National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Intake assessment of the food additives nitrites (E 249 and E 250) and nitrates (E 251 and E 252)

RIVM Letter report 2016-0208
R.C. Sprong | E.M. Niekerk | M.H. Beukers

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Synopsis

Intake assessment of the food additives nitrite (E 249 and E 250) and nitrate (E 251 and E 252).

Nitrate and nitrite are authorised as preservatives in certain food products, such as salami, ham (nitrite) and cheese (nitrate). They prevent food spoilage and protect the consumer against food-borne pathogens. Next to that, nitrate and nitrite play a role in food colour retention and contribute to flavour formation of the food.

RIVM estimated that the nitrate intake of the population aged 2 to 79 years does not exceed the acceptable daily intake (ADI). The intake of nitrite, however, exceeded the ADI. Because of the conservative assumptions, the real intake will probably much lower. Refinement is needed to obtain a more realistic intake assessment.

RIVM calculated the intake of nitrite and nitrate using the maximum permitted levels as laid down in the European Regulation on food additives. These levels are mostly expressed as maximum ingoing amounts. The actual concentration in food as consumed differs from the ingoing amounts because of chemical processes during processing and storage of foods. The nitrite concentration decreases, but derivatives, such as nitrosamines, may be generated. Analytical values of nitrite in meat products are desired to refine the intake assessment of nitrite. Some other European countries used analytical values of nitrite for their intake assessments. These studies showed lower nitrite intake estimates that remained below the ADI.

Chronic intake of high levels of nitrate, nitrite or their derivatives (such as nitrosamines) may have negative effects on health. Nitrate may hamper growth of young children and nitrite may have a negative effect on heart and lung functioning. Some nitrosamines (but not all) may induce cancer. RIVM did not perform an intake assessment of nitrosamines, because recent analytical data of these substances in food were not available. Analytical values of nitrosamines in food products are also desired to assess whether problems could be expected by current food additive use of nitrate and nitrite.

The study was performed on the initiative of the Dutch Ministry of Health, Welfare and Sport (VWS). The research described in this report is part of the programme on the development of an efficient system for monitoring intake of food additives (conform article 27 of EU Regulation 1333/2008).

Keywords: nitrite, nitrate, preservative, E 249, E 250, E 251, E 252, food additive, young children, adults, elderly, long-term dietary intake

Publiekssamenvatting

De inname van de voedseladditieven nitriet (E 249 en E 250) en nitraat (E 251 en E 252).

Nitraat en nitriet mogen als conserveermiddel aan bepaalde voedingsmiddelen worden toegevoegd, zoals aan salami of ham (nitriet) en aan kaas (nitraat). Hierdoor bederven de producten minder snel en is de consument beter beschermd tegen ziekteverwekkers. Daarnaast zorgen ze ervoor dat de kleur behouden blijft en dragen ze bij aan de smaakvorming van de producten.

Uit berekeningen van het RIVM blijkt dat in Nederland de inname van nitraat voor mensen tussen de 2 en 79 jaar binnen de veilige marge ligt. Voor nitriet lijkt dat niet het geval te zijn. Het is mogelijk dat de inname van nitriet in de praktijk lager is dan berekend omdat voor dit onderzoek conservatieve aannames zijn gebruikt. Verfijning van de berekening is nodig om een realistischere innameschatting te krijgen.

De innameberekeningen van nitraat en nitriet zijn berekend op basis van zogeheten maximum toegestane waarden, die zijn vastgelegd in de Europese additievenverordening. Dit zijn veelal de maximum hoeveelheden die aan een product mogen worden toegevoegd. De toegevoegde hoeveelheden kunnen echter veranderen tijdens opslag en bereiding van de producten. Zo verdwijnt een deel van het nitriet, maar kunnen afgeleide stoffen (zoals nitrosamines) juist worden gevormd. Metingen van de hoeveelheden nitriet in vleesproducten zijn gewenst om de innameberekeningen in Nederland te kunnen verfijnen. Meetwaarden van nitriet worden soms door andere Europese landen gebruikt voor innameberekeningen. Deze schattingen vallen doorgaans veel lager uit en vallen wel binnen de veilige marge.

Als consumenten langdurig te veel nitraat, nitriet en daarvan afgeleide stoffen binnenkrijgen (waaronder nitrosamines), kan dat schadelijk zijn voor de gezondheid. Nitraat kan dan de groei van jonge kinderen remmen en nitriet kan mogelijk effecten hebben op het functioneren van de longen en het hart. Sommige nitrosamines (maar niet alle) kunnen kankerverwekkend zijn. Van deze stoffen zijn echter geen innameberekingen gemaakt omdat het aan actuele meetgegevens van nitrosamines in voedingsmiddelen ontbrak. Daarom zijn ook van nitrosamines nieuwe meetwaarden gewenst om goed te kunnen beoordelen of ze bij het huidige gebruik van nitraat en nitriet een probleem vormen.

Het onderzoek is uitgevoerd in opdracht van het ministerie van VWS. Het draagt bij aan de ontwikkeling van een efficiënt systeem om de inname van levensmiddelenadditieven te monitoren (conform artikel 27 van Verordening 1333/2008).

Kernwoorden: nitraat, nitriet, conserveermiddel, E 249, E 250, E 251, E 252, jonge kinderen, volwassenen, ouderen, lange-termijn blootstelling, voedsel

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1 Introduction

1.1 Use of food additives E 249 – E 252

The food additives potassium nitrite (E 249), sodium nitrite (E 250), sodium nitrate (E 251) and potassium nitrate (E 252) are used as preservatives in some traditional meat preparations and/or in several meat products. The application of these food additives origins from the use of saltpetre (nitrate salts), that has been used to preserve meat for centuries. In the twentieth century, it became clear that nitrite generated out of nitrate under acidic conditions is the actual preserving agent (EFSA 2003). The food chain evaluation consortium (FCEC, 2016) recently reviewed the technological functions of nitrites. Nitrites are effective in reducing *Clostridium botulinum*, a Gram-positive microorganism which toxins are responsible for inducing botulism, a foodborne disease with high mortality rate. Some *C. botulinum* species can form heat-resistant spores, which is the rationale of authorisation of nitrites in heat-treated meat products. Nitrites are also effective against *Listeria monocytogenes*, another Gram-positive microorganism, under some conditions but not all (not further specified), but are ineffective to control Gram-negative enteric pathogens, such as Salmonellae (EFSA 2003). Microbial safety of meat not fully depends on nitrites, but on a combination of (additional) factors, such a heat-treatment, pH, salt, water content, redox potential and initial numbers of bacterial spores. Nitrates serve as a reservoir for nitrite generation, particularly in products that require long-ripening processes, such as long-ripened dry-fermented sausages or dry-cured ham (EFSA 2003).

In addition to antimicrobial activity, nitrites retain the colour of traditional meat preparations and meat products during shelf life, have effects on flavour formation and exert antioxidant activity. The role of nitrites in flavour formation is not clearly understood (EFSA 2003).

Appendix A of this report shows the authorisation of nitrites and nitrates. Nitrites are only allowed in certain traditional meat preparations and in meat products (see Box 1 for a description of these food categories). Nitrates are authorised in meat products, some types of ripened cheeses and whey cheeses, cheese products, dairy-based cheese analogues, and pickled herring and sprats (Regulation 1333/2008; EU 2008).

In the Netherlands, some interpretation issues exist for some meat-based foods. Some foods are regarded as meat products (for which use of nitrites may be allowed) according to the industry, but are classified as meat preparations (for which use of nitrites use is strictly limited to a small number of meat preparations) by the Dutch Food and Consumer Product Safety Authority (NVWA). Use of nitrites in these meat-based foods for which an interpretation issue exist may increase intake to nitrite in case of use in particular foods.

Box 1 Description of food categories for which the use of nitrites is authorised

The different food categories for which use of nitrites is described in the Guidance document describing the food categories in Part E of Annex II to Regulation (EC) No 1333/2008 on Food Additives (EU 2016) Below these descriptions are summarised.

8.2 Meat preparations as defined by Regulation (EC) No 853/2004

Fresh meat, including meat that has been comminuted or minced, that has had foodstuffs, seasonings or additives added to it or that has undergone processes insufficient to modify the internal muscle fibre structure of the meat and thus to eliminate the characteristics of fresh meat. Meat preparations can fall within the definition of 'unprocessed products' or that of 'processed products'. For example, a meat preparation will fall within the definition of 'processed products' if the actions mentioned in the definition of 'processing' that are applied are insufficient to modify the internal muscle fibre completely through to the centre of the product muscle fibre structure of the meat and thus to eliminate the characteristics of fresh meat.

For nitrites, use is only allowed in some specific traditional meat preparations: *lomo de cerdo adobado, pincho moruno, careta de cerdo adobada, costilla de cerdo adobada, Kasseler, Bräte, Surfleisch, toorvorst, šašlõkk, ahjupraad, kiełbasa surowa biała, kiełbasa surowa metka,* and *tatar wołowy (danie tatarskie)*

8.3. Meat Products
Processed products resulting from the processing of meat or from the further processing of such processed products, so that the cut surface shows that the product no longer has the characteristics of fresh meat. Processing means any action that substantially alters the initial product, including heating, smoking, curing, maturing, drying, marinating, extraction, extrusion or a combination of those processes.

8.3.1. Non-heat-treated processed meat
This category covers several treatment methods (e.g. curing, salting, smoking, drying, fermenting, marinating, pickling, maturing) that preserve and extend the shelf life of meats. Examples: cured and dried ham, fermented and dried sausages.

8.3.2. Heat-treated processed meat
Includes cooked (including cured and cooked, smoked and cooked, and dried and cooked), heat-treated (including sterilised) and canned meat cuts. Examples include: sterilised sausage, cured, cooked ham, cured, cooked pork shoulder, canned chicken meat and meat pieces boiled in soy sauce (tsukudani).

8.3.4. Traditionally cured meat products with specific provisions concerning nitrites and nitrates.
This comprises certain traditional meat products cured by:

- Immersion curing (meat products cured by immersion in a curing solution containing nitrites and/or nitrates, salt and other components);
- Dry curing (dry curing process involves dry application of curing mixture containing nitrites and/or nitrates, salt and other components to the surface of the meat followed by a period of stabilisation/maturation;
- Other traditionally cured products (immersion and dry cured processes used in combination or where nitrite and/or nitrate is included in a compound product or where the curing solution is injected into the product prior to cooking).

1.2 Hazard of nitrates and nitrites

Toxicity of nitrates is low and is mainly due to nitrite formation in food or in the human body. Nitrates are easily absorbed from the gastrointestinal tract and approximately 25% of plasma nitrate is taken up by the salivary glands which concentrate it by a factor of 10 (EFSA 2008) and excrete the nitrate in the saliva (EFSA 2008). The resident microorganisms of the tongue reduce nitrate to nitrite. Nitrite is also easily absorbed (JECFA 2002). Once absorbed, nitrite, either ingested as such or generated endogenously upon nitrate ingestion, reacts with oxyhaemoglobin in the blood to form methaemoglobin and nitrate.

Another possible toxic mechanism of nitrite is the formation of nitrosamines, such as N-nitrosodimethylamine (NMDA), which is classified as a probable human carcinogen (IARC, 2016). Nitrosamines can be generated out of nitrate and nitrite added to food at three levels:

- in the food to which nitrate and nitrite are added itself (e.g. in bacon or salami);
- during heating of the foods to which these food additives are added (e.g. when frying or baking bacon or salami at home);
- in the acidic environment of the stomach after ingestion of the foods (FCEC 2016).

Both JECFA (20002) and EFSA (2008, 2010) did not include nitrosamine formation in the derivation of the acceptable daily intake (ADI) for nitrite and nitrate, as they indicated that there was no quantitative evidence for endogenously (i.e. in the stomach) formation of carcinogenic nitrosamines. They based the ADI on the direct toxic effects of nitrites and nitrates. The ADI for nitrite is 0.07 mg/kg bw/day (expressed as nitrite ion and equivalent to 0.1 mg/kg bw/day sodium nitrate salt, NaNO2) and is based on its adverse effects on heart and lungs. For the nitrate anion, an ADI of 3.7 mg/kg bw/day nitrate ion (equivalent to 5.0 mg/kg bw/day sodium nitrate salt) was set, based on its adverse effects on growth.

