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DISCUSSION PAPER ON THE USE OF NITRATES (INS 251, 252) AND NITRITES (INS 249, 250)

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Background

1. The provisions for nitrates (INS 251, 252) and nitrites (INS 249, 250) were included in the paper CX/FA 16/48/7 for discussion at the 48th Session of the Committee on Food Additives. During the Physical Working Group (PWG) meeting held prior to the CCFA48 concerns were raised as to the expression of the maximum use levels for nitrates and nitrites as ingoing amount and/or residual amount, the appropriate maximum use levels, and safety of their use. After consideration of this issue, the PWG agreed to the proposal that the European Union (EU) drafts terms of reference for a discussion paper on this issue. As such, with the exception of provisions for nitrites in food categories 01.6.1 (Unripened cheese) and 01.6.2 (Ripened cheese) which were recommended for discontinuation, the PWG agreed to hold all provisions for nitrates and nitrites, pending the outcome of the consideration of the draft terms of reference for this discussion paper (CRD 2, CCFA48).

2. The issue was further discussed at CCFA48 where the JECFA Secretariat clarified that the basis for the ADI was on toxicological considerations of the nitrates and nitrites as such and that while nitrosamine formation was considered, it did not form the basis for the ADI. The formation of nitrosamines in the body or in foods was well known and could occur also from nitrates and nitrites occurring naturally in food and not only from their use as food additives. Therefore, nitrates and nitrites when used as food additives should be used at the minimum levels needed to achieve the functional purpose. Risk / benefit consideration were important because the use of nitrates and nitrites as a preservative was intended to improve the microbiological safety of the product (REP16/FA, para. 60).

3. Reflecting the discussion, the Committee agreed that the Netherlands would prepare a discussion paper with inputs from the JECFA Secretariat identifying concerns for the food additive use of nitrates (INS 251, 252) and nitrites (INS 249, 250) for consideration at CCFA49. The Committee also agreed that the scope of the discussion paper would address issues related in particular to:

(i) The expression of Maximum Use Levels as ingoing amount and/or residual amount taking into account the feasibility of controls, preserving effect (in particular the inhibitory activity against *C. botulinum*) and possible formation of nitrosamines

(ii) The technological need seeking a balance between the benefits (microbiological safety, desired effect on colour and flavour) and risks (formation of nitrosamines) taking into account existence of effective alternatives

(iii) Appropriate levels taking into account the ADI's for nitrites and nitrates and the discussion on point (i) and (ii) above (REP16/FA, paras. 61-63).

Analysis of the issues

4. In order to properly analyse the three topics, a short overview of the relevant background information was prepared (see Annex to this paper). That information was the basis to identify concerns and suggest possible approaches how to address them as formulated in the recommendations. The overview in Annex includes:

- General principles for the use of food additives
- Adopted provisions for nitrites and nitrates in the Codex standards
- Technological need for nitrates and nitrites

- Nitrosamine formation
- Available evaluations of processed meat, nitrosamines, nitrites and nitrates
- Estimation of the safety aspects of the proposed Maximum Use Levels for nitrites and nitrates following the GSFA guidelines (i.e. Annex A to the Preamble to the GSFA)

It should be noted that main information is provided for each of the addressed issues and that the Annex can be regarded as information to further reading.

(i) - The expression of Maximum Use Levels as ingoing amount and/or residual amount taking into account the feasibility of controls, preserving effect (in particular the inhibitory activity against C. botulinum) and possible formation of nitrosamines

5. Nitrites and nitrates can be expressed as ingoing or residual amounts. For the proposed provisions of CX/FA 16/48/7 it is not clear how they were expressed when submitted. Two provisions for nitrites currently included in the GSFA are expressed as residual amounts (no precise point in time when residues shall be determined is given). Some Codex members express nitrites and nitrates as ingoing amounts. Both ways of expressing maximum use levels have pros and cons, depending on the object in view.

Ingoing or residual amounts and control purposes

6. The Codex Committee on Processed Meat and Poultry Products (CCPMPP) have discussed the ingoing and residual amounts in their meetings. They noted in their 14th meeting in 1989 that there was a trend to control the level of “ingoing nitrite" rather than the "maximum level in the final product”, which was mainly dependent on the temperature and period of storage. The Committee noted that for purposes of control by food inspectors, there was also a need to retain a maximum level for residual nitrite (ALINORM 89/16 PAR 93).

7. JECFA did not address the issue of ingoing or residual amounts in their reports of 1995 and 2002 (JECFA 1995, JECFA 2002).

