeys the lowest dose levels associated with neurotoxic effects are 6.9 mg/kg body weight during 18 months for monkeys (110). Data regarding the bioavailability of manganese after oral administration of infant formula to monkeys are currently lacking. As non-human primates are more physiologically similar to humans than rodents in this respect, studies in monkeys provide information that to a higher extent applies to humans.

Humans

A number of epidemiological studies focusing on manganese neurotoxicity in children have been published. A review of those published 1977-2007 has been provided by Menez-Filho et al 2009 (99). Moreover, some additional studies have been published during the last five years (see below). Some examples and results from the epidemiological studies will be briefly mentioned in the following. It should be noted that most of these studies have been performed with a cross-sectional design and the quality of several of the studies may be questionable.

Children who drank water with an average concentration of manganese of at least 0.241 mg/L during 3 years performed more poorly in school and in the WHO neurobehavioural core test battery compared to children who drank water with manganese ≤ 0.04 mg/L (111, 112).

In some other studies it was observed that manganese levels in hair are higher in learning disabled children than in reference children, see Collipp *et al* (113), Pihl and Parkes (114). These authors concluded that it is possible that excess manganese ingestion could lead to learning or behavioural impairment in children. As a number of other agents, including lead, also might have affected the results, the observed association is not sufficient to establish a cause-effect relationship (114).

Takser *et al* (115) conducted a prospective epidemiological study to determine the long-term effect of manganese exposure *in utero* on children's psychomotor development. This French cohort consisted of 247 healthy pregnant Parisian women and their babies and the children were examined at 9 months, 3 years and 6 years. At 3 years of age negative relationships were found between blood levels of manganese and psychomotor sub-scales of attention, non-verbal memory and hand skills. However, no significant associations were observed between cord blood manganese concentration and general psychomotor indices at this age, or for the other studied age groups. These results suggest that early psychomotor development could be affected by environmental manganese exposure *in utero*.

Higher prenatal manganese exposure at gestational week 20 was found to be significantly correlated with distinct behavioural outcomes in a pilot study of 11-13 year old children by Ericson *et al* (116). These individuals were more impulsive, inattentive, aggressive, defiant, disobedient, destructive and hyperactive. A standardised test of cognitive ability and achievement performed by the children did not, however, show lower scores in comparison with reference children.

In a cross-sectional epidemiological study of 142 children (10-year-olds) in Bangladesh, a statistically significant relationship between decreasing intelligence scores and increasing manganese levels (800 µg manganese/L) in drinking water was found (11).

Khan *et al* (117) found dose–response associations between concentrations of manganese in drinking water and classroom behaviour, which suggests that those in the first quartile of exposure (< 265 µg/L) differed significantly from those consuming drinking water with higher levels of manganese. The study included 201 children (8-11 years) and was performed with a cross-sectional design in Bangladesh.

In Quebec, Canada, Bouchard *et al* (118) were able in an epidemiological study of 46 children (ages 6-15 years) to demonstrate a statistically significant relationship between increased levels of oppositional behaviours and hyperactivity and increased levels of manganese in drinking water. This study was followed up by another cross-sectional study of 362 children (ages 6-13 years), published in 2011 (100).

The main results of this study suggest that exposure to manganese at levels common in groundwater is associated with intellectual impairment (lower IQ scores) in children. A strong association between manganese concentrations and IQ scores was detected, with a difference of 6.2 full scale IQ points between the children exposed to water containing 1 and 216 µg manganese/L (median of lowest and highest quintiles). There was a significant association between manganese intake from drinking water, but interestingly not manganese from the diet, and elevated manganese concentration in children's hair.

Henn *et al* 2010 (119) studied 448 Mexican children born 1997-2000 with a longitudinal design in order to investigate associations between manganese exposure during early life and neurotoxic effects. Blood samples collected from children at 12 and 24 months of age were analysed for manganese levels. Bayley Scales of Mental and Psychomotor Development were used at 6-month intervals between 12 and 36 months of age to assess mental and psychomotor development. An inverted U-shaped association between 12-month blood manganese and concurrent mental development scores (compared with the middle 3 manganese quintiles) was found for the lowest manganese quintile. This 12-month manganese effect was apparent but diminished in mental development scores at later ages. At 24 months the levels of manganese were not associated with neurodevelopment. The authors´ interpretation is that these results indicate a biphasic dose-response relationship between manganese exposure at lower exposure levels and infant neurodevelopment.

The cohort mentioned above was also studied by Henn *et al* (101), in order to investigate possible interactions between manganese and lead in early childhood. In addition, possible interactions between manganese and potentially toxic metals such as lead have also been shown to occur. It was clearly shown that co-exposure of manganese and lead was associated with more severe neurodevelopmental effects than those expected from exposure to each metal alone.

According to Takser *et al* (115) and Henn *et al* (101), it is possible that there is a window of susceptibility to manganese exposure. They suggest that the strongest neurotoxic effects may occur during foetal life and early infancy possibly before 12 months of age.

When interpreting the results of the epidemiological studies it should be emphasised that most of them are performed with a cross-sectional design with a rather limited number of participants, with the exception of two prospective investigations of infants (101, 115). Moreover, in many of the studies it is not known whether the observed effects can be solely attributable to excess manganese or if other components of drinking water or diet could have influenced the result, as they were not monitored or accounted for in the analyses. Furthermore, control for potential confounders often seems to be insufficient. In most studies the participating children were 10 years old or older and it is not clear whether the observed associations may be the result of exposure in early infancy or later in childhood.

Another problem in these studies is that a validated biomarker for manganese exposure is lacking (99). When interpreting possible associations between manganese intake and studied outcomes in the mentioned studies these limitations should be considered. Even though there are many limitations, the results of these studies taken together indicate that neurotoxic effects after oral exposure to manganese can develop in children and that these effects are similar to those observed in adults environmentally or occupationally exposed to manganese.

NOAEL based on manganese intake

An NOAEL has been estimated to 11 mg manganese per day by WHO, 2004 (120). This NOAEL emanates from a Canadian study of 100 young women about 30 years old (121) and is based on calculated daily intakes of manganese and not on actual measurements of manganese intakes. Furthermore, the health status of the subjects in this study was not commented on. In the assessment by WHO (120) there were no comments regarding possible adverse/toxic effects in the study or why this value was chosen as NOAEL.

UL, TDI and RfD

No UL for infants could be established by EFSA, 2006 (88) or the British Expert Group on Vitamins and Minerals (EVM), 2003 (122) as relevant toxicological data were lacking. In a risk assessment performed by WHO (120) a TDI of manganese was established. This TDI was based on the estimated NOAEL of 11 mg/day (mentioned above) which was divided by an uncertainty factor of three. Using an adult body weight of 60 kg, a TDI of 60 µg Mn/kg body weight was derived. In addition, the American Environmental Protection Agency (EPA) established in 1996 an acute oral reference dose (RfD) at 0.14 mg/kg, i.e. 140 µg/kg body weight/day in an assessment based on oral intake studies (123). This RfD was based on an occasional intake of 10 mg manganese per day, which was considered safe by EPA, and an assumed body weight of 70 kg (124). Confidence in the oral RfD is regarded as medium by EPA and it should be observed that "quantitative information to indicate toxic levels of manganese in the diet of human is not available".

Biomarkers of manganese status

Several potential indicators of manganese exposure are available, for example manganese concentrations in blood, urine, hair and saliva. Manganese concentrations in blood could be used as a biomarker of exposure on a group basis and to measure recent exposure. Overall, however, none of the mentioned biomarkers is at present regarded as a sufficiently sensitive and valid indicator of exposure for individual biomonitoring. Moreover, the mechanisms of manganese toxicity are not yet clarified and hence no reliable biomarkers have been established to evaluate adverse effects of manganese exposure. As it is beyond the scope of this assessment to discuss these issues in detail, the reader is referred to Zheng *et al* (125) for a comprehensive review and discussion.

Maximum limits and guideline values for manganese in foodstuffs

Drinking water

WHO states in a background document (120) to the third edition of the drinking water guideline, 2004, that "A health-based value of 0.4 mg/l can be derived for manganese based on the upper range value of manganese intake of 11 mg/day, identified using dietary surveys, at which there are no observed adverse effects, using an uncertainty factor of 3 to take into consideration the possible increased bioavailability of manganese from water, allocating 20 % of the TDI to drinking-water and assuming the consumption of 2 litres of water per day by a 60 kg adult". However, in 2011 this guideline value was withdrawn; as it "is well above concentrations of manganese normally found in drinking-water, it is not considered necessary to derive a formal guideline value", according to WHO (126). Although the scientific background (including the derivation of the TDI) to the previously established WHO guideline value may be questionable, the decision by WHO not to apply any maximum limits in drinking water, has been criticised by Frisbie *et al* (127) who emphasise that: "drinking water or potential drinking water supplies with manganese concentrations above 400 µg manganese/L are found in a substantial number of countries worldwide".

Infant formula

For infant formula there is, according to the Commission Directive 2006/141/EC (128), a maximum limit of 100 µg manganese/100 kcal, which corresponds to about 650 µg/L (92). The maximum level of 100 µg manganese/100 kcal is the maximum limit in infant formula recommended by the SCF in its report 2003 (129), which was the basis for the Commission Directive (129). However, how this maximum limit in formula has been derived by the SCF is not clear. The SCF states that this value is: "below the estimated LOAEL in adults for manganese contents in water (4.2 mg/L)." This LOAEL is based on results from a study performed in Greece (102) from which an LOAEL of 4.2 mg per *day* – not *per litre* was derived. The consequence of this misinterpretation is that the calculations are based on an LOAEL which is twice that of the actual level in the mentioned study. In addition, this LOAEL is based on effects observed in persons of a different age category (older than 50 years), as neurological symptoms, indicating chronic poisoning by manganese, which clinically resembles symptoms of Parkinson's disease, were studied. Furthermore, the intake estimates in this study were based on calculations from the manganese contents in drinking water and not on actual intakes. These shortcomings in the process of establishing a maximum limit in infant formula described above, were initially discussed by Ljung *et al* (130). According to the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) a maximum level of 50 µg/100 kcal is recommended based on the concentration in unfortified soy-based formula (131).

Exposure assessment

Estimated intakes for all individual products are presented in Appendix V. Summary results for different product categories are presented in Tables 12 and 13 below. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 12) or a single portion (Table 13). The intake from breast milk is given as a reference in Table 12. The concentration of manganese was 4 µg per kg breast milk (See Appendix V, Table 7). This value is within the range for average manganese concentrations in breast milk reported in the literature (92).

Table 12. Summary of estimated daily intakes of manganese - expressed as µg/day and as µg/kg body weight/day from infant formula, follow-on formula, FSMP as the sole source of nutrition, FSMP as partial nutrition and from breast milk.

Product category	No. of products	Age (months)	Intake[a] (µg/day)	Intake (µg/kg bw/day)
Infant formula	9	0-4	66 (15-110)	10 (4-26)
Follow-on formula	4	6-8	136 (39-180)	21 (5-21)
FSMP as sole source of nutrition	21	0-12	316 (34-2256)	69 (8-230)
FSMP as partial feeding[b]	3	0-12	580 (200-780)	75 (48-80)
Breast milk	-	3 weeks	2.8 (-)	0.7 (-)

[a]Values are median (range)
[b]Nutramigen 2 lipil, XP Maxamaid and PKU anamix infant lcp+ (recommended daily intake)

Table 13. Summary of estimated intakes expressed as µg manganese per kg body weight *per consumed portion* from gruel, porridge, FSMP as partial feeding and other products [a]

Product category	No. of products	Age (months)	Intake[a] (µg/portion)	Intake (µg/kg bw/portion)
Gruel	14	6-12	257 (9-350)	33 (1-46)
Porridge	26	4-12	376 (114-989)	43 (16-128)
FSMP as partial feeding[b]	3	12	415 (351-764)	42 (36-78)
Foodstuffs for normal consumption	12	12	147 (16-1154)	15 (2-118)

[a]Values are median (range)
[b] Fresubin energy fibre drink, PKU gel and Frebini energy fibre drink

As is evident from Tables 12 and 13, the highest exposure is to be expected from intake of products categorised as FSMP as the sole source of infant nutrition and as partial infant nutrition and porridge.

The product category "Foodstuffs for normal consumption" contains a wide range of products and even within the same product category, for example oat drinks, manganese concentrations vary from 157 to 800 µg /kg due to variations in natural content. The analysed soy drinks generally had high concentrations of manganese (1,567-1,983 µg /kg) due to naturally high levels of manganese. Intakes of manganese from foodstuffs for normal consumption thus vary considerably and some products such as rolled oats, oat toasted and milled and some soy products may contribute to high exposure.

Estimation of the contribution of manganese from drinking water
As mentioned previously the concentrations of manganese in the water used for preparation and hence the potential contribution from water should also be considered. As manganese in a concentration of 300 µg/L is considered acceptable in private wells in Sweden, the total exposure could be considerably higher after consumption of products ready to eat with a low concentration of manganese. This could result in daily exposures with narrow margins to the TDI for formula products as well. The maximum level for manganese in drinking water supplied by the municipalities is, according to current Swedish legislation, 50 µg/L. Some examples of contributions of manganese from drinking water are presented in the risk characterisation below.

Risk characterisation

Daily intakes from the analysed products in relation to AI
According to the present intake assessment, the AI of 3 µg per day for 0-6 months will be reached after consumption of all analysed infant formulae as they contribute with 5-30 times the AI. A daily intake of 3 µg per day will also be reached with follow-on formulae from 6 months. One product recommended from 8 months contributes with 30 % of the AI and additional sources of manganese for the infant to reach an AI of 600 µg for the age 7-12 months are needed. Daily intakes from most FSMP products that may be used as the sole source of nutrition are well above the AI for the different age groups. However, the contribution of manganese from three FSMP products will not reach the AI level according to our calculations: Neocate Advance (42 % of AI at 12 months), Resource Minimax (47 % of AI at 12 months) and NutriniKid Multi Fibre (90 % of AI at 12 months). However, the products may be consumed together with other foods, adding to total manganese intake.

Table 14. Summary of estimated intakes expressed in terms of the number of portions required to reach the AI of 3 µg /day for 0-6 months, 600 µg/day for 7-12 months and 1,200 µg/day for products recommended from 12 months.

Product category	No. of products	Age (months)	Number of portions required to reach the AI [a]
Gruel	14	6-12	0 (0-4)
Porridge	26	4-12	0 (0-4)
Foodstuffs for normal consumption	12	12	1 (0-15)
FSMP as partial feeding [b]	3	12	3 (2-3)

[a]Values are median (range)
[b]Fresubin energy fibre drink, PKU gel and Frebini energy fibre drink

Daily intakes from the analysed products in relation to TDI

In the tables below, median and range for daily intakes and number of portions needed in order to reach TDI are displayed. The TDI applied in these calculations is 60 ug/kg body weight/day established by WHO (120).

Table 15. Summary of estimated intakes – as a percentage of the TDI.

Product category	No. of products	Age (months)	Intake as percent of TDI[ab]
Infant formula	9	0-4	17 (6-44)
Follow-on formula	4	6-8	30 (8-35)
FSMP as sole source of nutrition	21	0-12	115 (14-384)
FSMP as partial feeding	3	0-12	125 (79-133)

[a]Values are median (range)
[b]The tolerable daily intake (TDI) : 60 µg/kg bw/day (WHO, 2004) (120)

Table 16. Number of portions needed in order to reach TDI.

Product category	No. of products	Age (months)	Number of portions to reach TDI[ab]
Gruel	14	6-12	2 (1-53)
Porridge	26	4-12	1 (0-4)
FSMP as partial feeding	3	12	1 (1-2)
Foodstuffs for normal consumption	12	12	4 (1-37)

[a]Values are median (range)
[b]The tolerable daily intake (TDI) : 60 µg/kg bw/day (WHO, 2004) (120)

The exposure from infant formula and follow-on formula does not exceed the TDI and the margins seem to be sufficient in the products analysed. Some FSMP used as the sole source of infant nutrition and FSMP as partial feeding clearly exceed the TDI.