1.3 Intake of nitrates and nitrites

Given the low ADI of nitrite, nitrite intakes exceeding the health-based guidance value may easily occur. Intake of the Dutch population of nitrite added to food was assessed within the SCOOP project (EU 2001, EFSA 2010). Data reported in this project provided a range of intakes for the European population but did not specify the intake for the Dutch population. For several European countries, the mean intake of nitrite calculated with maximum permitted levels (MPLs) exceeded the ADI. More refined intake assessment, using average residual use levels, i.e. the levels in food at time of consumption, were available for Denmark and France. These studies indicated that the intake of adult high consumers (P95 or P99) was around or just above the ADI. For high consumer children, the intake was 2.5 times above the ADI, and the higher range of the mean intake of children is close to the ADI (EFSA 2010). Results from Dutch duplicate diets sampled in 1994 showed a median nitrite intake in adults of < 0.003 mg nitrite ion/kg bw/day (Vaessen & Schothorst, 1999), which is below the ADI. Because of the limitations of duplicate diet studies, such as small sample sizes (approximately 125 duplicate diets), adequate high usual intake percentiles cannot be derived from such studies.

Intake of nitrates is predominantly assessed in the context as a naturally occurring agent in vegetable foods and drinking water. The intake to nitrates as food additives should be regarded in view of this background intake. Intake of nitrates by the Dutch population has been estimated (Boon et al., 2009, Geraets et al., 2014). According to these studies, the health risk of the background nitrate intake of the Dutch population aged 2 to 69 years was negligible (see also section 4.3.2). These studies focused on nitrate naturally present in drinking water, fruit and vegetables, but did not included nitrates added to processed foods. In another study, a Dutch duplicate diet study sampled in 1994, a mean intake of 1.1 mg nitrate ion/kg bw/ day was shown in adults (Vaessen & Schothorst, 1999), which is below the ADI. As stated above for nitrites, adequate high usual intake percentiles cannot be derived from duplicate diet studies. In addition, these duplicate diet studies are quite outdated and may not reflect current nitrate intake.

1.4 Scope of the current study

The Dutch Ministry of Public Health, Welfare and Sports (VWS) requested RIVM to perform an intake assessment of nitrates and nitrites used as food additives. For a realistic intake assessment, preferably analytical data or use levels (see Box 2 for explanation of terminology used in this report) provided by the industry should be used. For the latter, a system was developed in 2011 by VWS, the Federation of Dutch Food and Grocery Industry (FNLI) and RIVM. The system has been used earlier to assess the intake of the food colours E 120 (carmine), E 133 (brilliant blue), E 150 (caramel colours), and E 171 (titanium dioxide) and smoke flavourings (Wapperom et al., 2011; Sprong et al., 2013; Sprong et al., 2014, Sprong et al., 2016). To assess the intake of nitrates and nitrites, FNLI also requested the food industry to supply use levels of these additives in processed foods, but no such levels were provided. Therefore, maximum permitted levels according to Annex II of Regulation 1333/2008 were used for the intake calculation. As these are predominantly ingoing amounts used in the production process, which, because of the reactivity of nitrites, does not necessarily reflect the actual residual amounts at moment of consumption, also maximum residual levels of nitrites according to the old Directive 95/2/EC were used to asses nitrite intake. The dietary intake was assessed for the Dutch population (children, adults and elderly people) according to 6 different scenarios. The estimated intakes are discussed regarding uncertainty and possible refinements, and are compared with results from other intake studies. The estimated intakes of nitrates and nitrite were compared with their ADIs to investigate whether further refinement is needed.

Box 2 Terminology nitrite and nitrate levels in food
Different terminologies for nitrite and nitrate used as food additives exist and are used in this report.

Use level: the amount of an additive added to food by the industry.

Maximum ingoing amount: type of maximum permitted level for nitrate and nitrite laid down in Annex II of Regulation 1333/2008. This is the maximum amount that may be added during manufacturing of the food. This type of maximum permitted levels is applicable on most types of foods.

Indicative ingoing amounts: indication of the amount added to food; used in Directive 95/2/EC.

Maximum residual amounts: maximum permitted level expressed as the residual amount at point of sale. This maximum permitted level is used for some foods in Annex II of Regulation 1333/2008 for which the ingoing amount cannot be established (e.g. some traditionally produced foods) and was used for maximum permitted levels in Directive 95/2/EC.

*Typical amounts: (*the range of) amounts most frequently used by the industry to obtained a certain effect.

2 Intake calculations

2.1 Maximum permitted levels

The maximum permitted levels of Annex II of Regulation 1333/2008 were used for the intake calculations (Appendix A). Many of these maximum permitted levels are expressed as ingoing amounts, i.e. the maximum amount that may be added during manufacturing. Because of processing, the actual residual amount, i.e. residue level at the end the production process, can differ from the ingoing amount (Honikel 2008, EFSA 2003). At present, we have no analytical values of the actual residual amounts of nitrites and nitrates in food. As a proxy, we used the maximum residual amounts of the old Directive 95/2/EC. Before 95/2/EC was amended by Directive 2006/52/EC, it contained two limits for both nitrates and nitrites for some food categories: one for the indicative ingoing amount and one maximum for the residual amount of nitrite. Table 1 summarizes both limits. The indicative ingoing amount is comparable to the current maximum ingoing amount, except for sterilised (canned) meat product, which now has a maximum ingoing amount of 100 mg/kg. Therefore, the maximum residual amounts of nitrites of the old directive were used for an additional scenario calculation (see section 2.5 scenario approach).

Table 1. Foods for which both indicative ingoing amounts and maximum residual amounts for nitrites were provided in the old Directive 95/2/EC, before it was amended by Directive 2006/52/EC and Regulation 1333/2006.

E number	Additive name	Food stuff	Indicative ingoing amount (mg/kg)	Residual amount (mg/kg)
E 249 E 250	Potassium nitrite Sodium nitrite	Non-heat-treated, cured, dried meat products	150[a]	50[b]
		Other cured meat products Canned meat products *Foie gras, foie gras entier, blocs de foie gras*	150[a]	100[b]

[a] Expressed as $NaNO_2$.
[b] Residual amount at point of sale to the final consumer, expressed as $NaNO_2$.

Because maximum limits are expressed as sodium salts, intake assessments are expressed as sodium salt and not as nitrate or nitrite ion.

2.2 Food consumption data

To estimate the intake of nitrates and nitrites, Dutch food consumption data were used of 1) young children aged 2 to 6 years, 2) the population aged 7 to 69 years and 3) the population aged 70 years or more. For young children, the food consumption data of the Dutch

National Food Consumption Survey (DNFCS)-Young children (Ocké et al., 2008) were used. This survey covers the dietary habits of young children aged 2 to 6 years and was conducted in 2005 and 2006. Regarding the population aged 7 to 69 years, food consumption data of the Dutch National Food Consumption Survey 2007-2010 (van Rossum et al., 2011) were used. This survey includes the dietary habits of people aged 7 to 69 years. The consumption data of the Dutch National Food Consumption Survey Older Adults (Ocké et al., 2013) were used for the population above 70 years. This survey includes the dietary habits of community dwelling older adults and was performed in 2010-2012. Results of the three consumption surveys were weighted for small deviances in socio-demographic characteristics in order to give results that are representative for the Dutch population.

2.3 Food coding

The above-mentioned food consumption surveys collected dietary data via the 24-hour recall method (by interview or record assisted interview), or in case of young children via the dietary record method, using the dietary recall software EPIC-Soft (IARC©) (Slimani et al., 1999). With this software, foods are identified using facets describing additional characteristics of a food, such as processing, fat content, preservation method, etc. The use of additives was not recorded in the Dutch food consumption surveys. For example, a low fat beef Frankfurter sausage is entered as food 'sausage Frankfurter' with facet 'beef' for its source and 'less fat' for its fat content, but not with facets relevant for preservation methods, such as 'smoked', 'canned' or 'preserved with nitrites'. Therefore, linking levels of E 249 – E 252 to foods consumed was performed using the Dutch EPIC-Soft codes neglecting facets. This means that E 250 levels in e.g. Frankfurter sausage were linked to the EPIC-Soft food 'sausage Frankfurter', irrespective of animal source, preservation method or fat content.

2.4 Food conversion

Several foods recorded in the food consumption databases, such as cheese, ham or salami, can be directly linked to a relevant maximum permitted level. Some compound foods consumed in the food consumption surveys only partly consist of an ingredient preserved with nitrates or nitrites. When these ingredients can be clearly separated (e.g. pizza with vegetables, ham and cheese), the foods were already coded according to their individual components in the food consumption survey. For example, consumption of 250 g ready-to-eat composite dishes like 'mashed potatoes with kale, gravy and cooked smoked sausage' are coded in the Dutch National Food Consumption Surveys according to their individual components, such as 51 g 'cooked kale', 113 g 'mashed potatoes', 31 g 'milk', 5 g cooking fat and 50 g cooked smoked sausage'. Those identified foods can be directly linked to a relevant maximum level. For some compounds foods, ingredients cannot be clearly separated. Examples are salty cheese crackers or spring roll. For these foods, a conversion table was made, using percentages of ingredients obtained from labels or from a standard Dutch cooking book (Henderson et al., 2010). For example, ham-cheese croissant was conversed to 6.7% cooked ham and 5.5% semi-hard cheese. These ingredients were subsequently linked to the relevant maximum permitted levels.

2.5 Scenario approach

Ideally, the calculations would have made use of use levels provided by the food industry. As mentioned in Section 1.5, such use levels were not provided. Therefore, the tiered approaches as used for E 150 and E 171 (Sprong et al., 2014; Sprong et al., 2016), starting with aggregated food categories using maximum reported use levels, followed by more refined tiers including less aggregated food categories, true zeroes and/or mean use levels, could not be used for nitrates and nitrites. Therefore, we used a scenario approach with maximum permitted levels.

Appendix A lists the food categories in which nitrites and nitrates are authorised; their corresponding maximum permitted limits and their restrictions of use. For the intake assessment, these authorised uses were taken into account using 3 scenarios:

- Scenario 1: Authorisation scenario. In this scenario, it was assumed that all foods which may contain added nitrites or nitrates according to Annex II of R 1333/2008 contain the food additive at maximum permitted levels;
- Scenario 2: Authorisation scenario excluding true zeroes. This scenario is the same as scenario 1, except for foods that do not contain the additive according to label information it was assumed they do not contain the food additive;
- Scenario 3: Scenario including foods for which an interpretation issue exists: This scenario is the same as scenario 2, but includes foods regarded as meat products according to the food industry, but which are classified as meat preparations by the NVWA. In this scenario, it is assumed that all these foods contain the food additive at the maximum permitted level of food category 8.3.1 (150 mg/kg).

As indicated in section 2.1, the residual amount of nitrate and nitrite do not equal the ingoing amounts due to loss of these additives during food processing. As the three-abovementioned scenarios resulted in exceeding the ADI for nitrites but not for nitrates (Section 3.2), intake calculations were refined using maximum residual levels of the old Directive 95/2/EC as proxy for the maximum amount of nitrite in a product at the moment of consumption (see Table 1). This was done using the following three additional scenarios:

- Scenario 4: Authorisation scenario using residual amounts of directive E95/2/EC. In this scenario, the maximum residual amount value of 50 mg/kg product for non-heat-treated, cured, dried meat products was used for foods in category 8.3.1 (non-heated meat products) that match the description. In addition, the maximum residual amount of 100 mg/kg for other cured meat products, canned meat products and *foie gras, foie gras entier, blocs de foie gras* was used for foods in category 8.3.1 and 8.3,2 that match this description;
- Scenario 5: Authorisation scenario using residual amounts and excluding true zeroes: This scenario is the same as scenario 4, except for foods which do not contain the additives according to

label information it was assumed that they do not contain the food additive;
- Scenario 6: Scenario using residual amounts and including foods for which an interpretation issue exists: This scenario is the same as scenario 5, but includes foods regarded as meat products according to the industry but classified as meat preparations by the NVWA.