8. This issue has been addressed by EFSA in 2003. EFSA concluded that there is no simple and direct relationship between the ingoing amount and the residual amount of nitrite. Decrease of nitrite depends on the storage temperature, heat treatment of meat products and the presence of other compounds such as ascorbate. Therefore, a low analytical value of nitrite may have several causes, e.g. recently manufactured product with an initial low amount of nitrite, product stored for several months with an initial modest amount of nitrite, or product manufactured in the presence of additional ascorbate. For these reasons, it was concluded that limits based on ingoing amount are more useful for control purposes than residual amounts (EFSA 2003).

9. One of the arguments against setting maximum limits on the ingoing amount is that it is difficult to define such values for some production processes, such as curing with immersion techniques or traditional dry curing (FCEC 2016).

Ingoing or residual amounts and preserving effects

10. JECFA did not address the issue of ingoing or residual amounts in their reports of 1995 and 2002 (JECFA 1995, JECFA 2002).

11. According to EFSA in 2003, there is no convincing evidence that the residual amount protects against *C. botulinum*. It was concluded that there is no simple and direct relationship between the ingoing amount and the residual amount of nitrite (EFSA 2003).

Ingoing or residual amounts and formation of N-Nitrosamines

12. N-nitrosamines can be generated out of nitrate and nitrite on three levels: in the product itself during the production process, during heating of the products in the domestic situation and endogenously in the gastrointestinal environment. The issue of ingoing and residual amounts of nitrate and nitrite in relation to N-nitrosamine formation is only relevant for the generation of these substances in the product itself. Regarding endogenous formation in the gastrointestinal tract, only residual amounts are relevant.

13. Although JECFA discussed N-nitrosamine formation in their reports of 1995 and 2002, they did not discuss the (quantitative) relation between ingoing or residual amounts of nitrate and nitrate and N-nitrosamine formation during the production process. Therefore, a scientific basis for setting limits on ingoing or residual amounts in relation to N-nitrosamine formation is not available from the JECFA reports. JECFA addressed the endogenous formation of N-nitrosamine out of nitrite and N-nitrosatable compounds in the gastrointestinal tract and concluded that there was no quantitative evidence of endogenous formation of carcinogenic N-nitrosocompounds.

14. The SCF in 1995 concluded that a clear correlation exists between the amount nitrite added for curing of meat and the formation of volatile nitrosamines in cured meat products (SCF 1995).

15. There is insufficient data on the relationship between the ingoing amounts of nitrite and nitrosamine formation (FCEC 2016).

16. An alternative for limits on ingoing or residual amounts nitrate and nitrite in relation to nitrosamines, may be maximum limits on N-nitrosocompounds in manufactured food to contribute to public health protection. For example, the USA has established a limit for total volatile nitrosamines in pumped bacon at 10 ppb (10 µg/kg, USDA 2013). However, also opposite arguments are available. According to Honikel (2008) N-nitrosamines occur only in small amounts in meat and are avoidable by proper heating. In 2013, the European Commission requested the EU Member States whether they were interested in setting limits on N-nitrosocompounds in the final products (EU 2013). Only a few Member States were in favour of such limits at that time, particularly because of lack of analytical methods and the complexity of the analysis. Recently, new methods for the analysis of nitrosamines have been developed (e.g. a LC-MS/MS, Hermann et al., 2014) and the usefulness of these methods could be further debated. It should be noted that whereas maximum limits on N-nitrosocompounds in manufactured food may be a tool to contribute to public health protection, it does not control N-nitrosocompounds formed during the home preparation of cured meat products. Neither does it take into account the possibility of N-nitroso compound formation within the gastrointestinal tract.

(ii) - The technological need seeking a balance between the benefits (microbiological safety, desired effect on colour and flavour) and risks (formation of nitrosamines) taking into account existence of effective alternatives

Benefits

17. The benefits of nitrites and nitrates (preservation, colour retention, flavour formation and anti-oxidative properties) are described under the technological need section (see Annex). There is a technological need following Section 3.2c of general principles for the use of food additives, as laid down in the Preamble to the GSFA (See para 53, Annex II), provided that nitrites and nitrates are not used to mask faulty raw materials or undesirable (including unhygienic) practices. Following the descriptions of the technological need section, there is no technological need in fresh and frozen meat.

18. There may be interpretation differences on the main purpose of nitrates: colouring vs preserving.

Risks

19. The risks of nitrate and nitrite can be attributed to their direct chronic effects, acute effects (methaemoglobinaemia) and formation of genotoxic and carcinogenic N-nitrosocompounds. Exceedance of the ADI may occur as well.