The exposure from porridge can in a number of cases be fairly high and the number of portions in order to reach the TDI may be rather small. This is also the case for a couple of gruel products. When the TDI is reached by consuming even less than one or two portion(s) daily, the concentration of manganese shuoldt not be regarded as acceptable. In this context it is, however, also important to be aware of the uncertainties in the establishment of the used TDI. (For more details see the "Drinking water" section below). Not all products have, however, been fortified. Some products contain manganese naturally in high concentrations. The products included in "Foodstuffs for normal consumption" create a heterogeneous category including a variety of foods. In some specific products concentrations are high and consumption of these products could thus be problematic.

Contribution from drinking water
A reasonable estimation of the contribution from drinking water, assuming a concentration of 50 µg/L and an intake of 630 mL water by a child with a body weight of 4.2 kg (about 3 weeks old) would be 32 µg, i.e. 8 µg/kg body weight. A consumption of 630 mL is assumed as it would correspond to the amount of water needed to prepare 700 mL of formula, which is our estimated consumption by infants of this age. The intake of manganese from formula would then increase almost twofold, but still below the TDI. If we assume a type of worst case scenario with a water concentration of 300 µg/L, the contribution of manganese from drinking water would amount to 189 µg, i.e. 45 µg/kg body weight under the same assumptions as above. Clearly, for formula this exposure would result in an intake below but close to the TDI.

Discussion

Manganese deficiency seems to be extremely rare in humans, because manganese is commonly present in foods and drinking water. Currently, the prevalence of manganese deficiency is not known. The risk of development of neurotoxicity is considered to be higher in infants than in adults as infants have not developed the ability either to regulate the absorption of manganese or to eliminate manganese effectively. These circumstances may result in an excessive body exposure of infants to manganese (92). In addition, children are more vulenerable, as the development of the neuronal system – including the brain – is intense during childhood. According to a recent literature search performed at the NFA, there is currently limited information about manganese homeostasis in infants. Furthermore, it is likely that different mechanisms may operate in the gastrointestinal absorption of manganese from human milk and infant formula (87).

Mild neurotoxic effects have been observed in monkeys at a dose level of 300 µg/kg body weight (109). When considering this study and the fact that the nervous system of younger animals in general seems to be more sensitive than that of adults (92), it may be argued that the TDI of 60 µg/kg body weight is too high as there should be safety factors for interspecies extrapolation and inter-individual variations and an extra safety factor as LOAEL has been used instead of NOAEL (which was not available). As relevant data are lacking it is not possible to propose a TDI. However, it seems reasonable to suggest a "provisional TDI for infants" in the range of 5-15 µg/kg body weight based on the the lowest found dose level associated with neurotoxic effects at 300 µg/kg body weight in the study by Golub (109) and a safety factor of at least 20-30 to allow for interspecies differences and the use of LOAEL.

Associations between intake of manganese and neurotoxicity have been demonstrated for different biomarkers (concentrations of manganese in blood and hair), different cognitive tests and sources of exposure. None of these studies is entirely convincing regarding toxic effects of manganese in children. In most epidemicological studies exposure data are commonly reported as blood levels of manganese, while some studies report concentrations in drinking water as the exposure parameter. In addition, kinetic studies dealing with associations between actual oral intake and blood levels are currently lacking. In consequence, it is not possible to relate blood levels to oral exposure. Moreover, many of the epidemiological studies have been performed in countries where malnutrition and concurrent infections in children may be common (for example Bangladesh and Mexico), which may result in a change in sensitivity towards manganese toxicity. These circumstances, as well as the fact that most studies have been performed with a cross-sectional design, make it difficult to use these studies in order to estimate a safe intake level. Nevertheless, these studies could support the findings in experimental studies.

Epidemiological studies that have detected some kind of association between manganese exposure and adverse effects indicate that children are more sensitive to negative health effects of manganese in comparison with adults. More, well designed epidemiological studies are, however, warranted in order to confirm these associations. In addition, further studies are required in order to develop appropriate animal models reflecting susceptible human subpopulations like infants and children.

In "Guidelines for Drinking-water Quality", 2004(126), WHO established a health-based guideline value for manganese of 400 µg/L, but the scientific background to this value has been questioned and it has been argued that the application of this guideline value probably does not protect against negative health effects in young children (younger than 1 year old) (92). Moreover, this guideline value was withdrawn in 2011, based on an opinion of WHO that it was not considered necessary to derive a formal guideline value because 0.4 mg/L would be well above concentrations of manganese normally found in drinking-

water. The highest concentration of manganese recommended by the SCF (90) in infant formula is 100 µg/100 kcal (corresponding to about 650 µg/L), but also in this case the scientific background has been questioned (130). Consequently, children receiving formula prepared from water containing manganese may be at risk of over-exposure to manganese.

According to ESPGHAN a maximum level of 50 µg/100 kcal is recommended based on the concentration in unfortified soy-based formula. It is possible that a higher concentration of manganese in formula in comparison with breast milk is justifiable, since manganese is an essential element, which is less bioavailable in formula than in breast milk. It is, however, questionable whether a 100-fold higher manganese concentration in formula is justifiable (92). This is also the conclusion drawn by the National Board of Health and Welfare in a report on environmental health (132). The maximum limit of manganese in formula has to be set at a level where additional input from the mixing water does not affect the safety of the final product ready for consumption.

In the present study of foods for infants and young children high concentrations of manganese have been detected mainly in FSMP as the sole source of nutrition, although in line with the current permitted range, and in porridge products intended for infants and young children as well as in some other products intended for consumption by this group of consumers. Similar analytical results have been found in an investigation performed by the IMM (3).

The use of AI and TDI for evaluating risk benefit of manganese in foods for infants and young children

In order to evaluate whether the content of a micronutrient in a particular food product is within the acceptable or optimal range, upper and lower levels of intakes must be established. However, when AI for manganese and this TDI are used for different age groups, the shortcomings of these values become apparent.

In Table 17 it is shown that the daily intake of manganese required to reach the AI varies according to age. These values are based on manganese intakes from human milk (< 6 months) and other foods (≥ 7 months). The daily intake of manganese that corresponds to the TDI (60 µg/kg bw/day according to WHO (120) at different ages and body weights is also displayed in this table.

It is not biologically plausible that manganese requirements would change to this extent between 6 months (3 µg/day) and 7 months (600 µg/day) and between 11 months (600 µg/day) and 12 months (1,200 µg/day). In addition, the scientific basis for the TDI is also weak. The calculation of the number of portions to reach the AI and TDI is misleading as this TDI at ages above 8 months (510 µg/day) is lower than the AI (600 µg/day). In this case, an optimal range of the manganese content in infant foods cannot be established and evaluation of the manganese concentration of the studied products is not possible. Hence, revision of the AI

and establishment of an UL for manganese are urgently needed in order to be able to define an optimal range of manganese in products intended for infants and young children.

Table 17. Examples of how the AI and the daily intake of manganese that correspond to the TDI vary with age and body weight.

Age (months)	Body weight (kg)	AI [a] of manganese (µg/day)	Daily intake of manganese that corresponds to TDI[b] (µg/day)
0 (3 weeks)	4.2	3	252
4	6.6	3	396
6	7.7	3	462
8	8.5	600	510
12	9.8	1,200	588

[a]The adequate intake (AI) 0-6 mo 3µg, 7-12 mo 600 µg, 1-3 years 1200 µg (IoM, 2001) (93)
[b]The tolerable daily intake (TDI) : 60 µg/kg bw/day (WHO, 2004) (120)

Conclusion

This overview of risks and benefits associated with the intake of manganese shows that more data are needed before a conclusive risk and benefit assessment can be performed. Manganese is an essential nutrient needed as a cofactor for many enzymes. Deficiency of manganese has, however, not been recognised as a nutritional problem in humans, probably due to the ubiquity of manganese in foods.

Neurotoxic effects associated with oral exposure to manganese have been reported from studies in experimental animals. In addition, data from several epidemiological studies in different countries such as Canada, Bangladesh and Mexico indicate associations between manganese exposure in children and impairments in behaveour and intelligence. Currently, relevant data on certain aspects of manganese toxicity and epidemiology are lacking. The adequacy and safety of manganese via foods intended for infants and young children should therefore be carefully considered in relation to potential benefits and risks.

In the present survey of food products intended for infants and young children, high concentrations of manganese have been detected mainly in FSMP used as sole sources of nutrition, porridge products and in some other products intended for consumption by this group of consumers. The detected concentrations of manganese are, however, in line with the current permitted range for FSMP products.

When considering recommended consumptions of these food products from the manufacturers or when estimating intakes per portion, the intake of manganese for some products is close to or even exceeds the TDI applied (60 µg/kg body weight/ day established by WHO in 2004). This does not seem to be scientifically justified, especially since this TDI for several reasons must be regarded as very uncertain. Consequently, more data regarding the daily requirements of manganese during infancy and childhood are urgently required in order to be able to define the optimal range of intake more accurately.

What is especially important is that the homeostatic regulation of manganese in infants may not yet have been developed at the time when the infants are consuming the products containing high concentrations of manganese. This is likely to result in considerably higher manganese exposure in infants in comparison with adults (103). According to Swedish paediatric expertise there are no advantages of such high manganese intakes during infancy – not even when considering products categorised as FSMP (133). Thus, manganese fortification of products intended for infants and possibly also young children could be questioned and even considered potentially harmful.

In conclusion, the current maximum limits for manganese in drinking water, infant formulae and FMSP seem to be based on unconvincing scientific data and a new risk benefit assessment is required as soon as sufficient scientific data are available.

Iron (Fe)

Nutritional background

Physiological function of iron

Iron is essential in oxygen supply as a component of haemoglobin and for oxygen storage as a component of myoglobin. Iron is also a component of enzymes with functions in the metabolism of energy and proteins and in the synthesis of proteins, tissues, hormones and neurotransmitters. Because iron easily reacts with oxygen, mechanisms have evolved that tightly limit the uptake of iron and control the reactivity of iron in the body (134).

Iron requirements in infancy

Full term, normal birth weight infants below 6 months do not generally need any iron in addition to the amounts provided by human milk. The newborn infant has a high blood concentration of haemoglobin, which declines during the first few weeks of life (135). The iron that was bound in Hb is then transferred to iron storage. Up to around 6 months of age the iron need of the infant is covered by the release of endogenous iron. Iron concentrations in the blood of infants, but not in human milk, depend on maternal iron status. At around 6 months, additional intake beyond what is available in breast milk becomes necessary. Estimated daily iron requirements in 6-12 month old children are 0.9-1.3 mg/kg body weight (135).

Iron absorption

Iron absorption depends on total iron intake, dietary factors and the iron status of the individual. Bioavailability of iron differs between different types of foods, and is assumed to be about 10 % from a mixed diet. Bioavailability of iron is lower in cereal-based foods (non-haem iron) than iron in meat products (haem iron). Phytates inhibit uptake of iron from many vegetable sources of iron, including iron in soy-based formulas. Humans do not actively excrete iron and protection from iron overload occurs through down-regulation of absorption (135). However, research indicates that down-regulation of iron absorption may be less effective up to 9 months of age (136). When iron stores are sufficient, the peptide hormone hepcidin blocks iron uptake by inhibiting ferroportin-mediated transport. On the contrary, in iron deficiency, hepcidin levels are low. Up-regulation of iron absorption does occur in infants with low iron status.

Recommendations for iron intake in infants and young children

A RI has not been set for infants below the age of 6 months because of the assumption that breast milk provides the iron to fulfil the iron requirements at this

age. From 6 months to 5 years of age, Swedish nutrition recommendations (SNR) state 8 mg/day as the RI (137). The RI is based on calculations of iron requirements in infancy and childhood in the Nordic nutrition recommendations (NNR) (138). The up-regulation of iron absorption when iron stores are low has not been accounted for in the factorial model from which the iron requirements of infants are obtained (135). This could lead to an overestimation of requirements. Consequently, the scientific background to determine iron requirements of infants would be strengthened by information from intervention studies.

Iron intake by infants and young children

The concentration of iron in human milk is approximately 0.3 mg/L and the literature show gastrointestinal absorption to be about 50 %. In infants who are exclusively breastfed, the iron intake is approximately 0.2 mg/day if they consume 700 ml milk per day. Infants consuming infant formula as the sole source of nutrition may reach an intake of 6 mg/day iron from formulas complying with iron content regulations (131). The higher concentrations of iron in infant formula than in breast milk could, at least partly, be explained by previous assumptions of much lower bioavailability of iron from infant formula than from breast milk. However, lower iron levels in infant formula have been recommended in recent years (139).

Important iron sources in older children and adults are meat and meat products, pulses, cereals and green vegetables. Breast milk provides sufficient iron for most infants below 6 months. In the second half of infancy and in young children, iron-fortified products are important iron sources. In a study of one-year-old Swedish children, iron-fortified gruel, follow-on formula and porridge contributed with 64 % of the total iron intake while meat contributed with 17 % of the total iron intake in this age group (140). Studies from the 1980s indicate that diets of the majority of infants at 6 and 12 months meet iron requirements (141, 142). A study of 90 one-year-old children in Sweden indicates a mean iron intake of 9 mg/day (140).

Hazard identification

Adverse effects of insufficient iron intake

A summary of the negative effects of iron deficiency can be found in the British Scientific Advisory Committee of Nutrition´s report Iron and Health (134). Iron deficiency anaemia is associated with impaired neurodevelopment, and the consequences seem to be irreversible. Iron deficiency anaemia has also been associated with impairment of several arms of the immune system.

Randomised controlled trials provide evidence that iron deficiency anaemia is associated with impaired development of motor function in children less than

three years of age (134). It is, however, not possible to identify cut-off levels of iron status indicators at which child development may be impaired. One potential mechanism could be impaired brain development as suggested by evidence both from animal and human studies. Iron is needed in the production of myelin, which builds up a lipid cover around nerve cells to facilitate/speed up neurotransmission. Iron is also a catalytic element involved in the synthesis of neurotransmitters. Definitions of anaemia and of iron deficiency vary between studies, making comparisons difficult. A number of factors that often coincide both with iron deficiency anaemia and with child development could act as confounders. Environmental factors such as psychosocial, economic and biomedical factors found to be associated with iron deficiency anaemia may explain some of the association between iron deficiency anaemia and impaired child development.

Adverse effects of excessive iron exposure

Acute iron toxicity in children is often due to accidental ingestion of iron supplements. The symptoms after ingestion of large amounts of iron are nausea, vomiting, loose stools, haemorrhagic necrosis of the gastrointestinal mucosa that, at very high doses, may result in hypovoalemic shock, multi-organ failure and death (134). High intakes of iron may lead to impaired liver function. Chronic iron toxicity may occur in primary haemochromatosis, when high iron uptake leads to high incorporation of iron in tissues and organs.

High iron intakes may lead to adverse effects through the capacity of facilitating oxidative reactions or by interactions with other transitional metals. Interactions have been found among iron, copper, manganese, cobalt, cadmium, lead, and zinc. One example is that iron in infant formula may reduce copper absorption and status (143, 144). To describe these interactions in detail is, however, beyond the scope of this report.

It has been hypothesised that high iron concentrations in tissues are associated with an increased risk of cancer, cardiovascular disease, infection and inflamemation and several other conditions (134). The data to support that these conditions are related to high intakes of iron are almost exclusively derived from investigations in adults. The exceptions are growth and infection, as evidence from randomised controlled trials suggests that iron supplementation of iron-replete infants and children may impair physical growth and increase the risk of certain infections (145). A recent study indicates that iron-replete infants may be at risk of adverse effects on development by consuming an infant formula with a high iron concentration (146).