2.6 Linking food consumed to relevant food categories of Regulation 1333/2008.

Detailed description and results of food classification are described in Appendix B. Below the linking of foods according to the scenarios listed in section 2.5 is described shortly.

2.6.1 Scenario 1

Foods consumed in the food consumption surveys and coded according to EPIC-SOFT were classified into the food categories in which nitrites and nitrates are authorized as laid down in Annex II of R 1333/2008 (see Appendix A for overview of these food categories). To this end, the 'Guidance document describing the food categories in Part E of Annex II to Regulation 1333/2008 on Food Additives' (EU 2016) was used. The NVWA was also consulted for linking food as consumed to the food categories in which nitrates and nitrites are allowed. Annex II of Regulation 1333/2008 contains different entries for traditionally and non-traditionally produced foods (see Appendix A of the current report). For many meat products on the market, it was not known whether these are traditionally produced or not. In addition, the available food consumption data did not distinguish between traditionally and non-traditionally produced meat products. Therefore, it was assumed that the products are non-traditionally produced, i.e. belong to food category 8.3.1 (non-heated meat products) and 8.3.2 (heated meat products).

Because of time passed since the data collection of food consumption surveys, some foods coded in the food consumption database are no longer available on the market, e.g. specific cheese (Trenta analogue cheese) or salty crisps (Pringles rice infusions). These were coded as similar foods still available.

To obtain information on compound foods containing ingredients preserved with nitrate and nitrites, the INNOVA database (www.INNOVAdatabase.com), a database on new food product releases, was searched. Also, for compound foods consumed in the food consumptions surveys and expected to contain ingredients preserved with nitrates or nitrites, labels were checked at web shops of large Dutch supermarkets. These compound foods, described by the percentage(s) of the relevant ingredient(s), were also included. The data set resulting from this exercise was used in the intake calculations.

2.6.2 Scenario 2

Since not all foods that may contain nitrates or nitrites contain these preservatives, the INNOVA database was also used to determine presence of these additives. In addition, three main brands (including private labels) for each food were checked at web shops of large Dutch supermarkets. If no use of E 249 – E 252 was declared, these foods were considered not to contain the preservatives (true zeroes). For several of these foods, there was also no technological need to use preservatives (for example heated meat-based snacks stored frozen). The data set resulting from this exercise was used for the calculation of scenario 2.

2.6.3 *Scenario 3*

The INNOVA search also retrieved meat-based foods subjected to interpretation issues. These foods, to be classified as meat preparation according to the NVWA, were classified as the food category matching best with the food. For example, 'gemarineerde beenham', 'gemarineerde varkenshaas', or 'filet American' were for the use of this project classified as 8.3.1 non-heat-treated meat products. These foods were added to the data set for scenario 2 described above and resulted in the data set used for the calculation of scenario 3.

2.6.4 *Scenario 4 to 6*

Scenarios 4 to 6 were built on the data sets obtained from scenario 1 to 3, except that food categories 8.3.1 and 8.3.2 were rearranged according to the old Directive 95/2/EC, and foods were linked to the relevant maximum residual amount. Websites of butcheries and meat industry were checked for descriptions of curing and drying of non-heat-treated meat to optimize the linkage with the maximum residual levels (Table 1).

2.7 Monte Carlo Risk Assessment

Although nitrite is associated with acute toxicity (JECFA 1995, JECFA 2002, EFSA 2003, 2010), no health-based guidance value for acute effects is available for this type of toxicity. Moreover, the acute effect, methaemoglobin formation is only relevant for infants up to the age of 3 months (Speijers & van de Brandt, 2002). As these infants do not consume foods to which nitrates/nitrites are added, acute intake was not assessed in the present study. As described in the introduction section, nitrates and nitrites exert chronic effects. Therefore, long-term intake (usual intake) to nitrates and nitrites was assessed using the Observed Individual Means (OIM) method. The Monte Carlo Risk Assessment programme (MCRA), Release 8.1 (de Boer and van der Voet, 2015) was used for the intake assessment.

By using the bootstrap approach, the uncertainty around the intake estimates due to the limited size of the food consumption data set was determined. Since for each scenario, only one fixed concentration level (the maximum permitted level) per food was used, the uncertainty due to the limited size of the concentration data is not relevant. The uncertainty is reported as the 95% confidence interval around the median (P50) and the 95^{th} percentile (P95) of intake.

3 Results

In this chapter, the results of the intake estimates of nitrite and nitrate and the contributors to their intake are presented.

3.1 Nitrite

Nitrite intake in the Netherlands is predominantly E 250 (sodium nitrite), as the search results of INNOVA and main brand information did not declare use of E 249 (potassium nitrite) on the labels. The intake estimates and main contributors are shown in Table 2 and Table 3, respectively. The results are described below per scenario.

3.1.1 Scenario 1: Authorisation scenario

The best estimate of the median intake exceeded the ADI (expressed as 100 µg sodium nitrite/kg bw/day) in children aged 2-6 years, but was below this health-based guidance value for the other two age groups. The best estimate for the 95th intake percentile exceeded the ADI (Table 2) in all age groups.

Foods belonging to food category 8.3.2 (heat–treated meat products, sterilised, non-sterilised) contributed most to the total intake, followed by food category 8.3.1 (non-heat-treated meat products), in all three age groups (Table 3). Because these food categories comprises a broad range of different meat-based foods, more detailed information on main foods contributing to total nitrite intake is shown in Appendix C. Main contributors (> 5%) to total nitrite intake observed in all populations were: liver sausage and pâté; smoked sausage; salami and other dried sausages; luncheon meat, boiled/grilled sausage, roasted cold cuts; and cooked ham. Frankfurter sausages were also a major contributor to nitrite intake in young children, and salted bacon contributed to intake in the population 7 -79 years. The Dutch meat snack 'Frikandel' was the main contributor to total nitrite intake in young children and the population aged 7-69 years. However, according to label information, 'Frikandel', together with many other heat-treated and subsequently frozen meat snacks, do not contain nitrites, and were therefore considered as a true zero in the next scenario.

3.1.2 Scenario 2: Authorisation scenario excluding true zeroes

For this scenario, foods that do not contain nitrites according to their food label were regarded as true zeroes. These foods are mostly frozen heat-treated meat snacks as mentioned above, but also comprise some cold cuts and sterilised or frozen compound foods containing meat products.

Excluding true zeroes resulted in a 8 to 23.6% decrease of the best estimate for the median intake (Table 2) compared to scenario 1. For children aged 2-6 years, the best estimate of the median intake of scenario 2 was near the ADI, with the upper limit of the uncertainty interval exceeding the ADI. The median nitrite intake of the Dutch population aged 7 -79 years was below the ADI. Regarding the best estimates of the 95th intake percentile, exclusion of true zeroes decreased the intake estimate with 2 to 23.2% compared to scenario 1. Estimated high intakes still exceeded the ADI for all age groups in this scenario.

Table 2. Median (P50) and high (P95) nitrite intake percentiles (µg sodium nitrite/kg bw/d) for different Dutch subpopulations according to six different scenarios. Intake estimates between brackets reflect the uncertainty around the best estimate for the particular intake percentile due to the limited size of the food consumption data.

Scenario	**Children aged 2-6 years**	**Population 7-69 years**	**Population > 69 years**
P50			
Scenario 1: Authorisation R 1333/2008	**123**[1] **(115-131)**	50 (48-52)	38 (34-42)
Scenario 2: Authorisation R 1333/2008 with true zeroes	94 (86-**106**)	40 (38-42)	35 (30-37)
Scenario 3: Scenario 2 plus foods with an interpretation issue	**116** (**102-126**)	51 (48-54)	41 (37-44)
Scenario 4: Authorisation scenario with maximum residual levels of Directive 95/2/EC	77 (71-84)	30 (29-32)	18 (14-23)
Scenario 5: Scenario 4 excluding true zeroes	59 (52-65)	24 (23-26)	17 (12-20)
Scenario 6: Scenario 5 plus foods with an interpretation issue	72 (65-79)	33 (31-34)	21 (17-29)
P95			
Scenario 1: Authorisation R 1333/2008	**519** (**490-539**)	**247** (**236-259**)	**151** (**139-158**)
Scenario 2: Authorisation R 1333/2008 with true zeroes	**399** (**380-442**)	**200** (**190-201**)	**148** (**132-155**)
Scenario 3: Tier 2 plus foods with an interpretation issue	**491** (**450-452**)	**236** (**230-244**)	**172** (**158-183**)
Scenario 4: Authorisation scenario with maximum residual levels of Directive 95/2/EC	**349** (**330-371**)	**160** (**153-167**)	94 (79-**106**)
Scenario 5: Scenario 4 excluding true zeroes	**279** (**258-312**)	**129** (**120-135**)	89 (71-**102)**
Scenario 6: Scenario 5 plus foods with an interpretation issue	**373** (**344-399**)	**170** (**163-185**)	**119** (**105-142**)

[1] Figures in bold means exceeding of the ADI expressed as sodium nitrite (100 µg/kg bw/d).

Table 3. Main contributors to total nitrite intake, classified according to the food categories of Regulation 1333/2008 for the different Dutch subpopulations estimated for scenarios 1 and 2.

	Young Children 2-6 years	**Population aged 7-69 years**	**Elderly > 69 years**
Scenario 1: Authorisation scenario			
08.2 Meat preparations as defined by Regulation (EC) No 853/2004	-	-	-
08.3.1 Non-heat-treated meat products	19.0%	26.7%	34.6%
08.3.2 Heat–treated meat products, sterilised	9.7%	4.4%	2.5%
08.3.2 Heat–treated meat products, non-sterilised	71.3%	68.9%	62.9%
Scenario 2: Authorisation scenario, excluding true zeroes			
08.2 Meat preparations as defined by Regulation (EC) No 853/2004 (M42)	-	-	-
08.3.1 Non-heat-treated meat products	24.2%	32.7%	35.7%
08.3.2 Heat–treated meat products, sterilised	11.8%	4.7%	2.3%
08.3.2 Heat–treated meat products, non-sterilised	64.0%	62.6%	62.0%

Main contributors to total nitrate intake in scenario 2 were the same as in scenario 1, being 08.3.2 (heat–treated meat products, sterilised, non-sterilised), followed by food category 08.3.1 (non-heat-treated meat products). On a more detailed level (Appendix C), main contributors also remained the same, except for 'Frikandel', which was assumed to be a true zero.

3.1.3 *Scenario 3: Inclusion of foods for which interpretation issues exist*

As expected, compared with scenario 2, inclusion of foods for which interpretation differences exist, increased both median and high intake (Table 2). The best estimate for the median intake increased with 17 to 27.5%. The median intake of young children exceeded the ADI, whereas that of the other age groups remained below this health-based guidance value. Inclusion of foods with an interpretation issue increased the best estimate of the 95th intake percentile with 16 to 23% compared with scenario 2. The P95 intake of all age groups exceeded the ADI.

Table 4 shows the contribution to the total nitrite intake for foods for which an interpretation issue exists. Frying sausage 'braadworst' was an important contributor, contributing 8.1 to 13.2% to the total nitrite intake. The contribution of 'filet Americain' and raw beef sausage ('ossenworst') to total nitrite intake varied from 1.6 to 6.9%. For marinated ham of the bone ('beenham'), the contribution to total nitrite intake varied between 0.2 and 2.5% and for marinated pork silverslide ('varkenshaas') between 0.8 and 3.5%. Regarding roast beef ('rosbief'), the contribution to total nitrite intake ranged between 0.1 and 1.8%

Table 4. Contribution of foods for which an interpretation issue exist to total nitrite intake of the Dutch population.