Existing alternatives

20. Key issue in the discussion of the technological need is whether alternatives are available to replace nitrate and nitrate. JECFA in their reports of 1995 and 2002 did not discuss the possibility of existing alternatives (JECFA 1995 and JECFA 2002).

21. The FAO in their Guidelines for slaughtering, meat cutting and further processing concluded that nitrites are indispensable for meat curing and there is no alternative (FAO 1991).

22. According to the EFSA opinion of 2003, no alternatives for nitrite were available at that time (EFSA 2003).

23. A recent report concluded that no single alternative that fulfils all four technological needs (colour, flavour, microbiological safety and antioxidant activity) is available, but that existing alternatives might be helpful in reducing the ingoing amount. The food chain evaluation consortium (FCEC) provided examples of alternatives, such as organic acids, nisins, ethyl lauroyl arginate and essential oils for preservation, fermented red rice, plant extracts, lycopene, tomato paste and phytochemicals for colour and taste, and ascorbic acid and rosemary extract for antioxidant function nitrite (FCEC, 2016).

24. According to an USDA regulation, use of nitrites could be lowered using lactic acid bacteria (USDA 2013).

Presence of nitrosation inhibitors

25. Nitrosation inhibitors (e.g. ascorbic acid) may be used to reduce the chance of nitrosamine formation (JECFA 1995, EFSA 2003, FCEC 2016). In the USA, addition of 550 ppm (mg/kg) of either sodium ascorbate or sodium erythorbate should be used together with ingoing amounts of 100 ppm (mg/kg) sodium nitrite (or 123 mg/kg potassium nitrite) to pumped bacon (USDA 2013) to minimize consumer exposure to preformed nitrosamines in bacon. It should be noted that the remaining nitrates and nitrites still may have direct toxic effects.

(iii) - Appropriate levels taking into account the ADI's for nitrites and nitrates and the discussion on point (i) and (ii)

Adequacy (proposed) levels taken into account ingoing or residual amounts (point i)

26. There are some identified concerns regarding expression of the maximum limit as ingoing amounts or residual amounts. Unless these issues are solved, the appropriateness of the proposed levels with respects to ingoing or residual amounts cannot be assessed.

Adequacy (proposed) levels taken into account the technological need (point ii)

27. According to Section 3.1c and 3.3a of general principles for the use of food additives, as laid down in the Preamble to the GSFA (CODEX STAN 192-1995), a food additive should be used at the lowest level necessary to achieve the intended technical effect. The proposed provisions for nitrites in meat products (listed in table 3 in the Annex of this paper) are above the existing maximum limits in the GSFA for food category 08.2.2 Heat-treated processed meat, poultry, and game products in whole pieces or cuts and food category 08.3 Processed comminuted meat, poultry, and game products (Table 1). It is not clear why higher use levels are needed.

28. 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 (EFSA 2003). Microbiological safety can also be obtained without nitrites if the correct combination of key parameters is met. Therefore, the level of nitrites and nitrates to be added to control botulism depends on the production process of the food.

29. The FAO in its document on Guidelines for slaughtering, meat cutting and further processing indicated that for nitrite the preserving effect could be obtained by 80 -150 mg/kg, colour protection by 3- 50 mg/kg and flavour formation by 20-40 mg/kg (FAO 1991). It is not clear whether these are in-going or residual amounts. The expression (as ion or sodium salt) is also not clear. Therefore, it is difficult to compare the proposed uses compared with the levels of the FAO document. In addition, as hygiene may have improved over time, indicated use levels for preservation published in 1991 may no longer be relevant.

30. EFSA in its opinion of 2003 concluded that 50 to 100 mg added nitrite (as sodium nitrite equal to 35 to 70 mg nitrite ion) per kg of meat products may suffice for many products. It was also concluded that for other products, especially those with a low salt content and having a prolonged shelf life, addition between 50-150 mg/kg nitrite (as sodium nitrite; equal to 35 to 105 mg nitrite ion) is necessary to inhibit the growth *of C. botulinum*. It is not clear how these ingoing use levels can be translated into residual amounts. Assuming that all the proposed uses of Table 3 of this paper are given as residual nitrite ion (note 32), most of the proposed maximum residual levels exceed the range for ingoing amounts mentioned by EFSA (EFSA 2003).

31. Recently, a European study put forward that lower nitrite amounts than the current European limits may be sufficient for microbiological safety of meat products, colouring and flavouring purposes based on current and formal practices in some EU Member States but emphasized that it was not possible to reach a firm conclusion for all products and all situations (FCEC, 2016).