Hazard characterisation

Adverse effects of insufficient iron intake

Iron deficiency anaemia is a worldwide problem, particularly prevalent in low income countries. Infants, young children and women of childbearing age are risk groups for developing iron deficiency anaemia. Low iron status of women, high prevalence of low birth weight and infections make infants and children in low income populations at high risk. Because iron is accumulated in the foetus in the last trimester of pregnancy, infants who are born premature or with a low birth weight have lower iron stores at birth and are at risk of iron deficiency (147, 148). There are reports of lower iron stores in children fully breastfed for 6 months compared to children who received complementary foods before 6 months (149, 150). Non-dietary factors associated with lower serum ferritin are male sex (148) and rapid weight gain (151). The prevalence of iron deficiency anaemia is very low during the first 6 months of life in European infants, and increases from 2-3 % at 12 months to 3-7 % at 1 to 3 years of age (135). In a study of 90 randomly selected Swedish one-year-old healthy children, about 10% were iron-depleted, as defined by having a serum ferritin $\leq$ 12 µg/L (140).

Adverse effects of excessive iron exposure

Intakes of 40-60 mg/kg body weight cause adverse health effects and intakes around 100 mg/kg body weight may lead to death (134). For individuals with primary haemochromatosis (0.5 % of the population), safety margins between normal iron intakes and risk of adverse effects are not evident and these individuals are at risk of developing negative health effects following iron supplementation (88).

Doses of 1 mg/body weight/day supplemental iron may cause impaired length gain in iron-replete infants aged between 4 and 9 months (152). Adverse effects of iron supplementation in low-income countries on morbidity caused by infections has been observed at doses of 12-200 mg ferrous sulphate/day (145). Some interactions between iron and other minerals may have implications for growth and development in infancy. The potential functional implications of lower copper status associated with the consumption of iron at high concentrations are not known.

A UL of 10 mg non-haeme iron per day in addition to habitual dietary iron was set by NNR to protect against biochemical iron overload (serum ferritin 300 µg/L) (138). EFSA has not established a UL for iron because of a lack of scientific data (153). The IOM in the USA set a UL of 45 mg/day from all sources for adults and children from 14 years of age (93). For children younger than 14 years, the UL was set at 40 mg/day by the IOM. The UL for adults was based on gastrointestinal side effects of supplementation. It is not clear how the extrapolation from the UL

value for adults to the value for infants and children was made. In the United Kingdom, a guidance level of 17 mg/day of supplemental iron was set, based on gastrointestinal side effects of supplementation, while data was considered too limited in order to propose an UL for iron intake. A provisional maximum tolerable daily intake of 0.8 mg/kg bw/day was established by JECFA in 1983 (154). This figure was used by Rasmussen *et al* (2006) to suggest a temporary guidance level of 10 mg/day for infants and children 1-3 years old (155). Because of the lack of scientific data for establishing UL values, we do not find it justified to use any value for the quantification of a possible risk of high iron exposures from infant foods. This should, however, not be interpreted as a lack of concern for adverse health consequences as a result of high iron intakes in infancy.

Biomarkers of iron status

The level of too low iron intake at which risks of development of adverse effects occur has been difficult to quantify. Studies often use biomarkers in blood or plasma to measure the risk of iron deficiency and iron deficiency anaemia. Anaemia is often used as an indicator of iron status of infants because testing haemoglobin concentrations in the blood is cheap and easy to perform. Haemoglobin levels may be low for a number of reasons other than iron deficiency, for example due to infections. A widely used indicator of iron status is serum ferritin, which is proportional to ferritin storage. One disadvantage of serum ferritin is that it is also an acute phase reactant that may be elevated in infection and inflammation. The cut-off values to identify infant anaemia (blood haemoglobin < 110 g/L) and iron deficiency (serum ferritin < 12 µg/L) used by WHO (156) have been criticised for overestimating anaemia and iron deficiency, and therefore lower levels have been suggested (157). Other indicators of iron status are, for example, concentrations of serum transferrin and zinc protoporphyrine. Optimally, several indicators should be used to identify iron deficiency. Studies where a distinction between anaemia and iron deficiency anaemia has not been made are difficult to evaluate because of the various potential causes of anaemia besides iron deficiency.

Exposure assessment

Estimated intakes for all individual products are presented in Appendix VI. Summary results for different product categories are presented in Tables 18 and 19. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 18) or a single portion (Table 19).

On average, the daily iron intake from infant formulae was 2.4-5.1 mg (Table 18). The iron concentrations in the studied infant formulae were 3.5-6.9 mg/kg. The levels stated in LIVSFS 2008:2 (which is the implementation of directive 2006/

141/EG): 0.3-1.3 mg/100 kcal corresponds to 2.0-9.1 mg/L when assuming 70 kcal/100 ml in infant formula. In breast milk, the concentration was 0.28 mg/L, which is in line with previously published breast milk concentrations (135). An infant consuming 700 ml breast milk per day would hence have an iron intake of 0.2 mg iron/day. The iron concentrations in the four studied follow-on formulae were 7.8-9.4 mg/kg. The products in the category of FSMP are used for treatment of malnutrition, allergy or PKU. The range of iron concentrations in this category was wide. Iron-fortified gruel or porridge is recommended during the second half of infancy because of the high iron requirements at this age. There is a large variation in the iron concentrations of gruel and porridge products. Most products in the category "foodstuffs for normal consumption" have low iron concentrations.

Table 18. Summary of estimated iron intakes from infant formula, follow-on formula, FSMP as the sole source of nutrition, FSMP as partial nutrition and from breast milk[a]

Product category	Age (months)	No. of products	Intake (mg /day)
Infant formula	0-4	9	4.0 (2.4-5.1)
Follow-on formula	6-8	4	7.0 (4.7-7.9)
FSMP as sole source of nutrition	0-12	21	5.3 (2.7-10.0)
FSMP as partial feeding[b]	0-12	3	4.8 (2.2-10.9)
Breast milk[c]	3 weeks		0.2

[a]Values are median (range)
[b]Nutramigen 2 lipil, XP Maxamaid and PKU anamix infant lcp+
[c]A composite sample of human milk collected week 3 post-partum, n=90

Table 19. Summary of estimated intakes of iron per consumed portion from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption[a]

Product category	Age (months)	No. of products	Intake (mg/portion)
Gruel[b]	6-12	12	2.6 (1.2-3.8)
Porridge [b]	4-12	21	2.1 (0.3-3.14)
FSMP as partial feeding[c]	12	3	3.0 (2.8-3.9)
Foodstuffs for normal consumption	12	12	0.21 (0.01-1.2)

[a]Values are median (range)
[b]Products to be mixed with any kind of milk are not included in this table
[c]Fresubin energy fibre drink, PKU gel and Frebini energy fibre drink

Risk characterisation

Intakes in relation to RI

We did not compare iron intakes from infant formulae below 6 months with any reference intake, as there is no RI for infants less than 6 months of age. The average iron intake from follow-on formulae (Table 18) is slightly below the RI. The estimated daily intake of BabySemp 3 follow-on formulae, recommended from 8 months of age, results in an intake of less than the RI. According to our calculations, additional sources of iron are needed in addition to this product in order to reach the RI. All products in the FSMP category recommended for infants 6 months or older (n = 8) contain iron sufficient to cover the RI, except for Neocate advance, recommended from 12 months (5.4 mg/day) and Minimax enteral formula for children, recommended from 6 months (5.4 mg/day). It is, however, possible that these products are prescribed for use in combination with other foods.

The number of portions required to reach the RI by consumption of gruel or porridge only varies from 3 to 10 for products recommended from 6 months. These products should be mixed with water (Table 20). Products that are recommended for infants from 4 months have not been compared with an RI since no RI is available below 6 months. However, those products have lower iron concentrations than products intended for infants from 6 months. For products recommendded from 6 months that should not be mixed with water, the iron concentration of added breast milk or follow-on formula will determine the iron concentration of the final product. First Flavour and Céréales Cacao should be mixed with the baby's usual milk according to the package information. One of the porridge products (Organic seven grain cereal) with a relatively low iron concentration should be mixed with a milk product. If mixed with Follow-on formula 2 from Holle the final concentration will be 0.9 mg/kg and 9 portions are needed to reach RI with this product. Some products that should be mixed with water contain iron concentrations in the lower range: Wholegrain porridge multigrain and Mild wholegrain porridge from HIPP and Oat porridge from Holle. These are non-fortified organically grown products. Rice, soy and oat drinks are not important sources of iron.

Table 20. Summary of estimated iron intakes expressed in terms of number of portions required to reach the RI of 8 mg/day[a]

Product category	Age (months)	No. of products	Number of portions to reach RI 8 mg/day
Gruel [b]	6-12	12	3 (2-7)
Porridge [b]	6-12	13	4 (3-10)
FSMP as partial feeding	12	3	3 (2-3)
Foodstuffs for normal consumption	12	12	55 (6-700)

[a]Values are median (range)
[b]Products recommended to infants less than 6 months and products to be mixed with any kind of milk are not included in this table

Contribution from water
Iron in groundwater may contribute to iron status (158). The general contribution of water to iron nutrition is probably small in Sweden, although high iron concentrations may occur in private wells. Public water may contain 0.2 µg/L when reaching the consumer (SLVFS 2001:30). For a 3-month-old infant, this corresponds to an additional intake of 126 µg per day from the 630 ml water needed to prepare 700 ml infant formula.

Discussion

Iron is an essential and particularly important nutrient for development of infants. There are still a number of questions concerning the risks and benefits of iron intake during this vulnerable period. Iron requirements increase rapidly in the second half of infancy and infants in risk groups may have difficulties in reaching sufficient intakes, although most infants meet dietary iron requirements according to older studies (141, 142). It is, however, possible that the feeding pattern of infants has changed in terms of product choices since these studies were performed. Data on 12-month-old children indicate that porridge and gruel are outstanding as sources of dietary iron (140). Our study shows that the choice of gruel or porridge could make a large difference to the iron intake of an infant. Swedish population based data on infant feeding practices are needed to increase our understanding of important determinants of iron nutrition in infancy.

The risk of possible adverse effects in relation to high iron intakes could not be evaluated based on established tolerable upper intake levels and hence no safe daily intake could be determined. Some products in the FSMP category contain concentrations of iron which lead to intakes of about 10 mg/day compared to daily intakes of up to 5 mg/ day from infant formula. We are not able to quantify a risk of development of adverse health effects at this or other levels of intake. Furthermore, we are not aware of the scientific justification for the higher iron concentrations in the FSMP category than in infant formulae.

A discussion about the risks following low and high iron intakes should take into account the physiological changes in iron metabolism during the first year of life. At an age of below 6 months, most infants need little iron. Breast milk or formula with intakes that correspond to the amounts absorbed from breast milk would be sufficient to cover iron needs for most infants at this age because endogenous iron compensates for low intakes. Around 6 months, most infants do need additional iron sources beside breast milk. Current RI does not take into account the increased efficiency of iron uptake when iron stores in the body are insufficient, which means that there may be an in-built overestimation of iron requirements. On the other hand, research indicates that iron absorption cannot be down-regulated efficiently by infants before 9 months of age and too high intakes could thus infer a health risk. Infants and children who are iron-replete are at risk of adverse consequences of excessive iron intake. It is, however, uncertain if the adverse effects on growth and infections noted in iron supplementation trials occur to the

same extent when food is fortified with iron. After 9 months of age, the benefits of iron for some individuals in a population could perhaps outweigh the potential risks of excess intakes as absorption is then under physiological regulation. The potential risks of high iron intakes from fortified products are poorly investigated in infants and young children. In particular, long term studies are few. Considering the seriousness of the potential adverse health effects, such as impaired growth and development, caution should be taken in assuring that infants and young children are not consuming excess iron. An important step would be to establish ULs for iron in infants and young children. A complete risk-benefit assessment of the iron intake from infant formula and other iron fortified products is yet to be done.

Conclusion

The iron intake from most of the studied follow-on formulae and FSMP for use as the sole source of nutrition meets the RI of iron from 6 months. There is no RI of iron before 6 months. There is a large variation in the iron concentrations of porridge and gruel and some products are important iron sources while others contribute less to iron nutrition in infancy. Infants and young children are at risk of iron deficiency because of high requirements due to growth and development. Infants with inadequate iron nutrition are at risk of irreversible negative effects on development. On the other hand, infants below 9 months may be particularly sensitive to high iron intakes because of immature regulation of iron. Excess iron intake in infants and young children may have serious implications such as impaired development and growth. It is a matter of concern that the level of iron intakes at which negative health effects may occur is not quantified for infants. Iron requirements for infants and the tolerable upper level of intake should be defined and established before an optimal level of iron fortification of food products for infants and young children can be determined. In particular, it is urgent that an UL of iron for infants and young children is established.

Copper (Cu)

Nutritional background

Physiological function of copper

Copper is an essential trace element, as it is a component of many enzymes and proteins in living organisms. As a cofactor in enzymes involved in the defence against oxidative stress, copper seems to play an important role (159). Copper is required for normal growth of infants, host defence mechanisms, bone strength, maturation of erythrocytes and leukocytes, iron transport, and brain development (160). Both deficiency and excess of copper can result in varied symptoms in, for example, the haematopoietic system, the skeleton, the liver, and the brain (160).

Dietary sources of copper

There is high variability in the copper content of different foods, depending on the type of food but also on the place of cultivation, season, processing and cooking methods. Copper is found in all kinds of food and the highest concentrations are found in nuts and seeds and cocoa (about 10 mg/kg). Meat, fish, vegetables and cereals generally contain lower concentrations of copper (0.5-2 mg/kg). Public drinking water pipes from municipal waterworks leading to private properties are not made of copper and the public drinking water contains no copper. In contrast, about 80% of the drinking water pipes inside private households are made of copper. Depending on the chemical composition of the water, temperature, pipe length and contact time copper can be dissolved in the water that has been stagnant in the private property pipes. The intake of copper from drinking water is estimated to a couple of milligrams daily, but variation in intake may be considerable (161).

Copper absorption

Normal adults regulate the amounts of copper absorbed and excreted. This regulation takes place in the liver. Whether an effective regulation of copper also operates in infants is at present not clarified. Copper accumulates in the foetus mainly during the third trimester of pregnancy. Premature and low birth weight infants are therefore at higher risk of copper deficiency than full term infants (160). Copper accumulates in the liver to a higher level than is tolerated in adults. For the neonate, this acts as a reserve to avoid copper deficiency in the first months of life. At about 6 months of age, liver reserves are found to contain the same concentrations as those of adults (160). Copper absorption depends on the copper nutrition of the individual and the type of animal or plant source of copper. Zinc, iron, certain amino acids, ascorbic acid, and fructose also affect copper uptake. Of special importance in infant nutrition is zinc. However, reduced Cu

absorption seems to be present only at high zinc intakes. Copper absorption from from breast milk is estimated to 80 % (160).

Recommendations and intakes of copper
The requirements of copper in infancy are high, due to rapid growth and brain development. The recommended intake for infants 0-23 months is 0.3 mg/day and for children 2-5 years old 0.4 mg/day (137). Daily intake of copper from foods has been found to be in the range of 1-2 mg/day in adults and 0.6-0.8 mg/day in young children (162). Analysis of market baskets representing a typical Swedish diet (exluding drinking water) showed intakes of 1.3 mg/day for adults.

Hazard identification

Adverse effects of insufficient copper intake
Severe deficiency of copper may be associated with a variety of symptoms related to reduced activity of enzymes containing copper, for example neutropaenia and anaemia and in addition impaired development in children (88). The symptoms of copper deficiency are well characterised due to the presence of conditions that lead to abnormal copper metabolism such as in Menke´s disease. Patients with Menke´s disease develop a severe copper deficiency with, for example, severe mental impairment, growth failure, hypothermia, loss of skin and hair pigmentation, bone fractures, retinal dystrophy and premature death (160).