Foods with interpretation issue	**Young Children 2-6 years**	**Population aged 7-69 years**	**Elderly > 69 years**
Frying sausage ('Braadworst')	13.2%	8.1%	9.8%
Filet American and raw beef sausage ('ossenworst')	1.6%	5.9%	2.5%
Marinated ham of the bone, hot ('beenham')	0.2%	1.2%	2.5%
Marinated Pork silverslide ('varkenshaas')	0.8%	3.5%	3.2%
Roast beef ('rosbief')	0.1%	1.3%	1.8%

3.1.4 Scenarios using residual amounts of directive E95/2/EC.

As explained in section 2.1, actual residual amounts are most likely to be lower than ingoing amounts and calculations using the maximum residual levels of the old Directive 95/2/EC were used as proxy as no information on actual residual amounts are present.

As shown in Table 2, median intake in scenarios using residual amounts decreased to levels below the ADI. However, estimated high intake still exceeded the ADI for young children and the population aged 7 to 69 years. For the elderly, the best estimate of high intake for scenario 4 (authorization scenario) and 5 (authorization scenario excluding true zeroes) was below the ADI, with the upper level of the uncertainty interval exceeding the ADI. The best estimate of high intake for scenario 6 (inclusion of foods with an interpretation issue) exceeded the ADI in the elderly population.

Main contributors to intake in scenarios 4 to 6 remained the same compared with the corresponding scenarios 1 -3, although the actual contribution and the order of the main contributors could vary (not shown).

3.1.5 Portion sizes 95th percentile of nitrite intake

MCRA is able to calculate the portion sizes of consumption around a specified percentile, the so-called drill down. To investigate whether the high intake is due to excessive portion sizes, drill downs around the 95th intake percentile were investigated per age group. Appendix D shows the drill down for young children for scenario 5 (maximum residual levels of the old Directive 95/2/EC, excluding true zeroes), which is the least conservative scenario. In the Netherlands, meat-based foods are predominantly eaten as sandwich filling at breakfast or lunch and as part of dinner. For sandwich filling, the typical serving size is 15 to 20 g. The consumption sizes in Appendix D indicate that children around the 95th

intake percentiles consume up to 3 or 4 sandwiches filled with meat-based food per day, which can be considered as high consumption of meat-based products but not as excessive. For the population aged 7-69 years and 70-79 years, also consumptions can be considered as high consumptions, but not as excessive (not shown).

3.2 Nitrate

According to label information, E 251 (sodium nitrate) was mainly used in cheese and foods with cheese as ingredient. E 252 (potassium nitrate) was mainly used in meat products and foods with meat as ingredient. No foods with an interpretation issue were found. Therefore, only exposure via scenario 1 and 2 was calculated. Table 5 summarizes the median and high (P95) intake of nitrates used as food additives for the two intake scenarios. The best estimate of median intake was not affected by the intake scenario excluding true zeroes. Regarding the best estimate of the 95th intake percentile, exclusion of true zeroes decreased the intake estimate, particularly for the elderly. In none of the calculation scenarios, nitrate intake exceeded the ADI.

The lower intake can predominantly be explained by pickled herring and sprat, which were important contributors to the total intake of elderly and the population aged 7 to 69 years in the authorization scenario, but were considered as true zero in the second scenario (table 6).

Table 5. Median (P50) and high (P95) nitrate intake percentiles (mg sodium nitrate/kg bw/d) for different Dutch subpopulations according to two different tiers. Values between brackets reflect the uncertainty around the estimated intake percentile due to the limited size of the food consumption data.

Scenario	**Children aged 2-6 years**	**Population 7-69 years**	**Population > 70 years**
P50			
Scenario1: Authorisation scenario	0.07 (0.06-0.08)	0.07 (0.06-0.07)	0.06 (0.06-0.07)
Scenario 2: Authorisation with true zeroes	0.06 (0.05-0.07)	0.06 (0.06-0.06)	0.06 (0.05-0.06)
P95			
Scenario1: Authorisation scenario	0.35 (0.32-0.39)	0.27 (0.26-0.29)	0.27 (0.22-0.33)
Scenario 2: Authorisation with true zeroes	0.32 (0.29-0.35)	0.22 (0.21-0.23)	0.16 (0.15-0.18)

Table 6. Main contributors to total nitrate intake classified according to the food categories of regulation 1333/2008 for the different Dutch subpopulations estimated using two different scenarios.

	Young Children 2-6 years	**Population aged 7-69 years**	**Elderly > 69 years**
Scenario 1: Authorisation scenario			
01.7.2 Ripened cheese	66.4%	66.6%	58.4%
01.7.4 Whey cheese	0.2%	0.1%	-
08.3.1 Non-heat-treated meat products	30.7%	22.3%	19.4%
09.2 Processed fish and fishery products including molluscs and crustaceans	2.7%	11%	22.1%
Scenario 2: Authorisation scenario, excluding true zeroes			
01.7.2 Ripened cheese	66.7%	73.6%	74.4%%
01.7.4 Whey cheese	-	-	-
08.3.1 Non-heat-treated meat products	33.3%	26.4%	25.6%
09.2 Processed fish and fishery products including molluscs and crustaceans	-	0.1%	-

Other main contributors to total nitrate intake were ripened cheeses (food category 7.2) and non-heat-treated meat products (food category 8.3.1). Ripened cheeses predominantly existed of 'Gouda' like cheeses and other typical Dutch hard and semi-hard cheeses. Most of these cheeses contained nitrates according to label information. Regarding the non-heat-treated meat products, these consisted of bacon (strips or cubes) and dried cured sausages, such as salami, and smoked sausage.

4 Discussion

4.1 Intake assessment

As for all intake assessments, the current intake assessment is subjected to uncertainties due to data gaps and assumptions to handle these data gaps. The following sections discuss the input data and settings, and their possible effects on the intake estimates.

4.1.1 Food consumption data

One of the limitations in the used food consumption data obtained from food consumption surveys was the incomplete information from participants on the type of products consumed, resulting in non-specific foods like ham for which the specific type was not known; this may have resulted in a small under- or overestimation of the exposure.

Fish consumption is very low in the Netherlands. Therefore, amounts and type of fish consumed may not represent the real fish consumption. However, as herring appeared to be a true zero for nitrates, and pickled sprat is not a frequently consumed fish product, it is estimated that the uncertainty regarding fish consumption will have hardly affected the exposure estimate.

Although facets for preservation method are available in EPIC soft, these facets were not included in the currently available Dutch National Food Consumption Surveys. The same applies for brand names. Including these facets in the new food consumption surveys would allow refinement using true zeroes for preservation methods other than nitrates and nitrites, and/or brands not using these additives.

4.1.2 Concentration data

4.1.2.1 Maximum levels used versus medium typical amounts

In the calculations described in the current report, maximum permitted levels according to Annex II of R 1333/2008 were used. Intake estimates would have been more accurate if data from the industry and butchers had been used. To assess the possible overestimation of intake by using maximum permitted limits the maximum permitted limits of nitrite were compared with use levels published in a recent European survey (FCEC, 2016). Table 7 shows the main findings of this study. For non-heat-treated processed meat and sterilized processed meat, the reported median typical ingoing amount of nitrite was 80 to 100% of the maximum ingoing amount laid down in R 1333/2008. Regarding non-sterilised heat-treated meat products, the percentages were 63 to 80%. Thus, using maximum ingoing amounts instead of median typical ingoing amounts may have resulted in overestimation of nitrite intake by a factor 1.6 (assuming all intake derived from non-sterilised heat-treated minced poultry meat) or less for scenarios 1 to 3. This would still have resulted in intakes exceeding the ADI for the populations aged 2 to 6 years and 7 to 69 years. This indicates that use levels (ingoing amounts) provided by the industry would very likely not have improved the exposure to a large extend.

Regarding nitrates, no information on typical amounts is available and therefore the magnitude of possible overestimation using maximum ingoing amounts instead of typical amounts could not be assessed.

Table 7. Reported nitrite use levels (mg/kg) in Europe, expressed as ingoing amounts of sodium nitrite of non-traditional meat-based foods in FCEC report.

Food Category	**N**	**Minimum**	**Maximum**	**Median typical amount**	**Maximum permitted level according to R1333/2008**	**Median typical amount as percentage of maximum permitted level**
8.3.1 Non-heat-treated processed meat						
Derived from whole pieces red meat	48	10	200	150	150	100%
Derived from whole pieces poultry meat	10	10	150	145	150	97%
Derived from minced red meat	37	10	200	120	150	80%
Derived from minced poultry meat	10	10	200	130	150	87%
8.3.2 Sterilised heat-treated processed meat						
Derived from whole pieces red meat	19	20	180	100	100	100%
Derived from whole pieces poultry meat	13	10	150	80	100	80%
Derived from minced red meat	21	20	180	100	100	100%
Derived from minced poultry meat	15	10	150	100	100	100%
8.3.2 Non-sterilised heat-treated processed meat						
Derived from whole pieces red meat	54	10	200	120	150	80%
Derived from whole pieces poultry meat	31	10	200	100	150	67%
Derived from minced red meat	43	10	200	120	150	80%
Derived from minced poultry meat	29	10	200	95	150	63%

4.1.2.2 Traditional versus non-traditional foods

For some traditionally produced foods, maximum levels cannot be set at ingoing amounts and are therefore provided as residual levels (Appendix A). Due to lack of information on the production method of consumed meat products, all meat products were assumed to be non-traditionally manufactured products. This may have resulted in an overestimation of nitrite intake in case of consumption of "*Röhschinken and similar products*" and "*dry cured ham*", because the maximum permitted levels (in those cases: residual levels) are lower for these traditionally meat products compared to the maximum permitted levels (ingoing amounts) of their non-traditionally counterparts (Appendix A). For "*dry cured bacon*", the use of the maximum permitted levels (ingoing amounts) of the non-traditionally counterparts may have resulted in a small underestimation of the nitrite intake as the maximum permitted levels assigned to 'bacon' are lower than the maximum residual levels for traditionally produced dry cured bacon (Appendix A).

Regarding nitrates, the residual levels for the traditional products "*Röhschinken and similar products*", "*dry cured ham*" and "*dry cured bacon*" are higher than the maximum ingoing amount for non-traditionally produced products. This may have resulted in an underestimation of the exposure.

4.1.2.3 Ingoing versus residual amounts

As mentioned above, most of the maximum permitted levels are provided as maximum ingoing amounts and not as residual amounts. Due to the reactivity of nitrate and nitrite, the residual amount is usually lower than the ingoing amount. To address this, the estimation of the nitrite intake was also performed using the maximum residual amount of the old legislation. According to this legislation, 33% of the added amount of nitrite in non-heat-treated dried meat products and 67% of the added amount in other cured meat products and canned meat products is maximally present as residual amount. Use of these residual amounts lowered the median intake with approximately 40 to 50% depending on the scenario and population group (Table 2). Regarding the 95th intake percentile, estimates reduced with approximately 25 to 50% (Table 2). These estimates may still overestimate the real intake. For emulsion type of sausages, the residual amount of nitrite ranged between 27 and 40% of added amount of nitrite immediately after heating. An additional storage time at 2 °C for 20 days resulted in residual nitrite levels between 7 and 10% of the added nitrite amounts (Honikel, 2008). Honikel (2008) concluded that 5-20% of added nitrite is present in meat products as residual nitrite, between 1-40% is present as nitrate, 5-15% is bound to myoglobin, 1-15% bound to sulfhydryl groups, 1-15% is bound to lipids, 20-30% to proteins, and 1-5% is present as gas. Overall nitrites and its metabolites summed up to 70 to 90%. When applying the range of 5-20% of added nitrite being present as residual amount, the 95th percentile of intake would range from 7 to 80 µg/kg bw/day (expressed as sodium nitrite) for scenario 2 (maximum levels excluding true zeroes). For scenario 3 (inclusion of foods for which an interpretation issue exists), applying the range of 5-20% of added nitrite being present as residual amount, the 95th percentile of intake would range between 9 and 99 µg/ kg bw/day (expressed as sodium nitrite). Thus, the real intake of sodium nitrite is likely to be lower than the estimates of the present study. This is supported by the results of the studies using analytical values, as explained in section 4.2. This indicates that the exposure assessment of nitrites can be refined using analytical data.