32. The function of nitrite and nitrate may be partially substituted by alternatives. Use of these alternatives may lower the required use levels of nitrite and nitrate.

ADI's and other health-based guidance values

33. JECFA has set an ADI of 0-0.07 mg/kg bw/day (expressed as nitrite ion) for the chronic effect of nitrites and an ADI of 0-3.7 mg/kg bw/day (expressed as nitrate ion) for chronic effects of nitrates (JECFA 2002).

34. Nitrites may have acute effects (methaemoglobin formation), but an acute reference dose has not been established.

35. Because of this effect, JECFA specifically excluded infants below the age of three months from both ADIs due to their increased sensitivity.

Adequacy (proposed) levels in relation to the ADI

36. JECFA recommended in 2002 that the Codex Committee of Food Additives and Contaminants (CCFAC) reconsider the list of maximum levels of nitrite and nitrate in the GSFA, as the ADI may be exceeded.

37. Most of the proposed uses of nitrites in Table 3 exceeds the FS*ADI*320 value of the guidelines for the development of maximum levels for the use of food additives with numerical ADIs as laid down in Annex A of the GSFA (Tables 2 and 3 in the Annex of this paper). According to the guidelines this implies that the use of nitrites is only accepted for products where calculation of potential intake from all uses show that exceedance of the ADI is unlikely, or if the estimation of the intake based on more exact methods show that the use levels are acceptable. Table 3 also shows that for most requested maximum use levels of nitrites, consumption of only small amounts of food will already result in exceedance of the ADI, particularly in young children. Also, nitrite intake exceeds the ADI in more refined estimates. Thus, at the particular proposed nitrite levels, negative effects on health cannot be excluded.

38. For nitrates, the proposed values in Table 4 are between the FS* ADI* 80 and FS*ADI*160 value of the guidelines for the development of maximum levels for the use of food additives with numerical ADIs a laid down in Annex A of the GSFA (Tables 2 in the Annex of this paper), implying that the use would be acceptable if the daily consumption of the foods containing the additive does not usually exceed one fourth of the assumed maximum sold food intake (i.e. 6.25 g/kg bw/day). This corresponds to a daily intake of 130 g food and 390 g food for a 20 kg child and a 60 kg adult, respectively), which is quite high. However, given a possible exceedance of the ADI indicated by JECFA (see Annex – Overview of nitrates evaluations) for which natural sources (e.g. vegetables and water) are the main contributors, maximum use levels should be seen in light of this background exposure in order not to violate the general principles on food additive safety laid down in Section 3.1 of the Preamble to the GSFA. In addition, nitrates, acting as a reservoir for nitrites, may further contribute to the exposure to nitrites.

Concerns identified and recommendations

39. JECFA evaluations are over fourteen years old. Several new studies and findings may have appeared since and therefore an update of the JECFA evaluation may be considered. Questions to be addressed here:

- Is there a need to re-evaluate safety of nitrites and nitrates?
- What are recent exposures to nitrate and nitrite taking into account exposure from all sources? Does exposure to nitrite and nitrate poses a health risk?
- What are recent exposures to N-nitrosamine generated out of nitrate and nitrite used as food additives during: i) the production process in foods; ii) heat-treatment in the domestic setting; and iii) gastrointestinal transit? Is there a safety concern?
- Do the new provisions for nitrates and nitrites included in the paper CX/FA 16/48/7 pose any health risk taken into account background exposures to nitrate, nitrite and N-nitrosamines?

40. Nitrite and nitrate food chemistry is complex and its relation to antimicrobial activity, colour and flavour relations is not always clear. Therefore, it is difficult to understand the technological need and required maximum limits. An updated overview of nitrite and nitrate food chemistry in relation to the additive function and required maximum limits may be needed. For this, clear input from the industry as well as from the research institutes may be needed. Questions to be addressed are:

- What chemical reactions are crucial in the additive function(s) of nitrate and nitrite. Why can they not be obtained otherwise?
- For which type of products or production processes (e.g. fresh, frozen, whole pieces, comminuted, non-heat-treated, pasteurised, sterilised, fermented, traditionally cured) is use of nitrates and nitrites indispensable? What is the (main) reason for nitrate and nitrite use: preservation, colour retention, antioxidative capacity and/or flavour formation? Why are there no alternatives?
- What realistic ranges of nitrate and nitrite levels are needed for certain food categories to achieve a particular technological effect?