Adverse effects of excessive copper exposure
An excessive intake of copper has an irritating effect on the gastrointestinal tract and has previously been used to induce vomiting in the event of poisoning. High intakes of copper may in the long run lead to liver damage. Certain heritable diseases are known to result in impairment of the normal metabolism of copper in the body. Wilson's disease, which is an autosomic recessive disorder, will lead to an accumulation of copper mainly in the liver and the brain. In Idiopathic Copper Toxicosis (ICT) abnormally high levels of copper in the liver have been found in infants and young children.

Hazard characterisation

Adverse effects of insufficient copper intake
Copper deficiency is not common in humans, but may occur, for example in patients receiving total parenteral nutrition for a long time (88). Of importance, mainly in low-income countries, is that infants recovering from malnutrition may

develop copper deficiency (160). In particular infants fed mainly cow´s milk and a high intake of refined carbohydrates such as polished rice are at high risk of developing symptoms of copper deficiency. Premature infants are at higher risk of developing copper deficiency in the neonatal period than infants born at term.

Adverse effects of excessive copper exposure

Acute effects (abdominal pain and vomiting) after ingestion of copper compounds may occur after doses in the range of 10-15 mg (163). In general chronic effects due to copper ingestion are rare as the mechanisms of homeostasis are effective, but certain subpopulations may be more vulnerable (88). There is probably a genetic susceptibility that explains that some individuals cannot tolerate moderate to high intakes of copper, but the extent and mechanism of this are not fully understood. There are some data suggesting an association between a high intake of copper from drinking water and diarrhoea in children and gastrointestinal disturbances and acute liver failure (88).

In a Swedish study from 2003, including 430 children, a total of 4,703 samples of drinking water from the homes of the children were analysed (161). A median concentration of 0.61 mg copper/L was found in the study, and the 10^{th} and 90^{th} percentiles were found to be 0.04 mg/L and 1.57 mg/L respectively. The occurrence of vomiting and diarrhoeas experienced by the children during 12 weeks were studied, but no associations between these outcomes and concentration of copper in the drinking water were found. In adults, studies from Chile have demonstrated symptoms of vomiting starting at concentrations of 4 mg/L in women and of 6 mg/L in men. No symptoms were observed at a concentration of 2 mg/L (164).

Wilson's disease is an uncommon disease and the incidence is estimated to 1 person in 30,000 (88). If untreated, Wilson´s disease will result in accumulation of copper in the liver and the brain. The consequences may be hepatitis, haemolysis and liver failure (88). A high liver copper concentration does not by itself necessarily lead to tissue damage. In healthy full term neonates hepatic copper concentrations may at birth be similar to those observed in individuals with Wilson´s disease. It is, however, not known why these large amounts of copper in the liver do not induce adverse effects (165).

The disease ICT, which is very rare (165), is probably caused by a combination of heredity and high intake of copper early in life (88). Studies from, for example, Germany on children up to 12 months old have not shown any effects on the liver after exposure to concentrations up to 2 mg/L (166).

Upper level of tolerable intake of copper

When establishing an upper level of tolerable intake of copper, the potential development of liver damage was considered, since this was regarded a better indicator of chronic exposure than the gastrointestinal effect which is the result of

acute exposure. In the United States, the IOM has set an UL of copper at 10 mg daily for adults on the basis of effects on the liver (93). EFSA has established an UL of copper at 5 mg per day based on the same study used by the IOM (88). The difference between these values is explained by the fact that EFSA has applied a safety factor of 2 in order to consider the potential variation in the population. In addition, EFSA (88) has set ULs of copper for children on the basis of relative body weights (standard body weights were used): 1-3 years old: 1 mg/day, 4-6 years old: 2 mg/day, 7-10 years old: 3 mg/day and 11-17 years old: 4 mg/day. Currently there is no UL established by EFSA or the IOM for infants 0-12 months old. According to a recently published paper (165), current copper ULs should be reevaluated as there are new experimental data (data from clinical trials and experimental studies in primates) as well as new biomarkers of copper status (such as some copper-dependent enzymes and chaperones.

Biomarkers of copper status

Sensitive and specific Cu status biomarkers have not yet been identified. The currently used biomarkers, cuproenzymes such as the acute phase protein ceruloplasmin and Cu-Zn-superoxide dismutase, are influenced by dietary and environmental factors (167). These biomarkers may also increase during inflammation, pregnancy, ageing and a number of diseases, and copper deficiency could be masked as a consequence of these conditions (165). Superoxide dismutase 3, the predominant form of SOD in serum, has also received attention as a potential index of copper status (165). Cu chaperones are considered potential promising biomarkers that responds to both Cu deficiency and excess, but their reliability has yet to be established (167).

Exposure assessment

Estimated intakes for all individual products are presented in Appendix VII. Summary results for different product categories are presented in Tables 21 and 22. Product categories have been divided into two main groups depending on whether the consumption scenario used for the products in a given category covers a whole day (Table 21) or a single portion (Table 22). As is evident from Tables 21 and 22, the highest exposure is to be expected from intake FSMP as sole source of infant nutrition and FSMP as partial infant nutrition (168). The intake from breast milk is given as a reference in Table 21. The concentration of copper was 1,120 µg per kg breast milk (1). However, this value does not seem to be within the range for most average copper concentrations (200-600/L) in breast milk reported in the literature (160, 168).

Table 21. Summary of estimated intake (µg/day) of copper from infant formula, follow-on formula, FSMP as sole source and partial source of nutrition and breast milk.

Product group	Age (Months)	Number of products	Intake (µg/day)[a]
Infant formula	0-4	9	252 (232-370)
Follow-on formula	6-8	4	340 (166-353)
FSMP as sole source of nutrition	0-12	24	340 (140-1233)
FSMP as partial feeding[b]	0-12	3	484 (170-786)
Breast milk[c]	3 weeks		787

[a]Values are median and (range)
[b]Nutramigen 2 lipil, XP Maxamaid and PKU anamix infant lcp+ (recommended daily intake)
[c]A composite sample of human milk collected week 3 post-partum, n=90

Table 22. Summary of estimated intakes of copper - as µg per consumed portion from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption

Product group	Age (Months)	Number of products	Intake (µg per consumed portion)[a]
Gruel products	6-12	14	39 (5-94)
Porridge products	4-12	26	55 (17-161)
FSMP as partial feeding[b]	0-12	3	308 (160-580)
Foodstuffs for normal consumption	12	12	51 (5-143)

[a]Values are median and (range)
[b]Fresubin energy fibre drink, PKU gel and Frebini energy fibre drink

Risk characterisation

Daily intakes from the analysed products in relation to RI

There is at present no recommended intake established for infants 0-6 months of age. For infants and children 6-23 months the RI is set at 0.3 mg/day. Intake of copper from products intended for infants > 6 months were compared to RI. All follow-on formula recommended from 6 months of age had concentrations which lead to intakes higher than the RI. According to our calculations, BabySemp 3 follow-on formula, from 8 months of age had a concentration (0.33 mg/kg), corresponding to 55 % of the RI, and additional sources of copper are needed to fulfil the RI. Products in the categories of FSMP, as sole and partial feeding, contribute to daily copper intakes well beyond the RI.

There is a large variation in the contribution of copper from gruel and porridge to the total intake of copper. Corn gruel from Nestlé had the lowest copper concen-

tration (0.02 mg/kg), which means that in the quite unlikely scenario of reaching the RI for copper from this product only, 66 portions are needed. All products based on maize have relatively low copper concentrations. Products to be mixed with other milks or infant formula are included in Table 23. These products (2 gruels and 1 porridge for infants from 6 months of age) did not have lower concentrations of copper than products to be mixed with water.

In the product category "Foodstuffs for normal consumption" oat toasted and milled and several soydrinks contribute to a high extent to total copper intake. Rolled oats and rice-based drinks do not contribute to the same degree.

Table 23. Summary of estimated intakes expressed in terms of the number of portions required to reach the RI of 0.3 mg/day.

Product group	Age (Months)	Number of products	Number of portions to reach the RI[a]
Gruel products	6-12	14	8 (3-66)
Porridge	6-12	14	5 (2-7)
FSMP as partial feeding	12	3	2 (1-2)
Foodstuffs for normal consumption	12	12	7 (2-59)

[a]Values are median and (range)
Products for infants < 6 months are not included in the table.

Daily intakes from the analysed products in relation to UL

In the present investigation the exposure from infant formula does not exceed the UL established by EFSA in 2006 (88). Intake of copper by consumption of this kind of products varies between 23 - 37% of the UL. However, infant formula is consumed by newborn infants and when considering potential effects of excessive intake of copper it should be emphasised that the current UL does not apply to children younger than 12 months. This implies that the UL of 1,000 µg/day probably would not be the adequate reference value to be used in a risk assessment of the exposure of younger infants.

The contribution of copper from FSMP as the sole source of nutrition can be quite high from some products in relation to the UL set by EFSA. The highest intake (about 1,230 g daily) is received from Fresubin soya fibre and intake of recommended daily amounts of two other FSMP products – Isosource junior and NutriniKid multi fibre – will result in intakes of about 900 and 780 µg per day. Fresubin energy fibre, results in exceeding the UL after an intake of about two portions daily. The contribution per portion from gruel and porridge seems to be modest and safety margins in relation to UL are rather wide in these product categories.

Table 24. Summary of estimated intakes – as a percentage of the tolerable upper level (UL). UL for 1- 3 years old, 1000 µg/day, was established by EFSA (2003) [a].

Product group	Age (Months)	Number of products	Percent of UL[a]
Infant formula	0-4	9	25 (23-37)
Follow-on formula	6-8	4	17 (33-35)
FSMP as sole source of nutrition	0-12	24	34 (14-123)
FSMP as partial feeding[b]	0-12	3	48 (17-79)

[a]Values are median and (range)
[b]Nutramigen 2 lipil, XP Maxamaid and PKU anamix infant lcp+ (recommended daily intake)
[c]A composite sample of human milk collected week 3 post-partum, n=90

Table 25. Number of portions needed in order to reach UL

Product group	Number of products	Number of portions to reach UL [a]
Gruel products	14	26 (11-221)
Porridge products	26	18 (6-61)
FSMP as partial feeding	3	4 (2-6)
Foodstuffs for normal consumption	12	23 (7-197)

[a]Values are median and (range)

Copper in drinking water – MRL and estimated contribution to intake from infant formula

The EU has established a common maximum residue limit (MRL) for copper in drinking water. The MRL is set at 2.0 mg copper/L in order to protect from transitional acute gastrointestinal effects. The guideline of WHO also recommends an MRL of 2.0 mg/L (169). According to Swedish regulations (SLVFS 2001:30 and SOSFS2003:17) water can be used for drinking, though with an adverse remark, at copper concentrations exceeding 0.20 mg/L. The risk of negative health effects due to increased concentrations of copper in drinking water is considered to be low. Infants receiving formula may, however, be more vulnerable. Some examples of contributions of copper from drinking water are presented below.

Assuming a concentration of copper at 200 µg/L and an intake of 630 mL water by a child about 3 weeks old, this would result in a daily intake of 126 µg. A consumption of 630 mL is assumed as it would correspond to the amount of water needed to prepare 700 mL of infant formula, which is our estimated consumption by infants of this age. The median intake of copper from infant formula would then increase from 252 µg daily (see Table 21) to about 378 µg daily, but still below the UL of 1000 µg daily. As mentioned earlier, this UL does not, however, apply to children younger than 12 months.

If we assume a type of worst case scenario assuming a water concentration of 2,000 µg/L (the MRL, set by WHO), the contribution of copper from drinking water would be 1,260 µg daily under the same assumptions as above and total maximal exposure could be estimated to 1,260 daily + 370* µg daily = 1,630 µg daily. For infant formula this exposure would thus result in an intake clearly exceeding the UL for children 1-3 years old of 1,000 µg daily.
*Maximum value in the range stated for infant formula in Table 21.

Discussion

Negative health effects due to copper may be related either to deficiency or excessive intake. Thus, there is an acceptable or optimal interval for intake of copper. Some gruels, especially those made from maize flour, had low copper concentrations. However, copper is common in a variety of foods and unless the diet has very low variation copper requirements are likely to be met by other foods in the diet.

Overall intake of copper from the analysed infant foods, except for some products categorised as FSMP, seems to be reasonable in relation to the current UL of 1000 µg/day for children 1-3 years old. However, applying the UL in assessments of risks of copper exposure in children less than 1 year may underestimate potential risks for infants younger than 12 months. The contribution of copper from drinking water to the products may be considerable, and the median concentration of infant formula will exceed the UL if the water contains copper in a concentration at the maximum guideline level (2.0 mg/L) established by WHO in 2004. However, applying the guideline level permitted in Sweden (0.2 mg/L) will not result in an intake exceeding the UL. As the UL is clearly exceeded after consumption of some product categorised as FSMP, the need for copper in the amounts provided in the products should be verified. These products are intended for children at an age of 12 months or older and hence the used UL is applicable. Regarding levels of copper in processed cereal-based foods and baby foods for infants and young children, the view of the SCF (4) is that since copper intake by children is generally sufficient it is not advisable to add copper. The maximum level according to legislation for FSMP intended for children at an age of 12 months or older is 0.5 mg/100 kcal (SLVFS 2000:15, which is the implementation of directive 1999/21/EG). Another issue which probably should be paid attention to in this context is the interactions associated with intakes of other essential minerals like iron and zink. As it is beyond the scope of this report to discuss these interactions, they should be considered in a full risk-benefit assessment.

Conclusion

Copper is common in a variety of foods and copper intakes are likely to cover the RI for most infants by the intake of the analysed products solely or in combination with other foods. Overall intake of copper from the analysed infant foods, except for some products categorised as FSMP, seems to be reasonable if the UL of 1000

µg/day for children 1-3 years old is applied for infants 0-1 year old. However, this approach may not be appropriate and may result in an underestimation of potential risks for infants younger than 12 months. Thus, the risk of high copper exposures in infancy and childhood is at present of greater public health concern than the risk of inadequate copper nutrition.

It is urgently needed to establish an UL for infants younger than 12 months. It should be noted that the contribution of copper from drinking water to the products may be considerable and precautionary measures should be taken in order to assure that infants and young children are not exposed to excess copper intakes.

General points to consider

It should be noted that the exposure assessments in this report are based on several assumptions. The calculations are made for an infant or child of average weight, for the age group for which the product is recommended, and for consumption of the product in the amount of the product recommended on the packaging, or an average intake for the age group, based on previous research. Variability due to individual differences in body weight and in consumption may be large, and this is not accounted for in this assessment. Variability in intakes may be particularly high for FSMP products, because the consumption of such products is tailored by a dietician or physician to satisfy the special needs of an infant or child with a particular medical condition. The variations in concentration of contaminants and minerals in the different products are assumed to be small, as the food products included in our assessment are manufactured under standardised protocols, perhaps with the exception of products in the category "Foodstuffs for normal consumption".

The additional contribution to the exposure by water used for product preparation was considered to some extent. The contribution from water may potentially be high in individual cases, particularly if water from private water wells is used.

We were not able to account for the bioavailabilty of minerals from the analysed products. More data on bioavailabilty of the minerals from analysed products would be needed for an in-depth assessment of risks and benefits associated with certain intakes.

Furthermore, effects of intakes of combinations of metals were not assessed, although there are indications of interactions between several of these contaminants and minerals. Thus, no attempts were made to quantify the total risk of high intakes of contaminants and minerals in products with a high concentration of more than one contaminant or mineral. Although infants or young children who consume several products with high concentrations of contaminants and minerals may be at particular risk of adverse health effects, our data did not allow for assessment of such scenarios.