We did not perform calculations with the residual amounts of nitrates of the old Directive 95/2/EC, because nitrate intake did not exceed the ADI. For meat products, the maximum residual levels of nitrate were higher than the maximum ingoing amount of R 1333/2008, indicating that these maximum residual levels were not valid as a proxy in our study. For cheese, the maximum residual level of Directive 95/2/EC was a factor 3 lower compared with the maximum ingoing amount of R 1333/2008. Because cheese contributed most to nitrate intake (Table 6), overestimation of exposure due to maximum ingoing amounts is most likely.

4.1.3 *Linking foods consumed to concentration data*

4.1.3.1 True zeroes

The use of label information for assigning 'true' zeroes to food products, as done in the present study, is similar to the strategy as advised by the Food Chain Evaluation Consortium (2014). This Consortium emphasizes the inclusion of true zeroes as a major tool for refining exposure assessments to additives. The use of true zeroes was also recognized by the RIVM in its reports on food additive intakes as an important refinement tool (Wapperom et al., 2011, Sprong et al., 2014a, 2016). In the present study, this was done by checking online label information of three brands, but this was time consuming and provided an incomplete data set. The limited survey on brands may have resulted in a small under- or overestimation of intake in scenarios 2, 3, 5 and 6. Use of specific databases with label information may be a more cost-efficient approach. As stated before by Sprong et al. (2014a, 2015), product databases like Mintel or INNOVA are less useful to assign true zeroes, since these databases cover only new product launches rather than food actually on the market, and are not updated for foods removed from the market or may miss reformulation of foods. Databases such as the GS1 data source (https://www.gs1.nl/gs1-data-source), which is the underlying database for label information of food products available via web shops, cover foods that are currently on the market and may therefore serve as a more reliable food label source. RIVM, together with the Netherlands Nutrition Centre ('Voedingscentrum') have started a pilot in the end 2016 (to be finalised in 2017) on the use of the GS1 database. The usefulness of the GS1 database for additive use will be part of the pilot study.

4.1.3.2 Foods with an interpretation issue

Foods for which an interpretation issue exists according to the NVWA were found by coincidence in the INNOVA database and at web shops, and were provided by the NVWA. Labels from some similar foods were checked in webshops, but it was not possible to check all meat-based foods for foods with an interpretation issue. Intake estimates of scenario 3 and 6 could therefore be underestimated to a minor extent in case of missing foods with an interpretation issue. However, as all 'beenham' and 'varkenshaas' were assumed to contain nitrites in scenario 3 and 6, the nitrite intake may have been slightly overestimated because not all consumed 'beenham' and 'varkenshaas' will be marinated ones. The facet 'marinated' for preservation method was available in the food consumption data but not used because marinated 'beenham' and 'varkenshaas' are relatively new products and hardly available during the data collection of the food consumption surveys.

4.1.4 *Chronic intake model*

Chronic intake was assessed with the Observed Individual Means model. Ideally statistical models should be used that correct the variation in long-term intake between individuals for the within individual (between days) variation (Hoffmann et al., 2002; Nusser et al., 1996; Slob, 1993). An important prerequisite to use these models is that the logarithmically transformed daily intake distribution is normally distributed (de Boer et al., 2009). Since the intake data were not normally distributed for nitrates and nitrites (not shown), the observed individual means (OIM) method was used. The OIM method calculates the intake per day per subject and averages the intake of the 2 recall or recording days per subject. This implies that the high intake percentiles are overestimated (Figure 1).

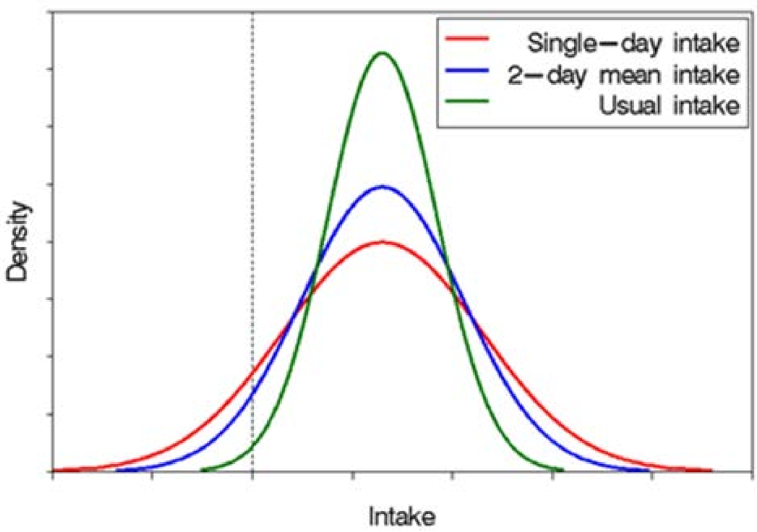

Figure 1. The Observed Individual Means (OIM) method used in this report is based on a 2-day mean intake. Therefore, this method deviates from the usual intake, since a mean intake based on two days is more sensitive to extreme consumption levels of foods than those based on a longer period. The OIM method may underestimate the mean intake and may overestimate the upper percentiles. Figure is obtained from the National Cancer Institute.

MCRA has an additional model available to estimate the long-term exposure called Model-Then-Add (van der Voet et al., 2014). In this approach, statistical modelling is applied to subsets of the diet (single foods or food groups) rather than the whole diet. The resulting usual exposure distributions are added to obtain an overall usual exposure distribution. The advantage of this approach is that separate foods or food groups may show a better fit to the normal distribution model as assumed in all common models for usual exposure (e.g. the LNN model) and therefore may result in a better estimate of the high exposure percentile. An exposure study into the intake of smoke flavours using Model-Then-Add showed that this resulted in a lower exposure estimate than reported by Sprong et al. (2013; van der Voet et al., 2014). Because this method is laboriously compared with the currently OIM methods, the Model-Then-Add method was not used in the present study. In addition, given the uncertainties in the real residual nitrate and nitrite concentrations in foods to which these additives are added, we advise to obtain analytical data before using more advanced statistical models to assess the intake of nitrites and nitrates, because it is expected that real residual levels would already result in a substantial refinement of the intake assessment.

4.1.5 Overall effect on intake

Overall, we assume that the intake is largely overestimated because of using maximum permitted levels instead of real residual concentrations and other conservative assumptions. Use levels provided by the industry would very likely not have improved the exposure assessment to a large extend as these levels also refer to ingoing amounts. Only with the use of analytical data, the intake assessment of nitrate and nitrite can be refined.

4.2 Results of the present study compared to other intake estimations

4.2.1 Nitrite

Two types of intake assessments of nitrite are available for other European countries: those performed with maximum permitted levels and those performed with analytical data. Table 8 shows the results of previously performed intake assessments of nitrites as summarized in the EFSA opinion on nitrites (ESFA 2010). Table 9 shows more recent studies performed with maximum permitted levels or analytical data. The intake estimates obtained in our study (Table 2) generally fits within the range of exposure estimates based on maximum permitted levels, although some deviations may occur due to differences in consumption patterns and assumptions used in the exposure calculation. Recent exposure assessments based on analytical data resulted in intake estimates below the ADI (Table 9). This was best illustrated by the study of Mancini et al. (2015), which assessed the nitrite intake using maximum permitted levels (comparable with scenario 1), maximum permitted levels excluding true zeroes (comparable with scenario 2) and analytical data for children aged 1 to 3 years. In the study of Mancini et al. (2015), median intake estimates with analytical data were a factor 14 lower compared with those obtained with maximum permitted levels. For high intake estimates, the use of analytical data resulted in a factor 54 lower intake estimates compared with maximum permitted levels.

Table 8. Summary of nitrite intake as sodium nitrite (µg/kg bw/day) in children and the adult population published by EFSA in 2010[1]

Tier	Children (3-14 years old)	Adults (> 18 years old)
Maximum permitted use levels for nitrites (from the report of EC 2001 for DK, ES, FR, IT, NL,UK, NO) • Mean exposure • Exposure 95th or 97.5th percentile	 71- **514**[4] -	 57-**329** -
Average reported nitrite levels in France and Denmark[2] • Mean exposure • Exposure 95th or 99th percentile[3]	 13-86 **157-243**	 7-43 86-**129**

[1] EFSA opinion on nitrites in meat products (EFSA, 2010)
[2] Based on average residual level of nitrite
[3] Range of exposures based on 95th percentile for French data and 99th percentile for Danish data
[4] Values in bold indicate exceeding of the ADI of 100 µg/kg bw/day (expressed as sodium nitrite).

Table 9. Summary of nitrite intake as sodium nitrite (µg/kg bw/day) in recent European studies

Country	Type of data	Population	Mean	High intake
France (Mancini et al., 2015)	Maximum ingoing amounts	Children aged 1 to 3 years	193	728[1]
France (Mancini et al., 2015)	Maximum ingoing amounts, excluding zeroes	Children aged 1 to 3 years	157	441[1]
France (Mancini et al., 2015)	Analytical data (cured) meat	Children aged 1 to 3 years	14	14[1]
France (Bemrah et al., 2012)	Second total diet study	Children Adults	1-7[2] 1-4[2]	13-36[2,3] 9-10[2,3]
France (Menard et al., 2009)	Monitoring data including meat	Children Adults	4-11[2] 3-6[2]	6-13[2,4] 3-7[2,4]
Sweden (Larsson et al., 2011)	Analytical data (cured) meat	Children	10-18[2]	27-49[2,3]
Belgium (Temme et al., 2011)	Analytical data (cured) meat	15 years and older	4.3	-

[1] P90
[2] Range of lower to upper bound estimate
[3] P95
[4] P97.5

The results from studies with analytical data indicate that the real intake of nitrites is most likely lower than those calculated in our study and support our conclusion to use analytical data for refinement (section 4.1.2). As a start, analysis of pooled meat products sampled by the Dutch mycotoxin-dedicated total diet study could be explored (Sprong et al., 2016). In this mycotoxin-dedicated total diet study, the following products that may contain nitrites were sampled: 'cervelaatworst', 'salami', 'boterhamworst', 'gekookte worst', 'rookworst' and 'knakworst'.

4.2.2 Nitrate

Mancini et al. (2015) also estimated the intake of nitrate as food additive in children aged 1 to 3 years using maximum permitted levels. The median intake was 65 µg/kg bw/day (expressed as sodium nitrate) and is comparable with the results obtained in our study. Their 90th percentile of nitrate intake was 419 µg/kg bw/day (expressed as sodium nitrate), which is higher than our 95th percentile of exposure. As the intake of nitrates as food additives did not exceed the ADI, Mancini et al. (2015) did not refine the intake assessment.

Intake assessments of nitrates in cured meat based on analytical data are available from three European countries, namely France (Menard et al., 2009), Sweden (Larsson et al., 2011) and Belgium (Temme et al., 2011). Table 10 summarizes these studies. The results are not univocal. The French study generally shows higher intake levels compared to the estimates of our study (Table 10), whereas the mean estimates of a Swedish and a Belgian study were approximately a factor 3 to 5 lower compared with the median nitrate intake in our study. High nitrate intake in the Swedish and Belgian study was a factor 4 to 9 lower compared with our study.

Table 10. European intake assessment of nitrates expressed as sodium nitrate (mg/kg bw/day) via meat and cheese using analytical data.

Country	**Type of data**	**Population**	**Mean**	**High intake**
France (Menard et al., 2009)	Analytical data meat and cheese	Children Adults	0.41-1.22[1] 0.27-0.66[1]	0.54-1.22[1,2] 0.27-0.66[1,2]
Sweden (Larsson et al., 2011)	Analytical data (cured) meat	Children	0.01-0.02[3]	0.02-0.04[3,4]
Belgium (Temme et al., 2011)	Analytical data (cured) meat	15 years and older	0.02	0.07[2]

[1] Range of lower to upper bound estimate
[2] P97.5
[3] Range reflects different age groups
[4] P95

4.2.3 Conclusion

Compared to European nitrite intake assessments using analytical data, our intake assessment using maximum ingoing amounts resulted in higher intake estimates, as in other European studies using maximum ingoing amounts. This further pinpoints that our study with current maximum limits can only be regarded as a first tier assessment. For nitrates, some European studies using analytical data suggest that the real intake of nitrate may also be lower.