The expression of Maximum Use Levels as ingoing amount and/or residual amount (i)

41. Regarding the issue of ingoing vs residual amount, there may be no 'one size fits all' solution, but for control purposes the ingoing amount may be most practical for the majority of products, although it may be difficult to obtain for some products. A lack of common understanding based on a good overview of production processes in relation to the (in)ability to express limits as ingoing or residual amounts may hinder the discussion on limits expressed as ingoing or residual amounts.

42. Regarding nitrosamines formation in the food during production and storage, the relationship between ingoing amounts and nitrosamine formation in the food during production is not clear. With respect to N-nitrosamine formation upon home heating and during transit in the gastrointestinal tract, the residual nitrite and nitrate amount may be more important than the ingoing amount. The lack of a good overview of each route of nitrosamine formation and their quantitative contribution to the overall oral exposure to nitrosamines from processed meat may hamper the discussion on relevance of maximum limits expressed as ingoing or residual amounts.

43. For the risk assessment of nitrite and nitrate as such, the residual amount in the meat product may be more important than the ingoing amount. The issue of ingoing vs residual amounts and protection of consumers was addressed during the 15th session of the Codex Committee on Processed Meat and Poultry Products. This Committee noted '*that figures for both ingoing and residual nitrite should be maintained since they provided useful information to processors and consumers*' (Consideration at Step 7 of the revision of existing Codex standards for processed meat and poultry products; agenda item 11; ALINORM 91/16 para. 68). The issue of ingoing amounts vs residual amounts in relation to risk assessment of nitrates and nitrites was addressed neither by JECFA in their meetings nor by EFSA in their opinions.

44. JECFA did not address the issue of ingoing or residual amounts as regards control purposes, preserving effects and formation of N-Nitrosamines in its reports of 1995 and 2002 (JECFA 1995, JECFA 2002).

Recommendation 1

The Committee is invited to consider requesting JECFA for an advice as regards the aspects of the ingoing and residual amounts in relation to the appropriateness for control purposes, preserving effect and nitrosamine formation in all possible routes. Existing literature data, together data obtained from industry and input from research institutes, could be the basis of such advice. Specific questions to be addressed are:

- What is the best expression of maximum permitted levels to protect human health (ingoing amounts and/or residual amounts, and/or limits on nitrosamines in products) in terms of chemical and microbiological food safety?
- Is this best expression of maximum permitted levels to protect human health practical/suitable in all cases? For which types of production processes and/or products this might not be the case? Why? What is the best alternative?
- Is this best expression of maximum permitted levels to protect human achievable for food control authorities. Are there any (analytical) issues that need to be solved?

The technological need seeking a balance between the benefits and risks taking into account existence of alternatives (ii)

45. Given the lack of alternatives completely replacing all benefits of nitrate and nitrite the criterion of Section 3.2 of general principles of food additive use as laid down in the Preamble to the GFSA '*objectives cannot be achieved by other means that are economically and technologically practicable*' may be followed for some uses. However, interpretation issues exist regarding the main technological function of nitrite and nitrate (colour retention or preserving). For a careful consideration of the technological justification for a proposed use, information is needed on the purpose(s) of the additive use, the production process, hygienic practices and presence or absence of existing alternatives. Without this information, a scientifically sound judgement of the technological justification cannot be made.

46. Because of the risk of nitrites, nitrates and nitrosamines and the possible exceedance of the ADI for nitrite and nitrate, use should be limited to only those foods for which the use of nitrates and nitrites is absolutely necessary and cannot be obtained by other means. Given the possible health risks of nitrates and nitrites, the technological need for colour retention and flavour formation may be of minor importance compared with the technological need for prevention of botulism. Sometimes the use of nitrites may be solely for colour retention. In that case, the use of nitrites should be carefully reconsidered.

47. The principles laid down in Sections 3.1c and 3.3a of the general principles of food additive use as laid down in Preamble to the GSFA (CODEX STAN 192-1995) should be the point of departure for maximum levels based on the technological need. The proposed levels for nitrites (Table 3 in the Annex of this paper) are higher than the current provisions in the GSFA (Table 1 in the Annex of this paper) and probably also above the appropriate levels indicated by EFSA in 2003. The reason for the higher proposed levels is not clear. To judge the required level of nitrates and nitrites, data is needed on the production process, hygienic practices and presence or absence of existing alternatives.

48. A full benefit-risk assessment weighing the protective effects on botulism against the negative impact of food additive use of nitrates, nitrites and formed N-nitrosocompounds is not available. A scientifically based benefit-risk analysis may help in the decision making process by being able to better weigh the benefits against the risks.

Recommendation 2

The Committee is invited to consider requesting JECFA for an advice as regards a risk-benefit analysis, weighing the benefits of use of nitrites and nitrates against their risks. For this, information as described under section 39 and 40 is needed as input for risk-benefit analysis.