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Appendix I. Labelling information on products included in the project

Table 1. Food for Special Medical Purposes for infants (0-12 months)

Product *(English translation)*	Id	Producer	Age group	Intended use	Labelled energy kcal/100 g	Labelled Copper µg/100g[1]	Labelled Manganese µg/100g[1]	Labelled Iron mg/100g[1]	Main ingredient	Sole source of nutrition	Product sold as
Althéra	M75	Nestlé	>1 w	Allergy	510	410		5.5	Lactose	X	P
Enfalac premature	M98	Mead Johnson	w 23-40[2]	Prenatal	490	515		8.3	Glucose syrup	X	P
Enfamil AR lipil	M78	Mead Johnson	>1 w	Reflux	500	330	300	5.5	Skimmed milk powder	X	P
Enfamil Human Milk Fortifier[4]	M61	Mead Johnson	w 23-40[2]	Prenatal	14[3]	44[3]	10[3]	1.4[3]	Medium chain tryglycerides		P
FM 85[4]	M60	Nestlé	w 23-40[2]	Prenatal	347	900	130	26	Maltodextrin		P
Galactomin 19 formula	M69	SHS	< 1y	Intolerance	534	380	440	3.9	Fructose	X	P
Minimax barnsondnäring *(Minimax enteral formula for children)*	M82	Nestlé	>6 mo	Malnutrition	120[5]	110[5]	70[5]	1.0[5]	Skimmed milk	X	RFU
Neocate LCP	M72	Nutricia	<1 y	Allergy	475	380	380	7.0	Glucose syrup	X	P
Nutramigen 1 lipil	M1	Mead Johnson	<6 mo	Allergy	500	380	300	9	Glucose syrup (corn)	X	P
Nutramigen 2 lipil	M48	Mead Johnson	>6 mo	Allergy	466	349	279	8.2	Glucose syrup (corn)		P
Pepti junior	M79	Nutricia	< 1 y	Allergy	515	314	327	6.0	Glucose syrup (corn)	X	P
Pepticate	M54	Nutricia	<1 y	Allergy	484	294	55	3.9	Whey protein	X	P
PKU anamix infant lcp+	M85	SHS	<1 y	PKU	457	430	430	8.1	Glucose syrup		P
Pregestimil lipil	M99	Mead Johnson	<6 mo	Allergy	500	380	300	9	Glucose syrup (corn)	X	P
PreNAN discharge	M95	Nestlé	w 23-40[2]	Prenatal	510	410	80	5.3	Whey protein	X	P
Profylac	M103	Semper	>1 w	Allergy	500	300	320	5.5	Maltodextrin	X	P

Id – identification of composite sample; w – week; mo-month; PKU – phenylketonuria; y – year; P – powder; RFU – ready for use

[1] Only presented if the mineral is labelled as an ingredient.

[2] Information from paediatric dieticians (not labelling).

[3] Per 100 ml product when reconstituted, i.e. four packets of Enfamil Human Milk Fortifier, the amount usually added to 100 ml of preterm human milk.

[4] The product should be diluted with breast milk.

[5] Per 100 ml ready for use product.

Appendix I. Labelling information on products included in the project

Table 2. Food for Special Medical Purposes for young children (1-3 years)

Product	Id	Producer	Age group	Intended use	Labelled energy kcal/100 ml	Labelled Copper µg/100ml[1]	Labelled Manganese µg/100ml[1]	Labelled Iron mg/100ml[1]	Main ingredient	Sole source of nutrition	Product sold as
Frebini energy fiber drink (chocolate flavour)	M97	Fresenius Kabi	1-12 y	Malnutrition	150	150	180	1.5	Maltodextrin		RFU
Fresubin energy fibre (pooled sample different flavours)	M26	Fresenius Kabi	>1 y	Malnutrition	150	300	400	2.0	Maltodextrin	X	RFU
Fresubin soya fibre	M70	Fresenius Kabi	>1 y	Malnutrition	100	130	270	1.3	Maltodextrin	X	RFU
Isosource junior	M71	Nestlé	>1 y	Malnutrition	122	100	200	0.8	Maltodextrin	X	RFU
Neocate advance	M81	SHS	>1 y	Allergy	400[2]	240[2]	200[2]	2.5[2]	Glucose syrup	X	P
Nutrini energy multi fiber	M83	Nutricia	1-6 y	Malnutrition	150	122	230	1.5	Maltodextrin	X	RFU
Nutrini multi fiber	M84	Nutricia	1-6 y	Malnutrition	100	81	150	1.0	Maltodextrin	X	RFU
NutriniKid multi fibre (pooled sample different flavours)	M27	Nutricia	1-6 y	Malnutrition	150	135	230	1.5	Maltodextrin	X	RFU
PKU gel (pooled sample different flavours)	M28	Vitaflo	> 1 y	PKU	342[2]	700[2]	1700[2]	10[2]	Sugar		P
Resource minimax (pooled sample different flavours)	M29	Nestlé	>1 y	Malnutrition	120	100	70	1.0	Skimmed milk	X	RFU
XP Maxamaid (pooled sample different flavours)	M53	SHS	1-8 y	PKU	309[2]	1800[2]	1600[2]	12[2]	Glucose syrup		P

Id – identification of composite sample; PKU – phenylketonuria;y – year; P – powder; RFU – ready for use

[1] Only presented if the mineral is labelled as an ingredient.

[2] Per 100 g in products sold as powder.

Appendix I. Labelling information on products included in the project

Table 3. Infant formulae

Product *(English translation)*	Id	Producer	Age group	Labelled energy kcal/100g	Labelled Copper µg/100g[1]	Labelled Manganese µg/100g[1]	Labelled Iron mg/100g[1]	Main ingredient[2]	Product sold as
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*	M30	Semper	0-6 mo	63[3]	401[3]		0.4[3]	Demineralized whey powder	RFU
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*	M2	Semper	0-6 mo	510	320		3.3	Demineralized whey powder	P
BabySemp 2 Lemolac modersmjölksersättning *(BabySemp 2 Lemolac infant formula)*	M14	Semper	4-12 mo	516	320		5.7	Demineralized whey powder	P
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	M15	HiPP	> 0 mo	507	280	80	4.1	Whey (partly demineralized)	P
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	M16	HiPP	>4 mo	496	285	51	5.3	Skimmed milk	P
Organic Infant milk	M80	BabyNat	0-6 mo	517	330	30	5.5	Demineralized whey powder	P
Eko Modersmjölksersättning 1 *(Organic Infant formula 1)*	M92	Holle	> 0 mo	519	290	88	3.2	Skimmed milk	P
NAN 1 Modersmjölksersättning *(NAN 1 infant formula)*	M10	Nestlé	> 0 mo	513	310	115	3.2	Demineralized whey powder	P
NAN HA 1 Modersmjölksersättning *(NAN HA 1 infant formula)*	M11	Nestlé	> 0 mo	510	410	125	5.5	Lactose	P

Id – identification of composite sample; mo – months; P – powder; RFU – ready for use

[1] Only presented if the mineral is labelled as an ingredient.

[2] All infant formulae were manufactured from cow's milk proteins.

[3] Per 100 ml ready for use product.

Appendix I. Labelling information on products included in the project

Table 4. Follow-on formulae

Product *(English translation)*	Id	Producer	Age group	Labelled energy kcal/100g	Labelled Copper µg/100g[1]	Labelled Manganese µg/100g[1]	Labelled Iron mg/100g[1]	Main ingredient[2]	Product sold as
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	M13	Semper	>8 mo	480	290		7.3	Demineralized whey powder	P
Eko tillskottsnäring 2 (Organic *follow-on-formula 2)*	M52	Holle	>6 mo	494	300	97	6.1	Skimmed milk	P
NAN Pro 2 Tillskottsnäring *(NAN Pro 2 follow-on-formula)*	M36	Nestlé	>6 mo	495	370		7.3	Maltodextrin	P
Optima organic Follow-on-milk	M76	BabyNat	>6 mo	490	325	33	6	Maltodextrin	P

Id – identification of composite sample; mo – months; P – powder

[1] Only presented if the mineral is labelled as an ingredient.

[2] All infant formulae were manufactured from cow's milk proteins.

Appendix I. Labelling information on products included in the project

Table 5. Processed Cereal-based Foods for infants and young children: porridge

Product *(English translation)*	Id	Producer	Age group	Labelled energy kcal/100g	Labelled Copper µg/100g[1]	Labelled Manganese µg/100g[1]	Labelled Iron mg/100g[1]	Main ingredient *(content of wholegrain in percent)*	Product sold as
Wholegrain									
Bio-Babybrei Grieβ *(Wheat porridge)*	M87	Holle	4 mo	359				Wholegrain wheat *(100 %)*	P
Eko dinkelgröt *(Organic spelt porridge)*	M65	Holle	6 mo	354				Wholegrain spelt *(100 %)*	P
Eko havregröt *(Organic Oat porridge)*	M63	Holle	6 mo	386				Wholegrain oat *(100 %)*	P
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	M4	Semper	12 mo	450			8.5	Wholegrain flour *(40 %)*	P
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	M17	HiPP	8 mo	432	142	670	3.9	Whey powder partly demineralized *(20 %)*	P
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	M39	HiPP	12 mo	422	Missing[2]	980	4.2	Whey powder partly demineralized *(41 %)*	P
Mild fullkornsgröt *(Mild wholegrain porridge)*	M32	Nestlé	8 mo	410			10	Skimmed milk powder *(37 %)*	P
Mild fullkornsgröt *(Mild wholegrain porridge)*	M42	HiPP	8 mo	424		1300	4.9	Whey powder partly demineralized *(38 %)*	P
Mild fullkornsgröt *(Mild wholegrain porridge)*	M33	Semper	8 mo	460			8.5	Demineralized whey powder *(47 %)*	P
Mild havregröt *(Mild oat porridge)*	M22	HiPP	6 mo	434	140	1060	4	Whey powder partly demineralized *(28 %)*	P
Musligröt päron-banan *(Musli porridge pear-banana)*	M9	Nestlé	12 mo	390			10	Oat meal *(39 %)*	P
Eko hirsgröt *(Organic millet porridge)*	M64	Holle	4 mo	393				Wholegrain millet *(100 %)*	P
Organic seven grain cereal[3]	M51	Organix	7 mo	374				Wholegrain wheat *(100 %)*	P
Rice porridge									
Baby´s first food The ultimate four grain porridge[3]	M90	Plum	4 mo	376				Quinoa and wholegrain rice *(100 %)*	P
Banangröt *(Banana porridge)*	M3	Semper	4 mo	460			8.5	Rice flour	P
Banangröt mjölkfri *(Banana porridge dairy free)*	M23	EnaGo	6 mo	450				Banana purée	P
Cerelac risgröt *(Cerelac rice porridge)*	M31	Nestlé	4 mo	420			7.5	Rice flour	P
First organic wholegrain baby rice[3]	M56	Organix	4 mo	374				Wholegrain rice *(100 %)*	P
God Natt! Risgröt med grönsaker *(Good night! Rice porridge with vegetables)*	M40	HiPP	4 mo	83[4]				Milk	RFU
Eko risgröt *(Organic rice porridge)*	M91	Holle	4 mo	382				Wholegrain rice *(100 %)*	P

Product ***(English translation)***	**Id**	**Producer**	**Age group**	**Labelled energy kcal/100g**	**Labelled Copper µg/100g**[1]	**Labelled Manganese µg/100g**[1]	**Labelled Iron mg/100g**[1]	**Main ingredient** ***(content of wholegrain in percent)***	**Product sold as**
Risgröt med banan och persika *(Rice porridge with banana and peach)*	M59	HiPP	4 mo	429	130	329	3.3	Whey powder partly demineralized	P
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	M25	Semper	5 mo	460			8.5	Rice flour	P
Sinlac specialgröt *(Sinlac special porridge)*	M12	Nestlé	4 mo	420			10	Rice flour	P
Others									
Cerelac fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	M37	Nestlé	6 mo	420			7.5	Wheat flour	P
Dinkelgröt naturell *(Spelt porridge natural)*	M86	Nestlé	6 mo	410			10	Spelt flour	P
Mild havregröt *(Mild oat porridge)*	M35	Semper	4 mo	460			8.5	Skimmed milk powder	P

(%) – content of main ingredient (wholegrain or rice); Id – identification of composite sample; mo – months; P – powder; RFU – ready for use

[1] Only presented if the mineral is labelled as an ingredient.

[2] According to the list of ingredients copper was added, but the content of copper is not declared in the nutrient declaration.

[3] The product could/should be diluted with other liquids than water.

[4] Per 100 ml ready for use product.

Appendix I. Labelling information on products included in the project

Table 6. Processed Cereal-based Foods for infants and young children: gruel (välling)

Product *(English translation)*	Id	Producer	Age group	Labelled energy kcal/100g	Labelled Copper µg/100g[1]	Labelled Manganese µg/100g[1]	Labelled Iron mg/100g[1]	Main ingredient *(content of wholegrain in percent)*	Product sold as
Gruel									
Drickfärdig mild fullkornsvälling *(Ready-to-drink mild wholegrain gruel)*	M34	Semper	8 mo	70[2]			1.2[2]	Skimmed milk	RFU
Fullkornsvälling *(Wholegrain gruel)*	M18	Nestlé	12 mo	450			10	Wholemeal flour *(44 %)*	P
Fullkornsvälling havre vete råg *(Wholegrain gruel oat wheat rye)*	M5	Semper	12 mo	450			8.5	Skimmed milk powder *(34 %)*	P
Mild fullkornsvälling *(Mild wholegrain gruel)*	M8	Semper	8 mo	460			8.5	Skimmed milk powder *(18 %)*	P
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	M21	Nestlé	8 mo	460			10	Skimmed milk powder *(33 %)*	P
Corn gruel									
Låglaktos majsvälling *(Low lactose corn gruel)*	M19	Nestlé	6 mo	480			8	Cornstarch	P
Majsvälling *(Corn gruel)*	M20	Semper	6 mo	470			8.5	Corn flour	P
Majsvälling *(Corn gruel)*	M96	HiPP	6 mo	496	255	50	4	Skimmed milk	P
Majsvälling *(Corn gruel)*	M7	Nestlé	6 mo	470			10	Skimmed milk powder	P
Rice gruel									
Céréales Cacao[3]	M74	Babybio	8 mo	389				Rice flour 84 %	P
First flavour[3]	M73	Babynat	6 mo	386				Rice flour 89 %	P
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	M55	Semper	6 mo	460			8.5	Skimmed milk powder	P
Välling mjölkfri *(Gruel dairy free)*	M24	EnaGo	6 mo	463			12	Flour (rice-. oat-. wheat-)	P
Oat gruel									
God natt mild havrevälling *(Good night mild oat gruel)*	M6	Nestlé	6 mo	470			10	Cornstarch	P

Id – identification of composite sample; mo – months; P – powder; RFU – ready for use.
[1] Only presented if the mineral is labelled as an ingredient.
[2] Per 100 ml ready for use product.
[3] The product could/should be diluted with other liquids than water.

Appendix I. Labelling information on products included in the project

Table 7. Breast milk and "foodstuffs for normal consumption"

Product ***(English translation)***	**Id**	**Producer**	**Intended use**	**Main ingredient** ***(content of main ingredient in percent)***	**Product sold as**
Breast milk (w 3 post-partum. n=90)[1]	M50		Breastfeeding	Human breast milk	RFU
Havredryck apelsin & mango *(Oat drink orange & mango)*	M46	Oatly	Oat drink	Oat base (oat 10 %)	RFU
Havredryck naturell *(Oat drink natural)*	M41	Carlshamn	Oat drink	Rolled oats (8.5 %)	RFU
Havregryn *(Rolled oats)*	M47	Lantmännen	Porridge	Rolled oats	P
Pama minutris *(Pama 'minute rice')*	M49	Quaker	Porridge	Rice, polished	P
Rice drink organic	M38	Rice Dream	Rice drink	Rice (14 %)	RFU
Risdryck naturell *(Rice drink natural)*	M45	Carlshamn	Rice drink	Rice (13 %)	RFU
Skrädmjöl *(Oat toasted and milled)*	M77	Saltå kvarn	Gruel or porridge	Oat, toasted & milled	P
Sojadryck *(Soya drink)*	M88	Garant	Soya drink	Soya beans (7.5 %)	RFU
Sojadryck original + Kalcium *(Soya drink original + calcium)*	M58	GoGreen	Soya drink	Soya beans (6.5 %)	RFU
Solhavre naturell *(Oat drink natural)*	M44	ICA Gott liv	Oat drink	Oat (10 %)	RFU
Soya drink natural fresh	M43	Alpro	Soya drink	Soya beans (6 %)	RFU
Soya natural	M57	Provamel	Soya drink	Soya beans (7.2 %)	RFU

Id – identification of composite sample; P – powder; RFU – ready for use

[1] Composite sample from 2008 (n=30), 2009 (n=30) and 2010 (n=30) from the ongoing biomonitoring project at the National Food Agency 'POPup'(personal communication with project leader Sanna Lignell). For details about sampling see Lignell S, Aune M, Darnerud P.O., Cnattingius S, and Glynn A (2009) Persistent organochlorine and organobromine compounds in mother´s milk from Sweden 1996-2006: Compound-specific temporal trend. Environmental Research 109:760-767.