4.3 Risk of nitrates and nitrites used as food additives

The calculations performed in scenario 1 to 3 can be regarded as first tier ('worst case') calculations. When not exceeding the ADI, no refinement is needed. When exceeding the ADI, this does not necessarily mean that a health risk exists but rather that refinement of the intake calculation is needed. For both nitrites and nitrates such considerations are described below. It should be noted that the derived ADI is also subject to uncertainties. In addition to nitrate and nitrite, this section addresses nitrosamine formation, which should also be taken into account in the risk of nitrate and nitrite added to food.

4.3.1 Nitrites

The 95th percentile of nitrite intake exceeded the ADI in all scenarios. However, as explained in sections 4.1.2.3 and 4.2.1, these scenarios likely overestimate the actual intake. Therefore, further refinement of exposure assessment using analytical data is needed.

With respect to meat-based foods for which an interpretation issue occur, the scenarios including these foods (Scenario 3 with maximum ingoing amounts and scenario 6 with maximum residual levels of the old Directive 95/2/EC) will probably also be largely overestimated and should be refined using analytical data.

4.3.2 Nitrates

The exposure estimates based on maximum ingoing amounts were below the ADI for the two scenarios, and therefore no further refinement is needed regarding nitrate intake from food additive use. However, nitrates also occur naturally in drinking water, fruit and vegetables (EFSA 2008). Nitrate intake due to its use as a food additive should therefore be viewed in light of this background intake. Table 11 shows the background intake for children aged 2 to 6 years as calculated in 2009 (Boon et al, 2009). The median intake estimates varied from 1.6 mg sodium nitrate/kg bw/day during winter for children aged 6 years to 2.6 mg sodium nitrate/kg bw/day during summer for children aged two years. As a conservative approach, the P95 intake estimate for nitrate as additive use of scenario 2 (0.32 mg/kg bw/d) was added to background intake of nitrates naturally occurring in food. This resulted in a summed intake ranging from 1.9 to 2.9 mg sodium nitrate/kg bw/day, which is lower than the ADI of 5 mg sodium nitrate/kg bw/day. The high intake estimate of background nitrate intake varies from 2.7 mg sodium nitrate/kg bw/day during winter for 6-year old children to 4.9 mg sodium nitrate/kg bw/day during summer for 2-year old children (Boon et al., 2009; Table 11). Adding the P95 intake estimate for nitrate as additive use of scenario 2 to P95 intake percentile for background intake, the summed intake varies from 3.0 to 5.2 mg sodium nitrate/kg bw/day, the latter being higher than the ADI of 5.0 mg sodium nitrate/kg bw/day. In 2008, the NVWA concluded that for children exceeding the ADI with a factor two or less poses a negligible health risk in case ADIs were derived from studies in which the doses administered were not corrected for bodyweight. This means that in the case young animals are exposed to constant concentrations (i.e. a dose per animal not corrected for body weight) of the compound via food or drinking water, they are exposed to concentrations about two times higher than adult animals. As a consequence, an exposure level exceeding the ADI with a factor two or less does not give reason for concern in such situations, unless other data in the toxicity database indicate otherwise. Since this situation is applicable for nitrate (Boon et al., 2009), the estimated intake from nitrates obtained from natural sources combined with the use as food additives, poses a negligible health risk for nitrates. In addition, the conservative scenario summing the P95 nitrate intake as food additive to the P95 back ground nitrate intake may not be realistic, because children probably do not consume high amounts of fruit, vegetables, cheese and nitrate-treated meat ever over a long-term period. Taken together, refinement of intake assessment of nitrate as a food additive is not needed.

Regarding the population aged 7 to 69 years, the median background nitrate intake varied from 1.2 to 1.6 mg nitrate ion/kg bw/day (Geraets et al., 2014; Table 12). Adding the P95 intake estimate of nitrate for the particular age group according to scenario 2 (0.22 mg sodium nitrate/kg bw/day; Table 5) to this background intake, did not result in exceeding of the ADI expressed as sodium nitrate (5 mg/kg bw/day). Also the use of the 95th percentile background intake did not result in intakes exceeding of the ADI expressed as sodium nitrate. Therefore, refinement of intake assessment of nitrate as a food additive is not needed.

Table 11. Median (P50) and high (P95) intake percentiles (expressed as mg sodium nitrate/kg bw/d) of background nitrate intake of the Dutch population aged 2 to 6 years as a function of age and season, assuming samples with a concentration below LOR[1] to equal ½ LOR, reported by Boon et al. (2009).

Age	**P50**	**P95**
Summer		
2	2.6	4.9
3	2.4	4.6
4	2.2	4.2
5	2.0	3.9
6	1.9	3.6
Winter		
2	2.4	3.9
3	2.2	3.5
4	1.9	3.2
5	1.8	3.0
6	1.6	2.7

Table 12. Median (P50) and high (P95) intake percentiles (expressed as mg sodium nitrate/kg bw/d) of background nitrate intake of the Dutch population aged 7 to 69 years assuming samples with a concentration below LOR[1] to equal ½ LOR, reported by Geraets et al. (2014).

Population	**P50**	**P95**
7-15 years	1.6	2.7
16-89 years	1.2	2.4

[1] LOR = limit of reporting

4.3.3 *Nitrosamines*

The present study did not take into account nitrosamines generated in foods to which nitrates or nitrites are added, because no recent concentration data of these substances were available. However, as outlined in section 1.1, nitrosamines are important in the discussion of nitrate and nitrite toxicity. The International Agency for Research on Cancer (IARC) classified in 2015 processed meat as carcinogenic to humans (Group 1; Bouvard et al., 2015). IARC did not distinguish between the types of processed meats. The exact nature of carcinogenicity of processed meat is not known, but may be due to the presence of known or suspect carcinogens as N-nitrosamines, polycyclic aromatic hydrocarbons and heterocyclic aromatic amines, depending on the production process (Bouvard et al., 2015). In 2002, IARC concluded there is sufficient evidence in experimental animals for the carcinogenicity of nitrite in combination with amines or amides. They stated that "*ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans (Group 2A). There is an active endogenous nitrogen cycle in humans that involves nitrate and nitrite, which are interconvertible in vivo. Nitrosating agents that arise from nitrite under acidic gastric conditions react readily with nitrosatable compounds, especially secondary amines and amides, to generate nitrosamines. These nitrosating conditions are enhanced following ingestion of additional nitrate, nitrite or nitrosatable compounds. Some of the N-nitroso compounds that could be formed in humans under these conditions are known carcinogens*" (IARC 2010). It should be noted that IARC concluded on the hazards of ingested nitrate and nitrite and not on the risk, which combines hazard and exposure (IARC 2010). In 1995 and 2002, JECFA concluded that there are quantitative data only on those nitrosamines that are readily formed endogenously, such as N-nitrosoproline, which are not carcinogenic. As there was no quantitative evidence of endogenous formation of carcinogenic N-nitroso compounds at the levels of intake of nitrate and nitrosatable compound achievable in the diet, a quantitative risk assessment on the basis of endogenously formed nitrosamines was not necessary according to JECFA. EFSA, in its opinion on nitrites of 2010, referred to JECFA (EFSA, 2010). A study taking into account nitrate levels in foods and consumption of fish, also indicated that *in-vivo* nitrosamine formation leads to marginal increases in cancer risk (Zeilmaker et al., 2010).

Addition of nitrite and nitrate to food can result in formation of nitrosamines in the food itself during manufacturing and storage (JECFA 1995, SCF 1995, FCEC 2016). Nitrosamines can also be generated during heating of cured meat products at home (e.g. frying bacon or baking salami on a pizza). Formation of nitrosamines upon baking and frying of cured meat products is complex, because varying effects (lowering or increasing the concentration of nitrosamines) of frying and baking were observed for different nitrosamines (Hermann et al., 2014). According to Honikel (2008), nitrosamines can be formed during heating above 130°C. In 1995, the SCF concluded that the dietary intake of nitrosamines is very low, but that due to the genotoxic and carcinogenic nature of these substances, efforts should continue to reduce dietary intake (SCF 1995). In 2005, EFSA, introduced a margin of exposure approach for genotoxic and carcinogenic substances, which implies that "*in general a margin of exposure of 10,000 or higher, if it is based on the BMDL10 from an animal study, and taking into account overall uncertainties in the interpretation, would be of low concern from a public health point of view; the magnitude of an MOE however only indicates a level of concern and does not quantify risk*." (EFSA, 2005). It should be noted that EFSA in this opinion also stated that "*substances which are both genotoxic and carcinogenic should not be approved for deliberate addition to foods or for use earlier in the food chain, if they leave residues which are both genotoxic and carcinogenic in food*" (EFSA, 2005). However, if the addition of nitrite to meat products and nitrate to cheese, meat products and fish products is the only way to prevent deleterious effects of pathogens, the risk manager may need to weigh the benefits and risks of nitrate and nitrite addition. Assessing the level of concern may help the risk manager to make such a risk-benefit analysis.

The margin of exposure approach was recently performed in a Danish study estimating the intake of N-nitrosamines known to be carcinogenic to humans from processed meat products (Hermann et al., 2015). The intake of volatile known carcinogenic N-nitrosamines was considered as of low concern. The exposure of non-volatile N-nitrosamines was substantially higher, but the toxicological relevance of these substances is not known (Hermann et al., 2015). In Denmark, because of derogation from R 1333/2008, lower concentrations of nitrite are allowed in meat products (FCEC 2016). Therefore, intake of N-nitrosamines known to be carcinogenic may be higher in the Netherlands. In the study of Hermann et al. (2015), mean volatile nitrosamine concentration in Belgian samples was about a factor 2 higher compared with the Danish samples. Volatile nitrosamine concentration in Dutch meat products was measured in 1986 (Ellen et al. 1986). The nitrosamine concentration in meat products varied from <0.1 to 91.9 μg/kg, with a mean of positive samples being 3 μg/kg, which is approximately a factor 4 higher than in the study of Herman et al. (2015). Heating of meat products increased the concentration of volatile nitrosamines (Ellen et al. 1986). Since use (lower maximum permitted levels) and production processes may have changed since then, these concentrations have very likely changed over time. To be able to assess todays level of concern of nitrosamines formed in foods to which nitrate or nitrite are added, more information on the nitrosamine concentration of the particular foods is needed. This should preferably be at the levels of foods as eaten (e.g. fried bacon or raw and oven-baked salami).

4.3.4 Conclusion

The exposure estimates performed in our study using maximum permitted levels can be regarded as a first tier exposure assessment, and exceeding of the ADI does not necessarily indicate a health risk but rather indicates that refinement is needed. For nitrites, it is concluded that such refined exposure assessment using analytical data is needed to better assess its risk. Regarding nitrates, the first tiers assessments indicate that no further refinement is needed. As nitrosamine formation may be important for the toxicity of nitrate and nitrites, it is important to include an exposure assessment of nitrosamines based on analytical values in foods as well.

5 Conclusion and recommendations

5.1 Conclusions

- Intake assessment of nitrites and nitrates using maximum ingoing amounts as laid down in Regulation 1333/2008 can only be used in lower tier ('worst-case') assessments. When the resulting intake does not exceed the ADI, health effects are unlikely, but when the ADI is exceeded, health effects cannot be excluded and further refinement of the assessment may be needed because of the conservative assumptions.
- For nitrites, upper intake levels of the calculated scenarios using maximum ingoing amounts exceeded the ADI. As these scenarios are highly conservative, refinement is needed.
- Refinement using maximum residual amounts of the old Directive 95/2/EC (for which most of the corresponding indicative ingoing amounts are similar to the current maximum ingoing amounts of Regulation 1333/2008 and thereby provide a proxy for the current maximum residual amount to be expected in food) still exceeded the ADI for the upper intake percentiles of the population aged 2 – 69 years. As studies of other European countries using analytical data showed lower residual nitrite levels and subsequently lower intake estimates, the true nitrite intake in the Netherlands may be lower. In this case, the intake assessment of nitrites should be further refined using analytical data.
- Intake of nitrates as food additive remained below the ADI in all calculated scenarios. When taking the background nitrate intake (because of its presence in drinking water, vegetables and fruit) into account, the ADI could be exceeded by a factor 1.04 in young children. As this is lower than a factor 2, the health risk is negligible as outlined in section 4.3.2 and by the NVWA (2008), and refinement of the exposure assessment is not needed.
- Nitrosamine formation is an important aspect of the toxicity of nitrates and nitrites, but could not be taken into account because no recent information on nitrosamine content of foods on the Dutch market is available. To better address the risk of nitrite and nitrate used as food additives, information on nitrosamine concentrations in food should be made available.