If possible, this risk-benefit analysis should be a quantitative one. To this end, data on use levels (ingoing as well as residual) and prevention of *C. botulinum* out growth and toxin formation and other type of food pathogens should be made available to perform such risk-benefit assessment.

Appropriate levels taking into account the ADI's for nitrites and nitrates (iii)

49. The principles regarding safe use as laid down in the Preamble to the GSFA should be the point of departure for deriving maximum use levels. The screening of the proposed ML indicates that negative effects on health cannot be excluded. From the exposure point of view it is clear that the proposed provisions for nitrites and nitrates should only be accepted where calculation of potential intake from all uses will show that exceeding the ADI is unlikely, or if estimation of the intake of the additive based on more exact intake estimates methods show that the use levels are acceptable. Otherwise, a careful reconsideration of the proposed uses and maximum levels is needed.

50. It is obvious that only when the Committee addresses the points (i) and (ii), the appropriate levels for nitrites and nitrates could be established. For the discussion it has to be clear whether the levels should be expressed as ingoing and/or residual amount, what are on the scientific basis the appropriate levels balancing the benefits and risks and what is the relation of the proposed levels to the ADI.

Recommendation 3

The Committee is invited to consider the appropriate use and use levels taking into account the outcomes of points (i) and (ii) and the ADI's for nitrites and nitrates

Annex

General principles for the use of food additives

1. General principles for the use of food additives, including nitrates and nitrates, are laid down in the Preamble to the GSFA. The compliance with these principles shall be scrutinised before a food additive provision is included in the GSFA. The principles include food additive safety (Section 3.1), justification for the use of additives (Section 3.2), good manufacturing practice (GMP; Section 3.3) and specifications for the identity and purity of food additives (Section 3.4). For the present discussion Section 3.1, 3.2 and 3.3a are particularly relevant.

2. Section 3.1 states with regards to food additive safety:

   a. *'Only those food additives shall be endorsed and included in this Standard that, so far as can be judged on the evidence presently available from JECFA, present no appreciable health risk to consumers at the use levels proposed'.*

   b. *The inclusion of a food additive in this Standard shall have taken into account any ADI, or equivalent safety assessment established for the additive by JECFA and its probable daily intake from all food sources.*

   c. *The quantity of an additive added to food is at or below the maximum use level and is the lowest level necessary to achieve the intended technical effect. The maximum use level may be based on the application of the procedures of Annex A, the intake assessment of Codex members or upon a request by the CCFA to JECFA for an independent evaluation of national intake assessments'.*

3. Section 3.2 states with regards to justification of use:

   'The use of food additives is justified only when such use has an advantage, does not present an appreciable health risk to consumers, does not mislead the consumer, and serves one or more of the technological functions set out by Codex and the needs set out from (a) through (d) below, and only where these objectives cannot be achieved by other means that are economically and technologically practicable:

   a. *To preserve the nutritional quality of the food; an intentional reduction in the nutritional quality of a food would be justified in the circumstances dealt with in sub-paragraph (b) and also in other circumstances where the food does not constitute a significant item in a normal diet;*

   b. *To provide necessary ingredients or constituents for foods manufactured for groups of consumers having special dietary needs;*

   c. *To enhance the keeping quality or stability of a food or to improve its organoleptic properties, provided that this does not change the nature, substance or quality of the food so as to deceive the consumer;*

   d. *To provide aids in the manufacture, processing, preparation, treatment, packing, transport or storage of food, provided that the additive is not used to disguise the effects of the use of faulty raw materials or of undesirable (including unhygienic) practices or techniques during the course of any of these activities'.*

4. Section 3.3a states with regards to GMP: '*The quantity of the additive added to food shall be limited to the lowest possible level necessary to accomplish its desired effect*'.

Adopted provisions for nitrites and nitrates in the Codex standards

5. Currently, no adopted provision exists for nitrates in the GSFA. Nitrites are only allowed in the food category 08.2.2: Heat-treated processed meat, poultry, and game products in whole pieces or cuts and in the food category 08.3: Processed comminuted meat, poultry, and game products. Table 1 shows the details of the adopted nitrite provisions in the GSFA.