APPENDIX II: Arsenic (As)

Table 1. Estimated daily intake of arsenic from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding.

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml /day)**	**As concentration (µg /kg)**	**As intake (µg/kg bw/day)**
Infant Formula						
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	0.78	0.13
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	0.71	0.12
BabySemp 2 Lemolac modersmjölks-ersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	0.69	0.08
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HiPP	0	4.2	700	0.89	0.15
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	0.77	0.09
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	0.69	0.12
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	0.90	0.15
Organic infant milk	Babynat	0	4.2	700	0.83	0.14
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	0.54	0.09
Follow-on-formula						
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	4.6	0.27
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	0.71	0.08
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	1.1	0.12
Optima Organic Follow-on-milk	Babynat	6	7.7	900	0.71	0.08
FSMP used as sole source of nutrition						
Neocate advance	SHS	12	9.8	900	0.63	0.06
Nutrini energy multi fibre	Nutricia	12	9.8	600	3.4	0.21
Nutrini multi fibre	Nutricia	12	9.8	900	2.7	0.24
Resource minimax	Nestlé	12	9.8	750	1.9	0.15
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	1.3	0.12

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml /day)**	**As concentration (µg /kg)**	**As intake (µg/kg bw/day)**
Isosource junior	Nestlé	12	9.8	900	1.3	0.12
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	1.5	0.24
Pepticate	Nutricia	0	4.2	700	0.57	0.10
Galactomin 19 formula	SHS	0	4.2	700	0.55	0.09
Neocate LCP	Nutricia	0	4.2	700	0.69	0.12
Althéra	Nestlé	0	4.2	700	0.58	0.10
Enfamil AR lipil	Mead Johnson	0	4.2	700	0.67	0.11
Pepti junior	Nutricia	0	4.2	700	0.69	0.11
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	11	0.86
Profylac	Semper	0	4.2	700	1.3	0.22
PreNAN discharge	Nestlé	Premature/LBW	2.5	400	0.84	0.14
Enfalac premature	Mead Johnson	Premature/LBW	2.5	400	0.97	0.16
Pregestimil lipil	Mead Johnson	0	4.2	700	0.90	0.15
FM 85[a]	Nestlé	Premature	2.5	400	0.62	0.10
Enfamil Human Milk Fortifier[a]	Mead Johnson	Premature	2.5	400	0.49	0.08
NutriniKid multi fiber	Nutricia	12	9.8	600	3.7	0.23
FSMP used as partial feeding[b]						
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	1.4	0.17
XP Maxamaid	SHS	12	9.8	300	0.7	0.02
PKU anamix infant lcp+	SHS	0	4.2	300	0.7	0.05

[a]Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water

[b]The intake of these products is calculated as daily intakes in accordance with calculations for intakes of follow-on-formula. LBW=low birth weight

Table 2. Estimated intake of arsenic *per consumed single portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**As concentration (µg /kg)**	**As intake (µg/kg bw/portion)**
Gruel						
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	0.68	0.02
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	0.65	0.02
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	1.5	0.05
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	0.74	0.02
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	19.2	0.58
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	0.94	0.02
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	0.67	0.02
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	8.4	0.26
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	0.74	0.02
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	0.63	0.02
First flavor[a]	Babynat	6	7.7	234	17.6	0.53
Céréales cacao[a]	Babybio	8	8.5	234	16.5	0.46
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	0.64	0.02
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	0.54	0.02
Porridge						
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	28.1	0.56
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	4.6	0.09
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	4.4	0.09
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	11.4	0.23
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	23.1	0.42
Banangröt *(Banana porridge)*	Semper	4	6.6	130	12.8	0.25

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**As concentration (µg /kg)**	**As intake (µg/kg bw/portion)**
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	28.6	0.56
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	1.3	0.02
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	1.1	0.02
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	0.9	0.02
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	1.9	0.03
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	2.8	0.05
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	1.4	0.02
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	22.0	0.63
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	4.6	0.09
Organic seven grain cereal[b]	Organix	7	8.1	105	3.1	0.04
First organic wholegrain baby rice[b]	Organix	4	6.6	51	41.4	0.32
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	4.0	0.10
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	3.0	0.09
Organic millet porridge	Holle	4	6.6	175	1.5	0.04
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	1.2	0.03
Dinkelgröt naturell (Spelt porridge natural)	Nestlé	6	7.7	155	0.9	0.02
Bio-Babybrei Grieβ (Wheat porridge)[a]	Holle	4	6.6	225	1.3	0.05
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	6.5	0.08
Baby´s first food The ultimate four grain porridge[a]	Plum	4	6.6	110	12.5	0.21
Rice porridge[a]	Holle	4	6.6	188	31.3	0.89
FSMP used as partial feeding						
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	2.3	0.05
PKU gel	Vitaflo	12	9.8	50	3.7	0.02
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	2.0	0.04

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**As concentration (µg /kg)**	**As intake (µg/kg bw/portion)**
Foodstuffs for normal consumption						
Havredryck apelsin & mango *(Oat drink orange & mango)*	Oatly	12	9.8	100 ml/portion	1.0	0.01
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	2.0	0.02
Pama minutris (Pama *'minute rice')*	Quaker	12	9.8	130	32.3	0.43
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	18.3	0.19
Risdryck naturell *(Rice drink natural)*	Carlshamn	12	9.8	100 ml/portion	30.4	0.31
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	0.5	0.007
Skrädmjöl *(Oat toasted and milled)*	Saltå Kvarn	12	9.8	130	0.6	0.008
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	0.8	0.009
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	0.8	0.008
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	130	0.9	0.009
Soya drink natural fresh	Alpro	12	9.8	130	1.7	0.018
Soya natural	Provamel	12	9.8	130	1.1	0.011

[a]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water.

APPENDIX III: Cadmium (Cd)

Table 1. Estimated daily intake of cadmium from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding.

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Cd concentration (µg/kg)**	**Cd intake (µg/kg bw/day)**	**% of TDI[a]**
Infant formula							
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	0.3	0.05	15
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	0.2	0.04	10
BabySemp 2 Lemolac Modersmjölksersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	0.3	0.04	11
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HIPP	0	4.2	700	0.1	0.02	5
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	0.6	0.08	21
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	0.3	0.06	15
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	0.1	0.01	3
Organic infant milk	Babynat	0	4.2	700	0.1	0.01	4
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	0.4	0.07	19
Follow-on-formula							
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	0.6	0.04	11
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	0.2	0.02	6
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	0.3	0.03	9
Optima Organic Follow-on-milk	Babynat	6	7.7	900	0.1	0.01	3
FSMP used as sole source of nutrition							
Neocate advance	SHS	12	9.8	900	0.1	0.01	4
Nutrini energy multi fibre	Nutricia	12	9.8	600	0.4	0.02	6
Nutrini multi fibre	Nutricia	12	9.8	900	0.3	0.03	8
Resource minimax	Nestlé	12	9.8	750	0.7	0.05	14

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Cd concentration (µg/kg)**	**Cd intake (µg/kg bw/day)**	**% of TDI[a]**
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	2.2	0.20	55
Isosource junior	Nestlé	12	9.8	900	0.4	0.04	10
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	0.2	0.03	10
Pepticate	Nutricia	0	4.2	700	0.2	0.03	9
Galactomin 19 formula	SHS	0	4.2	700	0.2	0.03	9
Neocate LCP	Nutricia	0	4.2	700	0.6	0.10	28
Althéra	Nestlé	0	4.2	700	0.2	0.03	9
Enfamil AR lipil	Mead Johnson	0	4.2	700	0.2	0.03	9
Pepti junior	Nutricia	0	4.2	700	0.4	0.07	19
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	0.3	0.02	6
Profylac	Semper	0	4.2	700	0.1	0.02	6
PreNAN discharge	Nestlé	Premature/LBW	2.5	400	0.5	0.08	22
Enfalac premature	Mead Johnson	Premature/LBW	2.5	400	0.3	0.04	12
Pregestimil lipil	Mead Johnson	0	4.2	700	0.3	0.04	12
FM 85[b]	Nestlé	Premature	2.5	400	0.2	0.03	9
Enfamil Human Milk Fortifier[b]	Mead Johnson	Premature	2.5	400	0.2	0.03	7
NutriniKid multi fiber	Nutricia	12	9.8	600	0.4	0.02	6
FSMP used as partial feeding[c]							
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	0.4	0.04	12
XP Maxamaid	SHS	12	9.8	300	0.5	0.01	4
PKU anamix infant lcp+	SHS	0	4.2	300	0.3	0.02	7

[a]The tolerable daily intake (TDI) is 0.36 µg/kg bw/day established by EFSA in 2009. [b]Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water

Table 2. Estimated intake of cadmium *per consumed portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cd concentration (µg/kg)**	**Cd intake (µg/kg bw/portion)**	**No. of portions to reach TDI[a]**
Gruel							
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	2.4	0.06	6
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	0.2	0.01	66
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	0.2	0.01	53
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	1.2	0.03	11
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	3.9	0.12	3
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	0.7	0.02	23
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	2.0	0.05	7
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	0.6	0.02	20
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	1.0	0.03	13
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	0.1	0.003	104
First flavor[b]	Babynat	6	7.7	234	3.0	0.09	4
Céréales cacao[b]	Babybio	8	8.5	234	6.9	0.19	2
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	1.3	0.04	10
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	0.1	0.003	105
Porridge							
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	5.3	0.11	3
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	1.5	0.03	12
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	2.5	0.05	7
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	6.0	0.12	3
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	2.4	0.04	8
Banangröt *(Banana porridge)*	Semper	4	6.6	130	3.3	0.07	6

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cd concentration (µg/kg)**	**Cd intake (µg/kg bw/portion)**	**No. of portions to reach TDI[a]**
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	3.8	0.08	5
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	3.7	0.06	6
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	3.8	0.06	6
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	2.3	0.05	8
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	1.6	0.03	14
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	2.2	0.04	10
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	4.3	0.06	6
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	5.4	0.16	2
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	2.2	0.04	9
Organic seven grain cereal[b]	Organix	7	8.1	105	2.2	0.03	13
First organic wholegrain baby rice[b]	Organix	4	6.6	51	0.3	0.002	175
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	0.9	0.02	16
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	2.7	0.08	5
Organic millet porridge	Holle	4	6.6	175	2.1	0.06	6
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	3.5	0.10	4
Dinkelgröt *naturell (Spelt porridge natural)*	Nestlé	6	7.7	155	1.9	0.04	9
Bio-Babybrei Grieβ *(Wheat porridge)*[b]	Holle	4	6.6	225	2.2	0.07	5
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	2.2	0.03	13
Baby´s first food The ultimate four grain porridge[b]	Plum	4	6.6	110	2.1	0.04	10
Rice porridge[b]	Holle	4	6.6	188	1.3	0.04	10
FSMP used as partial feeding							
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	1.1	0.02	16

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cd concentration (µg/kg)**	**Cd intake (µg/kg bw/portion)**	**No. of portions to reach TDI[a]**
PKU gel	Vitaflo	12	9.8	50	1.1	0.01	67
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	2.1	0.04	9
Foodstuffs for normal consumption							
Havredryck apelsin & mango *(Oat drink orange& mango)*	Oatly	12	9.8	100 ml/portion	0.3	0.003	105
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	2.4	0.02	15
Pama minutris *(Pama 'minute rice')*	Quaker	12	9.8	130	2.7	0.04	10
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	0.5	0.01	71
Risdryck naturell (Rice drink natural)	Carlshamn	12	9.8	100 ml/portion	4.5	0.05	8
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	4.9	0.07	6
Skrädmjöl *(Oat toasted and milled)*	Saltå kvarn	12	9.8	130	10.8	0.14	3
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	8.3	0.09	4
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	7.3	0.07	5
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	100 ml/portion	0.1	0.001	442
Soya drink natural fresh	Alpro	12	9.8	100 ml/portion	1.9	0.02	19
Soya natural	Provamel	12	9.8	100 ml/portion	1.9	0.02	19

[a]The tolerable daily intake (TDI) is 0.36 µg/kg bw/day established by EFSA in 2009.
[b]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water.

APPENDIX IV: Lead (Pb)

Table 1. Estimated daily intake of lead from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding.

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Pb concentration (µg/kg)**	**Pb intake (µg/kg bw/day)**	**% of RP[a]**
Infant Formula							
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	0.5	0.08	16
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	0.4	0.06	12
BabySemp 2 Lemolac modersmjölksersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	0.4	0.04	8
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HIPP	0	4.2	700	0.3	0.04	9
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	0.3	0.04	7
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	0.2	0.04	7
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	0.2	0.04	8
Organic infant milk	Babynat	0	4.2	700	0.3	0.04	8
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	0.3	0.06	11
Follow-on-formula							
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	0.5	0.03	6
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	0.6	0.07	14
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	1.2	0.14	27
Optima organic Follow-on-milk	Babynat	6	7.7	900	0.3	0.03	7
FSMP used as sole source of nutrition							
Neocate advance	SHS	12	9.8	900	0.3	0.03	6
Nutrini energy multi fibre	Nutricia	12	9.8	600	0.9	0.06	12
Nutrini multi fibre	Nutricia	12	9.8	900	1.1	0.10	21

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Pb concentration (µg/kg)**	**Pb intake (µg/kg bw/day)**	**% of RP[a]**
Resource minimax	Nestlé	12	9.8	750	0.7	0.05	11
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	1.2	0.11	21
Isosource junior	Nestlé	12	9.8	900	1.5	0.14	27
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	0.7	0.11	22
Pepticate	Nutricia	0	4.2	700	0.5	0.08	15
Galactomin 19 formula	SHS	0	4.2	700	0.8	0.13	27
Neocate LCP	Nutricia	0	4.2	700	0.4	0.07	14
Althéra	Nestlé	0	4.2	700	0.3	0.05	10
Enfamil AR lipil	Mead Johnson	0	4.2	700	0.5	0.08	17
Pepti junior	Nutricia	0	4.2	700	0.5	0.09	18
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	0.5	0.04	7
Profylac	Semper	0	4.2	700	0.3	0.04	8
PreNAN discharge	Nestlé	Premature /LBW	2.5	400	0.4	0.06	12
Enfalac premature	Mead Johnson	Premature /LBW	2.5	400	0.4	0.07	13
Pregestimil lipil	Mead Johnson	0	4.2	700	0.6	0.11	22
FM 85[b]	Nestlé	Premature	2.5	400	0.3	0.04	9
Enfamil Human Milk Fortifier[b]	Mead Johnson	Premature	2.5	400	0.5	0.08	15
NutriniKid multi fiber	Nutricia	12	9.8	600	0.9	0.06	11
FSMP used as partial feeding[c]							
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	0.9	0.10	20
XP Maxamaid	SHS	12	9.8	300	0.8	0.02	5
PKU anamix infant lcp+	SHS	0	4.2	300	0.6	0.04	8

[a]The reference point (RP) is 0.5 µg/kg bw/day established by EFSA in 2010.
[b] Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water
[c]The intake of these products is calculated as daily intakes in accordance with calculations for intakes of follow-on formulas.