5.2 Recommendations

- EFSA is currently performing a re-evaluation of nitrites and nitrates. This re-evaluation comprises both intake assessments and hazard assessment in case new toxicological data are available. It is currently not known whether EFSA has received sufficient analytical data to perform an exposure assessment. Since EFSA's re-evaluation is expected to be published by the end of 2016, we advise to await the outcome of this re-evaluation before starting any of the below-mentioned recommendations;
- In case EFSA could not perform intake assessments with analytical data, it is advised to measure nitrites in frequently

consumed foods and perform a refined exposure assessment. As nitrite and nitrate are convertible to each other in food, it is advised to measure them both in frequently consumed foods to which the preservatives are added.

- It is recommended to measure nitrosamine levels in food to which nitrate and nitrite are added. Because heating of the food during preparation at home may induce nitrosamine formation, it is advised to measure these substances in food as consumed (e.g. fried bacon, or raw and oven-cooked salami).

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Appendix A. Authorisations of nitrites and nitrates in the European Union.

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
01.7.2 Ripened cheese	E 251 – 252	Nitrates	150	(30)	***only hard, semi-hard and semi-soft cheese***
01.7.4 Whey cheese	E 251 – 252	Nitrates	150	(30)	***only cheese milk of hard, semi-hard and semi-soft cheese***
01.7.6 Cheese products (excluding products falling in category 16)	E 251 – 252	Nitrates	150	(30)	***only hard, semi-hard and semi-soft ripened products***
01.8 Dairy analogues, including beverage whiteners	E 251 – 252	Nitrates	150	(30)	***only dairy-based cheese analogue***
08.2 Meat preparations as defined by Regulation (EC) No 853/2004	E 249-250	Nitrites	150	(7) (7')	***only lomo de cerdo adobado, pincho moruno, careta de cerdo adobada, costilla de cerdo adobada, Kasseler, Bräte, Surfleisch, toorvorst, šašlõkk, ahjupraad, kiełbasa surowa biała, kiełbasa surowa metka, and tatar wołowy (danie tatarskie)***
08.3.1 Non-heat-treated meat products	E 249 - 250	Nitrites	150	(7)	
	E 251 - 252	Nitrates	150	(7)	
08.3.2 Heat–treated meat products	E 249 – 250	Nitrites	100	(7) (58) (59)	***only sterilised meat products*** (Fo > 3.00)
	E 249 – 250	Nitrites	150	(7) (59)	***except sterilised meat products*** (Fo > 3.00)

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
08.3.4.1 Traditional immersion cured products (Meat products cured by immersion in a curing solution containing nitrites and/or nitrates, salt and other components)	E 249 - 250	Nitrites	50	(39)	**only *cured tongue***: Immersion cured for at least 4 days and pre-cooked.
	E 249 - 250	Nitrites	50	(39)	**only *rohschinken, nassgepökelt* and similar products**: Curing time depending on the shape and weight of meat pieces for approximately 2 days/kg followed by stabilisation/maturation
	E 249 - 250	Nitrites	100	(39)	**only *Wiltshire ham* and similar products**:Meat is injected with curing solution followed by immersion curing for 3 to 10 days. The immersion brine solution also includes microbiological starter cultures
	E 249 - 250	Nitrites	150	(7)	**only *kylmâsavustettu poronliha/kallrökt renkött***: Meat is injected with curing solution followed by immersion curing. Curing time is 14 to 21 days followed by maturation in cold-smoke for 4 to 5 weeks
	E 249 - 250	Nitrites	150	(7)	**only *bacon, filet de bacon* and similar products**: Immersion cured for 4 to 5 days at 5 to 7 ^{o}C, matured for typically 24 to 40 hours at 22 ^{o}C, possibly smoked for 24 hrs at 20 to 25 ^{o}C and stored for 3 to 6 weeks at 12 to 14 ^{o}C

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
08.3.4.1 Traditional immersion cured products continued	E 249 - 250	Nitrites	175	(39)	**only *Wiltshire bacon* and similar products**: Meat is injected with curing solution followed by immersion curing for 3 to 10 days. The immersion brine solution also includes microbiological starter cultures
	E 249 - 250	Nitrites	175	(39)	**only *Entremeada, entrecosto, chispe, orelheira e cabeca (salgados), toucinho fumado* and similar products:** Immersion cured for 3 to 5 days. Product is not heat-treated and has a high water activity
	E 251 - 252	Nitrates	10	(39) (59)	**only *cured tongue***: Immersion cured for at least 4 days and pre-cooked
	E 251 - 252	Nitrates	250	(39) (59)	**only *Wiltshire bacon* and similar products**: Meat is injected with curing solution followed by immersion curing for 3 to 10 days. The immersion brine solution also includes microbiological starter cultures
	E 251 - 252	Nitrates	250	(39) (59)	**only *Wiltshire ham* and similar products**:Meat is injected with curing solution followed by immersion curing for 3 to 10 days. The immersion brine solution also includes microbiological starter cultures

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
08.3.4.1 Traditional immersion cured products continued	E 251 - 252	Nitrates	250	(39) (59)	**only *Entremeada, entrecosto, chispe, orelheira e cabeca (salgados), toucinho fumado* and similar products:** Immersion cured for 3 to 5 days. Product is not heat-treated and has a high water activity
	E 251 - 252	Nitrates	250	(7) (40) (59)	**only *bacon, filet de bacon* and similar products**: Immersion cured for 4 to 5 days at 5 to 7 °C, matured for typically 24 to 40 hours at 22 °C, possibly smoked for 24 hrs at 20 to 25 °C and stored for 3 to 6 weeks at 12 to 14 °C
	E 251 - 252	Nitrates	250	(39)	**only *rohschinken, nassgepökelt* and similar products**: Curing time depending on the shape and weight of meat pieces for approximately 2 days/kg followed by stabilisation/maturation
	E 251 - 252	Nitrates	300	(7)	**only *kylmâsavustettu poronliha/kallrökt renkött***: Meat is injected with curing solution followed by immersion curing. Curing time is 14 to 21 days followed by maturation in cold-smoke for 4 to 5 weeks
08.3.4.2 Traditional dry cured products. (Dry curing process involves dry application of curing mixture containing	E 249 - 250	Nitrites	50	(39)	**only *rohschinken, trockengepökelt* and similar products**: Curing time depending on the shape and weight of meat pieces for approximately 10 to 14 days followed by stabilisation/maturation

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
nitrites and/or nitrates, salt and other components to the surface of the meat followed by a period of stabilisation/maturation)	E 249 - 250	Nitrites	100	(39)	**only *dry cured ham* and similar products**: Dry curing followed by maturation for at least 4 days
	E 249 – 250	Nitrites	100	(39)	**only *presunto, presunto da pa and paio do lombo* and similar products**: Dry cured for 10 to 15 days followed by a 30 to 45 day stabilisation period and a maturation period of at least 2 months
	E 249 – 250	Nitrites	175	(39)	**only *dry cured bacon* and similar products** Dry curing followed by maturation for at least 4 days
	E 251 - 252	Nitrates	250	(39) (59)	**only *dry cured bacon* and similar products**: Dry curing followed by maturation for at least 4 days
	E 251 - 252	Nitrates	250	(39) (59)	**only *dry cured ham* and similar products**: Dry curing followed by maturation for at least 4 days
	E 251 - 252	Nitrates	250	(39) (59)	**only *jamon curado, paleta curada, lomo embuchado y cecina* and similar products**: Dry curing with a stabilisation period of at least 10 days and a maturation period of more than 45 days

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
08.3.4.2 Traditional dry cured products continued	E 251 - 252	Nitrates	250	(39) (59)	**only *presunto, presunto da pa and paio do* lomboand similar products**: Dry cured for 10 to 15 days followed by a 30 to 45 day stabilisation period and a maturation period of at least 2 months
	E 251 - 252	Nitrates	250	(39) (40) (59)	**only *jambon sec, jambon sel* and other similar dried cured products**: Dry cured for 3 days + 1 day/kg followed by a 1 week post-salting period and an ageing/ripening period of 45 days to 18 months
	E 251 - 252	Nitrates	250	(39) (59)	**only *rohschinken, trockengepökelt* and similar products**: Curing time depending on the shape and weight of meat pieces for approximately 10 to 14 days followed by stabilisation/maturation
08.3.4.3 Other traditionally cured products. (Immersion and dry cured processes used in combination or where nitrite and/or nitrate is included in a compound	E 249 - 250	Nitrites	50	(39)	**only *rohschinken, trocken-/nasgepökelt* and similar products**: Dry curing and immersion curing used in combination (without injection of curing solution). Curing time depending on the shape and weight of meat pieces for approximately 14 to 35 days followed by stabilisation/maturation

Food category	Food Additive		Maximum level (mg/l or mg/kg as appropriate)	Footnotes[1]	Restrictions/Exceptions
product where the curing solution is injected into the product prior to cooking)	E 249 - 250	Nitrites	50	(39)	**only *jellied veal and brisket***: Injection of curing solution followed, after a minimum of 2 days, by cooking in boiling water for up to 3 hours
	E 249 - 250	Nitrites	180	(7)	**only *vysocina, selsky salam, turisticky trvanlivy salam, polican,herkules, lovecky salam, dunjaska klobasa, paprikas* and similar products**: Dried product cooked to 70 °C followed by 8 to 12 day drying and smoking process. Fermented product subject to14 to 30 day three-stage fermentation process followed by smoking
	E 251 - 252	Nitrates	10	(39) (59)	**only *jellied veal and brisket***: Injection of curing solution followed, after a minimum of 2 days, by cooking in boiling water for up to 3 hours
	E 251 - 252	Nitrates	250	(39) (59)	**only *rohschinken, trocken-/nasgepökelt* and similar products**: Dry curing and immersion curing used in combination (without injection of curing solution). Curing time depending on the shape and weight of meat pieces for approximately 14 to 35 days followed by stabilisation/maturation
	E 251 - 252	Nitrates	250	(40) (7) (59)	**only *Salchichon y chorizo traducionales de larga curacion* and similar products**: Maturation period of at least 30 days.

Food category	**Food Additive**		**Maximum level (mg/l or mg/kg as appropriate)**	**Footnotes[1]**	**Restrictions/Exceptions**
08.3.4.3 Other traditionally cured products continued	E 251 - 252	Nitrates	250	(40) (7) (59)	**only *saucissons sec* and similar products *s***: raw fermented dried sausage without added nitrites. Product is fermented at temperatures in the range of 18 to 22 °C or lower (10 to 12 °C) and then has a minimum ageing/ripening period of 3 weeks. Product has a water/protein ratio of less than 1,7
	E 251 - 252	Nitrates	300	(40) (7)	**only *rohwürste (salami and kantwurst)***: Product has a minimum 4-week maturation period and a water/protein ratio of less than 1,7
09.2 Processed fish and fishery products including molluscs and crustaceans	E 251 - 252	Nitrates	500		only pickled herring and sprat

[1] Footnotes according to R1333/2008:

(7): Maximum amount that may be added during manufacturing

(7'): Maximum amount is expressed as Sodium nitrite

(30): In the cheese milk or equivalent level if added after removal of wh0ey and addition of water

(39): Maximum residual amount, residue level at the end the production process

(40): Without added nitrites

(58): Fo-value 3 is equivalent to 3 minutes heating at 121 °C (reduction of the bacterial load of one billion spores in each 1 000 cans to one spore in thousand cans)

(59): Nitrates may be present in some heat-treated meat products resulting from natural conversion of nitrites to nitrates in a low-acid environment

Appendix B. Detailed description of linking of food as consumed to food categories of Annex II of regulation 1333/2008

01.7.2 Ripened cheese; only hard, semi-hard and semi-soft cheese
This food category is relevant for nitrate use only and comprises most of the frequently consumed cheeses, such as ‘Gouda’ and ‘Edam’. This category was not checked thoroughly for true zeroes, because the impact was assumed to be low as the most frequently consumed cheeses declare use of nitrates on their label. A lot of cheeses in the food consumption data were identified by brand name. Some cheeses are no longer available on the market and for some no information on type of cheese could be found in web shops of supermarkets. These cheeses were classified as semi-hard ripened cheese in order to avoid underestimation of nitrates intake.