Table 1 Adopted provisions for nitrites (INS 249 and INS 250) in the GSFA

Food Categories	**Maximum Limit (mg/kg)**	**Notes[1]**
08.2.2 Heat-treated processed meat, poultry, and game products in whole pieces or cuts	80	32 288
08.3 Processed comminuted meat, poultry, and game products	80	32 286 287

[1]Notes

- **32**: As residual NO2 ion
- **286**: For use in products conforming to the Standard for Luncheon Meat (CODEX STAN 89-1981) and the Standard for Cooked Cured Chopped Meat (CODEX STAN 98-1981).
- **287**: Except for use in products conforming to the Standard for Corned Beef (CODEX STAN 88-1981) at 30 mg/kg as residual NO2 ion.
- **288**: For use in products conforming to the Standard for Cooked Cured Ham (CODEX STAN 96-1981) and Cooked Cured Pork Shoulder (CODEX STAN 97-1981).

6. The above provisions for nitrites were adopted in the GSFA in 2014 as a consequence of the alignment exercise, which was done on the five meat standards. The individual food additive provisions in the meat standards were replaced by the general reference to the GSFA after the commodity standards provisions had been "aligned" with the GSFA provisions applying the agreed decision-tree. It should be noted that before the alignment all 5 meat standards had two Maximum Use Levels for nitrites – i.e. "Maximum Ingoing Amount" and "Maximum Level Calculated on the Total Net Content of the Final Product", the latter ML being approx. a half of the former ML.

7. Apart from the five meat standards no other Codex standards permit the use of nitrites. However, nitrates are permitted for use according to the *Standards for Cheddar* (CODEX STAN 263-1966), *Danbo* (CODEX STAN 264-1966), *Edam* (CODEX STAN 265-1966), *Gouda* (CODEX STAN 266-1966), *Havarti* (CODEX STAN 267-1966), *Samsø* CODEX STAN 268-1966), *Emmental* (CODEX STAN 269-1967), *Tilsiter* (CODEX STAN 270-1968), *Saint-Paulin* (CODEX STAN 271-1968) and *Provolone* (CODEX STAN 272-1968). In all those standards nitrates are permitted at 35 mg/kg, singly or in combination, expressed as nitrate ion. In addition, the *General Standard for Cheese* (CODEX STAN 283-1978) permits the use of nitrates at 50 mg/kg, expressed as $NaNO_3$.

Technological need for nitrates and nitrites

8. JECFA in its evaluation reports mention that nitrites and nitrates are used for their preservative effect (particularly on *Clostridum botulinum*) and colour fixation in some processed foods, but did not further explain on the mechanism by which nitrite and nitrate exert their food additive function (JECFA 1995, JECFA 2002).

9. According a publication of the Regional Office for Asia and the Pacific of the FAO of 2007: '*the primary purpose of nitrite is to create a heat resistant red colour in a chemical reaction with the muscle pigment, which makes cured meat products attractive for consumers. Nitrite has a certain inhibitory effect on the growth of bacteria. This effect is particularly pronounced in canned meat products which are usually stored without refrigeration, where small numbers of heat resistant bacteria may have survived but their growth is inhibited by the presence of nitrite. Nitrite has the potential of attributing a specific desirable curing flavour to cured products. In the presence of nitrite fats are stabilized and rancidity in meat products retarded i.e., an antioxidant effect*'' (RAP 2007).

10. The European Food Safety Authority (EFSA) in 2003 reviewed the technological need of nitrite and nitrate in meat products. Meat, because of its nutrient availability, pH and water activity is a good medium for microorganisms. Although good hygienic practices can reduce microbiological contamination, sterile fresh meat is not likely to be obtained. *C. botulinum* spores occur in soil throughout the whole world. Toxins of *C. botulinum* can cause botulism, a food-borne disease with a high mortality rate. Whereas for fresh meat, appropriate storage condition, storage time and heating would be sufficient to reduce microbiological risk, growth of (heat-resistant) spores and the subsequent formation of botulism toxins during production (e.g. maturation, fermentation) and storage of meat products, cannot be excluded. Thus, botulism, is a potential health threat. Nitrites are effective in reducing *C. botulinum* and meat products cured with nitrites have a good record of safety regarding *C. botulinum*. Under some conditions (not further specified by EFSA), nitrites are also effective against *L. monocytogenes*, another Gram-positive microorganism. Nitrites were ineffective to control Gram-negative enteric pathogens, such as Salmonellae (EFSA 2003). Thus, nitrite (partially) contributes to the microbiological safety.

11. Nitrites have also an effect on flavour, colour and anti-oxidative stability of cured meat products, but often at lower levels than needed for preservation. The effect of nitrite on flavour formation is not fully understood (EFSA 2003, FCEC 2016).

12. Nitrites may not exert an antimicrobial effect in all meat products as the Codex Committee on Processed Meat and Poultry Products noted in their 14th meeting in 1989 that "nitrite" as far as corned beef was concerned had no preservative role and was needed mainly for the development of colour (ALINORM 89/16).