LBW=low birth weight

Table 2. Estimated intake of lead *per consumed portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Pb concentration (µg/kg)**	**Pb intake (µg/kg bw/portion)**	**No. of portion to reach RP[a]**
Gruel							
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	0.5	0.01	39
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	0.7	0.02	23
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	0.3	0.01	59
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	3.1	0.09	6
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	6.9	0.21	2
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	0.2	0.01	86
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	0.3	0.01	65
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	0.6	0.02	27
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	0.6	0.02	30
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	0.3	0.01	51
First flavor[b]	Babynat	6	7.7	234	0.2	0.01	76
Céréales cacao[b]	Babybio	8	8.5	234	0.4	0.01	49
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	0.3	0.01	73
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	0.3	0.01	63
Porridge							
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	1.4	0.03	18
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	1.3	0.02	20
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	0.5	0.01	50
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	12.6	0.26	2
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	1.3	0.02	22
Banangröt *(Banana porridge)*	Semper	4	6.6	130	0.6	0.01	39
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	0.5	0.01	56

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Pb concentration (µg/kg)**	**Pb intake (µg/kg bw/portion)**	**No. of portion to reach RP[a]**
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	0.9	0.01	38
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	0.5	0.01	62
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	2.2	0.04	12
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	0.6	0.01	47
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	0.4	0.01	76
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	0.7	0.01	55
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	1.9	0.05	9
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	0.4	0.01	62
Organic seven grain cereal[b]	Organix	7	8.1	105	0.5	0.01	75
First organic wholegrain baby rice[b]	Organix	4	6.6	51	0.5	0.004	119
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	1.5	0.04	13
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	0.3	0.01	52
Organic millet porridge	Holle	4	6.6	175	0.9	0.02	22
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	0.3	0.01	56
Dinkelgröt *naturell (Spelt porridge natural)*	Nestlé	6	7.7	155	0.5	0.01	54
Bio-Babybrei Grieβ *(Wheat porridge)*[b]	Holle	4	6.6	225	0.3	0.01	55
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	1.9	0.02	22
Baby´s first food The ultimate four grain porridge [b]	Plum	4	6.6	110	0.6	0.01	46
Rice porridge[b]	Holle	4	6.6	188	0.3	0.01	64
FSMP used as partial feeding							
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	1.9	0.04	13
PKU gel	Vitaflo	12	9.8	50	22.6	0.12	4
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	2.2	0.04	11
Foodstuffs for normal consumption							
Havredryck apelsin & mango *(Oat drink orange& mango)*	Oatly	12	9.8	100 ml/portion	0.2	0.003	198
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	1.3	0.01	39

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Pb concentration (µg/kg)**	**Pb intake (µg/kg bw/portion)**	**No. of portion to reach RP[a]**
Pama minutris *(Pama 'minute rice')*	Quaker	12	9.8	130	0.1	0.002	308
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	0.2	0.002	302
Risdryck naturell (Rice drink natural)	Carlshamn	12	9.8	100 ml/portion	1.4	0.01	36
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	0.3	0.004	127
Skrädmjöl *(Oat toasted and milled)*	Saltå kvarn	12	9.8	130	0.6	0.01	63
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	1.3	0.01	37
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	1.1	0.01	43
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	100 ml/portion	0.1	0.001	454
Soya drink natural fresh	Alpro	12	9.8	100 ml/portion	0.2	0.002	277
Soya natural	Provamel	12	9.8	100 ml/portion	0.1	0.001	340

[a]The reference point (RP) is 0.5 µg/kg bw/day established by EFSA in 2010.
[b]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water.

APPENDIX V: Manganese (Mn)

Table 1. Estimated daily intake of manganese from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding.

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Mn concentration (mg/kg)**	**Mn intake (µg/day)**	**% of AI[a]**	**Mn intake (µg/kg bw/day)**	**% of TDI[b]**
Infant Formula									
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	0.16	110	3680	26	44
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	0.13	90	3000	21	36
BabySemp 2 Lemolac modersmjölksersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	0.07	57	1910	9	14
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HIPP	0	4.2	700	0.10	68	2260	16	27
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	0.08	66	2210	10	17
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	0.02	15	510	4	6
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	0.05	32	1070	8	13
Organic infant milk	Babynat	0	4.2	700	0.05	35	1170	8	14
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	0.11	76	2540	18	30
Follow-on-formula									
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	0.36	180	30	21	35
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	0.12	111	3720	14	24
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	0.18	161	5380	21	35
Optima Organic Follow-on-milk	Babynat	6	7.7	900	0.04	39	1300	5	8
FSMP used as sole source of nutrition									
Neocate advance	SHS	12	9.8	900	0.56	508	42	52	86
Nutrini energy multi fibre	Nutricia	12	9.8	600	2.01	208	101	123	205
Nutrini multi fibre	Nutricia	12	9.8	900	1.62	461	122	149	248

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Mn concentration (mg/kg)**	**Mn intake (µg/day)**	**% of AI[a]**	**Mn intake (µg/kg bw/day)**	**% of TDI[b]**
Resource minimax	Nestlé	12	9.8	750	0.76	566	47	58	96
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	2.51	2256	188	230	384
Isosource junior	Nestlé	12	9.8	900	1.65	1489	124	152	253
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	0.48	336	11190	80	133
Pepticate	Nutricia	0	4.2	700	0.10	73	2440	17	29
Galactomin 19 formula	SHS	0	4.2	700	0.39	275	9170	66	109
Neocate LCP	Nutricia	0	4.2	700	0.45	316	10530	75	125
Althéra	Nestlé	0	4.2	700	0.05	34	1140	8	14
Enfamil AR lipil	Mead Johnson	0	4.2	700	0.41	290	9680	69	115
Pepti junior	Nutricia	0	4.2	700	0.42	297	9890	71	118
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	0.76	454	15130	59	98
Profylac	Semper	0	4.2	700	0.45	312	10390	74	124
PreNAN discharge	Nestlé	Premature/LBW	2.5	400	0.12	48	1590	19	32
Enfalac premature	Mead Johnson	Premature/LBW	2.5	400	0.11	42	1420	17	28
Pregestimil lipil	Mead Johnson	0	4.2	700	0.46	323	10760	77	128
FM 85[c]	Nestlé	Premature	2.5	400	0.12	48	1600	19	32
Enfamil Human Milk Fortifier[c]	Mead Johnson	Premature	2.5	400	0.14	57	1920	23	38
NutriniKid multi fiber	Nutricia	12	9.8	600	0.14	1074	90	9	15
FSMP used as partial feeding[d]									
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	0.64	580	19333	75	125
XP Maxamaid	SHS	12	9.8	300	2.60	780	130	80	133
PKU anamix infant lcp+	SHS	0	4.2	300	0.67	200	6666	48	79

[a]The Adequate intake (AI) is for 0-6 months 3µg, for 7-12 months 600 µg and for 1-3 years 1200 µg (IOM, 2001).
[b]The tolerable daily intake (TDI) is 60 µg/kg bw/day established by WHO in 2003.
[c] Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water
[d]The intake of these products is calculated as daily intakes in accordance with calculations for intakes of follow-on formula.

LBW=low birth weight.

Table 2. Estimated intake of manganese *per consumed portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Mn concentration (mg/kg)**	**Mn intake (µg/portion)**	**No. of portions to reach AI[a]**	**Mn intake (µg/kg bw/portion)**	**No. of portions to reach TDI[b]**
Gruel									
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	1.42	340	4	34	2
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	0.07	20	0	2	28
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	0.21	50	0	6	10
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	1.43	340	2	40	2
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	1.51	350	0	46	1
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	0.74	150	4	17	3
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	1.39	330	4	34	2
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	0.50	120	0	15	4
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	1.18	260	0	34	2
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	0.04	10	0	1	53
First flavor[c]	Babynat	6	7.7	234	1.09	260	0	33	2
Céréales cacao[c]	Babybio	8	8.5	234	1.32	310	2	36	2
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	1.27	290	2	34	2
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	0.08	20	0	2	26
Porridge									
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	4.63	610	0	93	1
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	2.33	390	2	46	1
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	2.25	370	0	49	1
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	3.27	520	0	67	1
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	0.88	110	0	16	4

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Mn concentration (mg/kg)**	**Mn intake (µg/portion)**	**No. of portions to reach AI[a]**	**Mn intake (µg/kg bw/portion)**	**No. of portions to reach TDI[b]**
Banangröt *(Banana porridge)*	Semper	4	6.6	130	1.11	140	0	22	3
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	1.53	200	0	30	2
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	2.57	330	2	39	2
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	3.32	430	2	51	1
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	1.76	230	0	35	2
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	1.64	210	0	28	2
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	2.51	400	3	40	1
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	2.26	300	4	31	2
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	1.24	240	0	36	2
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	2.70	430	2	50	1
Organic seven grain cereal[c]	Organix	7	8.1	105	3.59	380	2	47	1
First organic wholegrain baby rice[c]	Organix	4	6.6	51	2.59	130	0	20	3
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	0.75	120	0	19	3
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	4.40	990	0	128	0
Organic millet porridge	Holle	4	6.6	175	0.89	160	0	24	3
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	3.21	720	0	94	1
Dinkelgröt naturell *(Spelt porridge* natural)	Nestlé	6	7.7	155	3.24	500	0	65	1
Bio-Babybrei Grieβ *(Wheat porridge)*[c]	Holle	4	6.6	225	2.81	630	0	96	1
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	3.76	440	3	45	1
Baby´s first food The ultimate four grain porridge[c]	Plum	4	6.6	110	1.47	160	0	24	2

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Mn concentration (mg/kg)**	**Mn intake (µg/portion)**	**No. of portions to reach AI[a]**	**Mn intake (µg/kg bw/portion)**	**No. of portions to reach TDI[b]**
Rice porridge[c]	Holle	4	6.6	188	2.93	550	0	84	1
FSMP used as partial feeding									
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	3.82	760	2	78	1
PKU gel	Vitaflo	12	9.8	50	8.30	420	3	42	1
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	1.76	350	3	36	2
Foodstuffs for normal consumption									
Havredryck apelsin & mango *(Oat drink orange & mango)*	Oatly	12	9.8	100 ml/portion	0.80	80	15	8.2	7
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	0.67	67	18	6.8	9
Pama minutris *(Pama 'minute rice')*	Quaker	12	9.8	130	1.06	138	9	14.1	4
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	0.22	22	53	2.3	26
Risdryck naturell (Rice drink natural)	Carlshamn	12	9.8	100 ml/portion	0.70	70	17	7.1	8
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	4.65	605	2	61.7	1
Skrädmjöl *(Oat toasted and milled)*	Saltå kvarn	12	9.8	130	8.87	1154	1	117.7	1
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	1.95	195	6	19.9	3
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	1.56	156	8	15.9	4
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	100 ml/portion	0.16	16	76	1.6	37
Soya drink natural fresh	Alpro	12	9.8	100 ml/portion	1.57	157	7	16.0	4
Soya natural	Provamel	12	9.8	100 ml/portion	1.98	198	6	20.2	3

[a]The Adequate intake (AI) is for 0-6 months 3µg, for 7-12 months 600 µg and for 1-3 years 1200 µg (IOM, 2001).
[b]The tolerable daily intake (TDI) is 60 µg/kg bw/day established by WHO in 2003.
[c]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water.

APPENDIX VI: Iron (Fe)

Table 1. Estimated daily intake of iron from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding.

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml /day)**	**Fe concentration (mg/kg)**	**Fe intake (mg/day)**	**% of RI[a]**
Infant Formula							
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	3.8	2.7	NA
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	6.2	4.3	NA
BabySemp 2 Lemolac modersmjölksersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	5.6	4.5	NA
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HIPP	0	4.2	700	5.7	4.0	NA
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	6.4	5.1	NA
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	3.5	2.5	NA
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	4.1	2.9	NA
Organic infant milk	Babynat	0	4.2	700	6.9	4.8	NA
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	3.5	2.4	NA
Follow-on-formula							
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	9.4	4.7	59
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	8.8	7.9	99
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	7.9	7.1	89
Optima Organic Follow-on-milk	Babynat	6	7.7	900	7.8	7.0	88
FSMP used as sole source of nutrition							
Neocate advance	SHS	12	9.8	900	6.0	5.4	68
Nutrini energy multi fibre	Nutricia	12	9.8	600	13.0	7.8	98
Nutrini multi fibre	Nutricia	12	9.8	900	9.9	8.9	111
Resource minimax	Nestlé	12	9.8	750	10.7	8.0	100

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml /day)**	**Fe concentration (mg/kg)**	**Fe intake (mg/day)**	**% of RI[a]**
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	11.6	10	125
Isosource junior	Nestlé	12	9.8	900	8.2	7.4	93
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	11.4	8.0	NA
Pepticate	Nutricia	0	4.2	700	5.0	3.5	NA
Galactomin 19 formula	SHS	0	4.2	700	3.9	2.7	NA
Neocate LCP	Nutricia	0	4.2	700	7.4	5.2	NA
Althéra	Nestlé	0	4.2	700	6.5	4.6	NA
Enfamil AR lipil	Mead Johnson	0	4.2	700	7.3	5.1	NA
Pepti junior	Nutricia	0	4.2	700	7.1	4.9	NA
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	9.0	5.4	68
Profylac	Semper	0	4.2	700	6.2	4.3	NA
PreNAN discharge	Nestlé	Premature/LBW	2.5	400	7.5	3.0	NA
Enfalac premature	Mead Johnson	Premature/LBW	2.5	400	10.2	4.1	NA
Pregestimil lipil	Mead Johnson	0	4.2	700	11.5	8.0	NA
FM 85[b]	Nestlé	Premature	2.5	400	10.4	4.2	NA
Enfamil Human Milk Fortifier[b]	Mead Johnson	Premature	2.5	400	13.4	5.3	NA
NutriniKid multi fiber	Nutricia	12	9.8	600	13.4	8.0	100
FSMP used as partial feeding[c]							
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	12.1	10.9	136
XP Maxamaid	SHS	12	9.8	300	15.9	4.8	53
PKU anamix infant lcp+	SHS	0	4.2	300	7.3	2.2	NA

[a]The recommended daily intake (RI) from 6 months is 8.0 mg/d established by SNR 2005.
[b] Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water
[c]The intake of these products is calculated as daily intakes in accordance with calculations for intakes of follow-on formula.