01.7.4 Whey cheese; only cheese milk of hard, semi-hard and semi-soft cheese
This category is relevant for nitrates only. It mainly consists of ricotta, which was found a true zero for nitrates in scenario 2 and 3.

01.7.5 Processed cheese
This food category mostly comprises of cheese powder and cheese spread. Although use of nitrates is not allowed in processed cheese, according to the label information processed cheese may contain nitrates. This is probably due to carry over of ripened cheese as a (main) ingredient.

01.7.6 Cheese products (excluding products falling in category 16); only hard, semi-hard and semi-soft ripened products
This category is relevant for nitrates only. Cheese products were not coded in the Dutch food consumption surveys and therefore not included in the exposure assessment.

01.8 Dairy analogues, including beverage whiteners; only dairy-based cheese analogue
This category is relevant for nitrates only. Dairy-based cheese analogues were coded in Dutch consumption surveys, but the brands have disappeared from the market and true zeroes could therefore not be established.

08.2 Meat preparations as defined by Regulation (EC) No 853/2004; only *lomo de cerdo adobado, pincho moruno, careta de cerdo adobada, costilla de cerdo adobada, Kasseler, Bräte, Surfleisch, toorvorst, šašlõkk, ahjupraad, kiełbasa surowa biała, kiełbasa surowa metka,* and *tatar wołowy (danie tatarskie)*
This category is relevant for nitrites only. The foods in which nitrites are allowed according to this food category are expected not to be consumed in the Netherlands, as they are not recorded in the Dutch consumption surveys.

Meat preparations for which an interpretation issue exists regarding their classification into meat products (nitrites allowed) or meat preparations (nitrite not allowed) included marinated raw meat (‘beenham’ and ‘varkenshaas’, raw frying sausages, ‘rosbief als broodbeleg’, ‘ossenworst’ and ‘filet americain’). These foods were assumed to have the maximum permitted level of food category 08.3.1 ‘non-heat-treated meat products’ in scenarios 3 and 6. Within the Dutch food consumption survey, marinating of meat is described with the facet ‘preservation method’. From the data it is not clear whether the marinating was done by butcher, industry or a by the consumer himself just before cooking. Facets were not used in the coding of this study. Hence, it was assumed that all consumed ‘beenham’ and ‘varkenhaas’ was marinated. This may have resulted in an overestimation. However, if the facet ‘marinated’ from the food consumption data was used, an underestimation would very likely have occurred, as marinating meat has become more popular during the last years.

08.3.1 Non-heat-treated meat products
This food category is relevant for both nitrates and nitrites and comprises a.o. dried sausages (e.g. salami and ‘cervelaat’), raw ham and bacon. This food category also includes the non-heated smoked sausage ‘rookworst’. As the Dutch food consumption survey does not distinguish between heated and non-heated ‘rookworst’, it was assumed that 30%, the percentage of ‘rookworst’ bought at butcheries, was non-heat-treated. The other 70% was assumed to be heat-treated (FC 08.3.2)

Non-heat-treated meat products are used as decoration of meat preparations, such as ‘slavink’. In those compound foods, true zeroes were found.

08.3.2 Heat–treated meat products; only sterilised meat products
This food category is relevant for nitrites only. All canned meat products recorded as such in the food consumption survey (such as ‘ham in blik’) were assumed to be sterilised meat products. However, for most meat products no such information was recorded. The Dutch food consumption surveys do not distinguish between canned and non-canned Frankfurter sausages. Therefore, it was assumed that Frankfurter sausages were canned and thus sterilised, although also non-canned Frankfurter sausages are available on the market.

08.3.2 Heat–treated meat products; except sterilised meat products
This food category is relevant for nitrites only. This food category comprises a.o. cooked ham, cooked smoked sausages, several types of cold cuts (e.g. ‘boterhamworst’, ‘kipfilet’) and liver sausages. This category also contains frozen heated meat products like ‘frikandel’, which were found to contain no E 249 – 252, and therefore treated as a true zero in scenario 2,3, 5 and 6.

08.3.4 Traditional meat products
This food category is relevant for nitrites and nitrates. Most traditional cured products were not coded in the Dutch consumption surveys. It

was assumed that all meat products consumed in the Dutch food consumption surveys are non-traditionally produced meat products. An exception is '*jellied veal*', which was coded as such in the food consumption survey.

09.2 Processed fish and fishery products including molluscs and crustaceans; only pickled herring and sprat
This food category is relevant for nitrates only. The category was interpreted according to the Dutch translation of Annex II of Regulation 1333/2008, in which pickled herring is translated as 'gepekelde haring', which is salted herring. Herring was found to be a true zero in scenario 2 and 3. For sprat no information was found.

Compound foods
Compound foods are relevant for both nitrates and nitrites. All EPIC-Soft coded foods which may contain relevant ingredients for the exposure to nitrates and nitrites, such as ripened cheese (including cheese powder and cheese spread), whey cheese (ricotta) or meat products were checked. These compound foods comprised sauces, soups and salty snacks, such as potato crisps. For each applicable ingredient, a percentage was derived from label information or recipe books, and the ingredients were coded according to the same food categories as mentioned above. For some compounds foods, several flavours are on the market. Those flavours may the consequence of use ingredients with nitrites and nitrates (e.g. cheese), but may also be the consequence of ingredients that do not contain nitrites or nitrates (e.g. bacon flavour, which is not real bacon but only flavouring molecules). In the case that a product with several flavours was on the market, the frequency of use was assumed 25%. For instance, crisps have a lot of flavours, e.g. plain, paprika, cheese-onion, barbecue-ham, cream-chives etcetera, so it was assumed 25% of consumption is with cheese flavour with the remaining 75% having another flavour.

Appendix C. Foods contributing ≥ 5% to the total intake to nitrite for the different Dutch subpopulations for three different scenarios.

Table C1. Scenario 1. The authorization scenario.

Young Children 2-6 years	**Population aged 7-69 years**	**Elderly > 69 years**
Dutch meat snack Frikandel (20.9%)	Cooked ham (16.1%)	Cooked ham (18.3%)
Liver sausage, paté (20.3%)	Dutch meat snack Frikandel (14.6%)	Liver sausage, pate (11.7%)
Luncheon meat, boiled/grilled sausage, roasted cold cuts (15.4%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (9.8%)	Smoked sausage ‘rookworst’ (11.6%)
Salami and other dried sausages (8%)	Salami and other dried sausages (9.8%)	Salami and other dried sausages (10%)
Smoked sausage ‘rookworst’ (7.8%)	Liver sausage, pate (7.8%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (6.8%)
Cooked ham (5.3%)	Smoked sausage ‘rookworst’ (7.7%)	
Frankfurter sausages (5.3%)	Salted bacon (6.9%)	

Table C2. Scenario 2. The authorization scenario excluding true zeroes.

Young Children 2-6 years	**Population aged 7-69 years**	**Elderly > 69 years**
Liver sausage, pate (26.8%)	Cooked ham (20.2%)	Cooked ham (19.8%)
Luncheon meat, boiled/grilled sausage, roasted cold cuts (20.2%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (12.3%)	Liver sausage, pate (12.7%)
Salami and other dried sausages (10.5%)	Salami and other dried sausages (12.3%)	Smoked sausage ‘rookworst’ (12.6%)
Smoked sausage ‘rookworst’ (10.3%)	Liver sausage, pate (9.8%)	Salami and other dried sausages (10.8%)
Cooked ham (7%)	Smoked sausage ‘rookworst’ (9.7%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (7.4%)
Frankfurter sausages (6.9%)	Salted bacon (8.7%)	

Table C3. Scenario 3. Same as Scenario 2, including foods for which interpretation issues exits between the industry and the Dutch Food and Consumer Products Safety Authority.

Young Children 2-6 years	**Population aged 7-69 years**	**Elderly > 69 years**
Liver sausage, pate (22.5%)	Cooked ham (16.2%)	Cooked ham (15.9%)
Luncheon meat, boiled/grilled sausage, roasted cold cuts (17%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (9.9%)	Liver sausage, pate (10.2%)
Sausage ‘Braadworst’ (13.2%)	Salami and other dried sausages (9.8%)	Smoked sausage ‘rookworst’ (10.1%)
Salami and other dried sausages (8.8%)	Sausage ‘Braadworst’ (8.1%)	Sausage ‘Braadworst’ (9.8%)
Smoked sausage ‘rookworst’ (8.7%)	Liver sausage, pate (7.9%)	Salami and other dried sausages (8.6%)
Cooked ham (5/8%)	Smoked sausage ‘rookworst’ (7.7%)	Luncheon meat, boiled/grilled sausage, roasted cold cuts (5.9%)
Frankfurter sausages (5.8%)	Salted bacon (7%)	
	Filet American and raw beef sausage ‘ossenworst’ (5.9%)	

Appendix D. Portion sizes of nine children aged 2 to 6 years with intakes around estimated value of the 95th intake percentile. Scenario 5: Authorisation scenario using the residual amounts of Directive 95/2/EC and excluding true zeroes.

Subject	Consumption day	Food as eaten	Consumption (g)	Standard portion size (g)	Use level E250 (mg/kg)	Intake (µg/kg bw/day)[1]	Scenario
1	2	Salami	50	15	50	120.8	5
	2	Sausage, "Knakworst"	40	20	100	193.2	5
	1	Sausage, smoked	15	50	100	72.46	5
	1	Ham n.s.	15	20	100	72.46	5
	1	"Worst, boterham"	24	15	100	115.9	5
2	1	"Worst, snij"	15	15	50	65.22	5
	1	Sausages, boiled n.s.	16	20	100	139.1	5
	1	Sausage based on liver	42	20	100	365.2	5
3	2	Bacon, strips/cubes lean	15	50	100	57.25	5
	2	Sausages n.s.	25	50	100	95.42	5
	1	Chicken fillet for sandwich	7.5	15	100	28.63	5
	1	"Worst, paling"	10	15	100	38.17	5
	1	Minced meat, roasted, cold cuts	15	15	100	57.25	5
	1	Sausages n.s.	75	50	100	286.3	5
4	1	Sausage, "Knakworst"	80	20	100	559.4	5
5	2	Sausage based on liver	10	20	100	47.39	5
	2	Sausage, "Knakworst"	80	20	100	379.1	5

Subject	Consumption day	Food as eaten	Consumption (g)	Standard portion size (g)	Use level E250 (mg/kg)	Intake (μg/kg bw/day)[1]	Scenario
	1	"Worst, boterham"	8	15	100	37.91	5
	1	Pate	20	15	100	94.79	5
6	2	Ham, back	40	20	100	239.5	5
	2	Bacon, strips/cubes lean	45	50	100	269.5	5
	1	Sauce warm/hot n.s.	12	25	4.5	3.2	5
	1	Cervelaat	15	15	50	44.9	5
7	2	"Worst, boterham"	8	15	100	56.74	5
	2	Ham, boiled	20	20	100	141.8	5
	2	Casselerrib	50	20	100	354.6	5
8	1	Sausage based on liver	20	20	100	87.72	5
	2	Sausages, boiled n.s.	25	20	100	109.6	5
	2	Liver sausages n.s.	25	20	100	109.6	5
	2	Sausage based on liver	54	20	100	236.8	5
9	2	Liver sausage	19.5	20	100	88.64	5
	2	Sausage, smoked	100	50	100	454.5	5

[1] Values in red exceed the ADI of 100 μg sodium nitrite/kg bw/day.

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