NA=not applicable because the product is intended for infants less than 6 months for which there is no RI.
LBW=low birth weight

Table 2. Estimated intake of iron *per consumed portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Fe concentration (mg/kg)**	**Fe intake (mg/portion)**	**No. of portions to reach RI[a]**
Gruel							
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	11.4	2.7	3
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	10.8	2.6	3
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	12.1	2.8	3
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	11.1	2.6	3
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	16.2	3.8	2
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	9.4	1.9	4
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	13.0	3.1	3
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	11.4	2.7	3
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	11.9	2.6	3
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	10.1	2.4	3
First flavor[b]	Babynat	6	7.7	234	0.6	0.1	(55)
Céréales cacao[b]	Babybio	8	8.5	234	1.8	0.4	(20)
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	12.8	2.9	3
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	5.4	1.2	7
Porridge							
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	23.8	3.1	NA
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	12.0	2.0	4
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	6.2	1.0	8
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	13.2	2.1	4
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	21.6	2.8	NA

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Fe concentration (mg/kg)**	**Fe intake (mg/portion)**	**No. of portions to reach RI[a]**
Banangröt *(Banana porridge)*	Semper	4	6.6	130	18.8	2.4	NA
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	17.2	2.2	NA
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	22.3	2.8	3
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	18.7	2.4	3
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	20.2	2.6	NA
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	16.5	2.2	4
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	5.4	0.9	9
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	21.0	2.8	3
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	1.5	0.3	NA
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	11.2	1.8	5
Organic seven grain cereal[b]	Organix	7	8.1	105	4.3	0.5	(18)
First organic wholegrain baby rice[b]	Organix	4	6.6	51	2.1	0.1	NA
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	3.2	0.5	NA
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	3.6	0.8	10
Organic millet porridge	Holle	4	6.6	175	3.3	0.6	NA
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	3.6	0.8	10
Dinkelgröt naturell *(Spelt porridge natural)*	Nestlé	6	7.7	155	19.1	3.0	3
Bio-Babybrei *Grieß (Wheat* porridge)[b]	Holle	4	6.6	225	2.7	0.6	NA
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	19.5	2.3	3
Baby´s first food The ultimate four grain porridge[b]	Plum	4	6.6	110	2.7	0.3	NA
Rice porridge[b]	Holle	4	6.6	188	1.1	0.2	NA
FSMP used as partial feeding							
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	19.7	3.9	2

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Fe concentration (mg/kg)**	**Fe intake (mg/portion)**	**No. of portions to reach RI[a]**
PKU gel	Vitaflo	12	9.8	50	60.3	3.0	3
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	14.0	2.8	3
Foodstuffs for normal consumption							
Havredryck apelsin & mango *(Oat drink orange & mango)*	Oatly	12	9.8	100 ml/portion	0.9	0.09	86
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	0.8	0.08	94
Pama minutris *(Pama 'minute rice')*	Quaker	12	9.8	130	0.2	0.03	315
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	0.1	0.01	700
Risdryck naturell (Rice drink natural)	Carlshamn	12	9.8	100 ml/portion	0.8	0.08	103
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	5.5	0.71	11
Skrädmjöl *(Oat toasted and milled)*	Saltå kvarn	12	9.8	130	9.4	1.22	7
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	6.5	0.65	12
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	5.0	0.50	7
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	100 ml/portion	0.5	0.05	12
Soya drink natural fresh	Alpro	12	9.8	100 ml/portion	4.2	0.42	16
Soya natural	Provamel	12	9.8	100 ml/portion	3.3	0.33	25

[a]The recommended daily intake (RI) is 8.0 mg/d established by SNR in 2005.
[b]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water.NA=not applicable because the product is intended for infants less than 6 months for which there is no RI.

APPENDIX VII: Copper (Cu)

Table 1. Estimated daily intake of copper from ready-to-eat infant formula, follow-on formula, FSMP as sole source of nutrition and FSMP as partial feeding

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Cu concentration (mg/kg)**	**Cu intake (µg/day)**	**% of RI[a]**	**% of UL[b]**
Infant Formula								
NAN 1 Modersmjölksersättning *(NAN 1 Infant formula)*	Nestlé	0	4.2	700	0.35	246	NA	25
NAN HA 1 Modersmjölksersättning *(NAN HA 1 Infant formula)*	Nestlé	0	4.2	700	0.51	354	NA	35
BabySemp 2 Lemolac modersmjölks-ersättning *(BabySemp 2 Lemolac infant formula)*	Semper	4	6.6	800	0.46	370	NA	37
ECO 1 Modersmjölksersättning *(ECO 1 infant formula)*	HIPP	0	4.2	700	0.33	232	NA	23
ECO 2 Modersmjölksersättning *(ECO 2 infant formula)*	HIPP	4	6.6	800	0.39	308	NA	31
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula), powder*	Semper	0	4.2	700	0.34	239	NA	24
BabySemp 1 Modersmjölksersättning *(BabySemp 1 infant formula)*, RFU	Semper	0	4.2	700	0.38	263	NA	26
Organic infant milk	Babynat	0	4.2	700	0.36	252	NA	25
Eko 1 Modersmjölksersättning, *(Infant formula 1)*	Holle	0.5	4.2	700	0.34	239	NA	24
Follow-on-formula								
BabySemp 3 Tillskottsnäring *(BabySemp 3 follow-on-formula)*	Semper	8	8.5	500	0.33	166	55	17
NAN Pro 2 Tillskottsnäring *(NAN PRO 2 follow-on-formula)*	Nestlé	6	7.7	900	0.47	419	140	42
Eko tillskottsnäring 2 *(Follow-on-formula 2)*	Holle	6	7.7	900	0.36	327	109	33
Optima Organic Follow-on-milk	Babynat	6	7.7	900	0.39	353	118	35
FSMP used as sole source of nutrition								
Neocate advance	SHS	12	9.8	900	0.57	511	170	51
Nutrini energy multi fibre	Nutricia	12	9.8	600	1.11	666	222	67
Nutrini multi fibre	Nutricia	12	9.8	900	0.76	684	228	68
Resource minimax	Nestlé	12	9.8	750	1.01	755	252	76

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (ml/day)**	**Cu concentration (mg/kg)**	**Cu intake (µg/day)**	**% of RI[a]**	**% of UL[b]**
Fresubin soya fibre	Fresenius Kabi	12	9.8	900	1.37	1233	411	123
Isosource junior	Nestlé	12	9.8	900	1.02	914	305	91
Nutramigen 1 lipil	Mead Johnson	0	4.2	700	0.46	325	NA	33
Pepticate	Nutricia	0	4.2	700	0.44	311	NA	31
Galactomin 19 formula	SHS	0	4.2	700	0.39	270	NA	27
Neocate LCP	Nutricia	0	4.2	700	0.46	324	NA	32
Althéra	Nestlé	0	4.2	700	0.57	398	NA	40
Enfamil AR lipil	Mead Johnson	0	4.2	700	0.49	345	NA	35
Pepti junior	Nutricia	0	4.2	700	0.37	258	NA	26
Minimax barnsondnäring *(Minimax enteral formula for children)*	Nestlé	6	7.7	600	1.09	655	218	66
Profylac	Semper	0	4.2	700	0.40	278	NA	28
PreNAN discharge	Nestlé	Premature/ LBW	2.5	400	0.56	225	NA	23
Enfalac premature	Mead Johnson	Premature/ LBW	2.5	400	0.76	303	NA	30
Pregestimil lipil	Mead Johnson	0	4.2	700	0.51	360	NA	36
FM 85[c]	Nestlé	Premature	2.5	400	0.35	140	NA	14
Enfamil Human Milk Fortifier[c]	Mead Johnson	Premature	2.5	400	0.54	220	NA	22
NutriniKid multi fiber	Nutricia	12	9.8	600	1.30	778	259	78
FSMP used as partial nutrition[d]								
Nutramigen 2 lipil	Mead Johnson	6	7.7	900	0.54	484	161	48
XP Maxamaid	SHS	12	9.8	300	2.62	786	262	79
PKU anamix infant lcp+	SHS	0	4.2	300	0.57	170	NA	17

[a]The recommended intake (RI) from 6 months is 0.3 mg/day established by SNR in 2005.
[b]The tolerable upper intake level (UL) is 1000 µg/day established by EFSA in 2003.
[c] Products to be mixed with breast milk according to instruction, calculation in table based on product diluted with water
[d]The intake of these products is calculated as daily intakes in accordance with calculations for intakes of follow-on formulas.

NA=not applicable because the product is intended for infants less than 6 months for which there is no RI
LBW=low birth weight

Table 2. Estimated intake of copper *per consumed portion* from gruel, porridge, FSMP as partial feeding and foodstuffs for normal consumption (products not intended for infants)

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cu concentration (mg/kg)**	**Cu intake (µg/portion)**	**No. of portions to reach RI[a]**	**No. of portions to reach UL[b]**
Gruel								
Fullkornsvälling *(Wholegrain gruel)*	Nestlé	12	9.8	236	0.23	55	5	18
Låglaktos majsvälling *(Low lactose corn gruel)*	Nestlé	6	7.7	237	0.04	9	33	110
Majsvälling *(Corn gruel)*	Semper	6	7.7	229	0.06	15	20	67
Mild fullkornsvälling havre *(Mild wholegrain gruel oat)*	Nestlé	8	8.5	236	0.17	40	7	25
Välling mjölkfri *(Gruel dairy free)*	EnaGo	6	7.7	233	0.38	89	3	11
Drickfärdig mild fullkornsvälling *(Ready for use mild wholegrain gruel)*	Semper	8	8.5	200	0.11	22	14	46
Fullkornsvälling havre vete råg *(Wholgrain gruel oat wheat rye)*	Semper	12	9.8	237	0.21	50	6	20
Kvällsvälling ris och vete *(Evening gruel rice and wheat)*	Semper	6	7.7	237	0.10	24	12	41
God natt mild havrevälling *(Good night mild oat gruel)*	Nestlé	6	7.7	220	0.12	27	11	37
Majsvälling *(Corn gruel)*	Nestlé	6	7.7	236	0.02	5	66	221
First flavor[c]	Babynat	6	7.7	234	0.21	48	6	21
Céréales cacao[c]	Babybio	8	8.5	234	0.40	94	3	11
Mild fullkornsvälling *(Mild wholegrain gruel)*	Semper	8	8.5	228	0.16	37	8	27
Majsvälling *(Corn gruel)*	HIPP	6	7.7	220	0.33	73	4	14
Porridge								
Sinlac specialgröt *(Sinlac special porridge)*	Nestlé	4	6.6	132	1.22	161	NA	6
Fullkornsgröt med äpple *(Wholegrain porridge with apple)*	HIPP	8	8.5	169	0.45	76	4	13
Mild havregröt *(Mild oat porridge)*	HIPP	6	7.7	167	0.34	57	5	17
Banangröt mjölkfri *(Banana porridge dairy free)*	EnaGo	6	7.7	158	0.84	133	2	8
Risgröt med äpple och mango *(Rice porridge with apple and mango)*	Semper	5	7.2	130	0.19	25	NA	40

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cu concentration (mg/kg)**	**Cu intake (µg/portion)**	**No. of portions to reach RI[a]**	**No. of portions to reach UL[b]**
Banangröt *(Banana porridge)*	Semper	4	6.6	130	0.25	32	NA	31
Cerelac risgröt *(Cerelac rice porridge)*	Nestlé	4	6.6	130	0.22	29	NA	35
Mild fullkornsgröt *(Mild wholegrain porridge)*	Nestlé	8	8.5	128	0.33	43	7	23
Mild fullkornsgröt *(Mild wholegrain porridge)*	Semper	8	8.5	130	0.46	59	5	17
Mild havregröt *(Mild oat porridge)*	Semper	4	6.6	130	0.26	33	NA	30
Cerelac Fruktgröt banan apelsin *(Cerelac fruit porridge banana orange)*	Nestlé	6	7.7	130	0.39	50	6	20
Fullkornsgröt multikorn *(Wholegrain porridge multigrain)*	HIPP	12	9.8	158	0.37	58	3	17
Fruktgröt fullkorn *(Fruit porridge wholegrain)*	Semper	12	9.8	133	0.39	52	4	19
God Natt! Risgröt med grönsaker *(Rice porridge with vegetables)*	HIPP	4	6.6	190	0.35	66	NA	15
Mild fullkornsgröt *(Mild wholegrain porridge)*	HIPP	8	8.5	158	0.38	60	5	17
Organic seven grain cereal[c]	Organix	7	8.1	105	0.53	55	5	18
First organic wholegrain baby rice[c]	Organix	4	6.6	51	0.32	17	NA	61
Risgröt med banan och persika *(Rice porridge with banana and peach)*	HIPP	4	6.6	167	0.32	54	NA	18
Eko havregröt (*Organic oat porridge)*	Holle	6	7.7	225	0.41	91	3	11
Organic millet porridge	Holle	4	6.6	175	0.70	123	NA	8
Eko dinkelgröt *(Organic spelt porridge)*	Holle	6	7.7	225	0.58	130	2	8
Dinkelgröt naturell *(Spelt porridge natural)*	Nestlé	6	7.7	155	0.34	52	6	19
Bio-Babybrei Grieβ *(Wheat porridge)*[c]	Holle	4	6.6	225	0.38	85	NA	12
Musligröt päron-banan *(Musli porridge pear-banana)*	Nestlé	12	9.8	118	0.46	54	6	18
Baby´s first food The ultimate four grain porridge[c]	Plum	4	6.6	110	0.37	41	NA	24

Product *(English translation)*	**Producer**	**Age (months)**	**Weight (kg)**	**Consumption (g/portion)**	**Cu concentration (mg/kg)**	**Cu intake (µg/portion)**	**No. of portions to reach RI[a]**	**No. of portions to reach UL[b]**
Rice porridge[c]	Holle	4	6.6	188	0.22	42	NA	24
FSMP used as partial feeding								
Fresubin energy fiber, chocolate flavour	Fresenius Kabi	12	9.8	200 ml/portion	2.90	580	1	2
PKU gel	Vitaflo	12	9.8	50	3.19	160	2	6
Frebini energy fiber drink	Fresenius Kabi	12	9.8	200 ml/portion	1.54	308	1	3
Foodstuffs for normal consumption								
Havredryck apelsin & mango *(Oat drink orange & mango)*	Oatly	12	9.8	100 ml/portion	0.27	27	11	36
Havredryck naturell *(Oat drink natural)*	Carlshamn	12	9.8	100 ml/portion	0.22	22	14	46
Pama minutris *(Pama 'minute rice')*	Quaker	12	9.8	130	0.24	31	10	33
Ricedrink organic	Rice Dream	12	9.8	100 ml/portion	0.05	5	59	197
Risdryck naturell (Rice drink natural)	Carlshamn	12	9.8	100 ml/portion	0.09	9	32	107
Havregryn *(Rolled oats)*	Lantmännen	12	9.8	130	0.56	72	4	14
Skrädmjöl *(Oat toasted and milled)*	Saltå kvarn	12	9.8	130	1.02	132	2	8
Sojadryck *(Soya drink)*	Garant	12	9.8	100 ml/portion	1.43	143	2	7
Sojadryck original + kalcium *(Soya drink original + calcium)*	GoGreen	12	9.8	100 ml/portion	1.10	110	3	9
Solhavre naturell *(Oat drink natural)*	ICA	12	9.8	100 ml/portion	0.15	15	20	65
Soya drink natural fresh	Alpro	12	9.8	100 ml/portion	1.02	102	3	10
Soya natural	Provamel	12	9.8	100 ml/portion	0.90	90	3	11

[a]The recommended intake (RI) is 0.3 mg/day established by SNR in 2005.
[b]The tolerable upper intake level (UL) is 1000 µg/day established by EFSA in 2003.
[c]Products to be mixed with milk product according to instruction, calculation in table based on product diluted with water. NA=not applicable because the product is intended for infants less than 6 months for which there is no RI.

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9. Kontroll av restsubstanser i levande djur och animaliska livsmedel. Resultat 2010 av I Nordlander, Å Kjellgren, A Glynn, B Aspenström-Fagerlund, K Granelli, I Nilsson, C Sjölund Livsmedelsverket och K Girma, Jordbruksverket.
10. Råd om fullkorn 2009 – bakgrund och vetenskapligt underlag av W Becker, L Busk, I Mattisson och S Sand.
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1. Contaminants and minerals in foods for infants and young children – analytical results, Part 1, by V Öhrvik, J Engman, B Kollander and B Sundström.

   Contaminants and minerals in foods for infants and young children – risk and benefit assessment, Part 2 by G Concha, H Eneroth, H Hallström and S Sand.

   Tungmetaller och mineraler i livsmedel för spädbarn och småbarn. Del 3 Risk- och nyttohantering av R Bjerselius, E Halldin Ankarberg, A Jansson, I Lindeberg, J Sanner Färnstrand och C Wanhainen.

   Contaminants and minerals in foods for infants and young children – risk and benefit management, Part 3 by R Bjerselius, E Halldin Ankarberg, A Jansson, I Lindeberg, J Sanner Färnstrand and C Wanhainen.

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