13. According to a recent report of the food chain evaluation consortium (FCEC), if a correct combination of key parameters, such as water activity, pH, storage temperature and shelf life are achieved, microbial safety can be ensured without the presence of nitrites (FCEC 2016).

14. 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). Nitrates are allowed by some CODEX members in ripened cheese (e.g. EU, Australia and New Zealand, Canada), meat products (e.g. EU, Australia and New Zealand, Canada), pickled fish products (e.g. EU), some smoked, cured fish products (e.g. USA) and cured cod roe (USA) (EU 2008, FSANZ 2011, Health Canada 2012, CFR 2015).

Nitrosamine formation

15. Addition of nitrite and nitrate to food can result in formation of N-nitrosocompounds in the food itself during manufacturing and storage of food (JECFA 1995, SCF 1995, FCEC 2016). A clear correlation exists between the amount nitrite added for curing of meat and the formation of volatile nitrosamines in cured meat products (SCF 1995).

16. According to the FCEC report, there is insufficient data on the relationship between the ingoing amounts of nitrite and nitrosamine formation (FCEC 2016).

17. N-Nitrosamine formation requires free amines, which can be generated during ageing and fermentation of meat. In addition, for N-nitrosamine formation, the pH in meat must be low enough or metal ions must be present in order to form NO+, the active agent in N-nitrosamine formation (Honikel 2008). Only secondary amines give stable N-nitrosamines. According to Honikel (2008), meat mostly contains primary amino acids, which form unstable N-nitrosamines that easily degrade to alcohols.

18. N-Nitrosocompounds can also be generated during heating of cured meat products at home (e.g. frying bacon or baking salami on a pizza). Formation of N-nitrosocompounds upon baking and frying of cured meat products is complex, because varying effects (lowering or increasing the concentration of N-nitrosocompounds) of frying and baking of processed meat were observed for different N-nitrosocompounds (Hermann et al., 2014). According to Honikel (2008), N-nitrosamines can be formed dung heating above 130˚C.

19. In addition, N-nitrosocompounds can be formed endogenously in the gastrointestinal tract when both nitrite and nitrosatable compounds such as amines are present together at high concentrations (JECFA 1995, EFSA 2003). With respect to endogenous N-nitrosocompounds formation out of nitrates, it should be noted that ingested nitrate is known to be readily absorbed in the human body, concentrated in salivary glands, excreted in saliva and reduced to nitrite in the gastrointestinal tract (JECFA 1995, JECFA2002, EFSA 2003).

Overview of evaluations on processed meat

20. JECFA at its 44th meeting noted that several studies showed that food preparation techniques such as malting, smoking, drying and broiling of meat and fish products, as well as frying of cured meats including bacon, can, under certain conditions (not further specified) promote formation of nitrosamines. It therefore emphasized the need for good manufacturing practices in the preparation of these products to reduce the exposure to these nitrosamines (JECFA 1995).

21. 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 type of processed meats, nor did it consider any quantitative exposure of identified compounds in the processed meat. 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-nitrosocompounds, polycyclic aromatic hydrocarbons and heterocyclic aromatic amines, depending on the production process (Bouvard et al., 2015).

Overview of N-nitrosocompounds evaluations

<u>General</u>

22. JECFA only addressed N-nitrosocompounds as substances that can be generated in food or in the gastrointestinal tract in relation to nitrite and nitrate ingestion (JECFA 1995, 2002).

23. Several N-nitrosocompounds are classified as probably or possibly carcinogenic to humans by IARC (IARC 2016).

24. The International Programme on Chemical Safety (IPCS) in 2002 evaluated N-nitrosdimethylamine (NMDA), one of the N-nitrosocompounds that can be generated in food or endogenously in the gastrointestinal tract, and concluded that 'NDMA is a genotoxic carcinogen, and exposure should be reduced to the extent possible' (IPCS 2002).

25. The US department of Health and Human services in their report on carcinogens stated that human exposure to nitrosamines can result from formation of N-nitroso compounds either in food during storage or preparation or in vivo, usually in the stomach. They classified several N-nitrosamines as reasonably anticipated to be a human carcinogen (USSSH 2014).

26. FCEC in their report mention that nitrosamines formed during preparation of cured meat products at home and during gastrointestinal digestion upon consumption of cured meat are likely to be more relevant routes than nitrosamines formed during the production process (FCEC 2016).

In food

27. JECFA in 1995 at their 44th meeting stated that nitrite with and without nitrosatable precursors is genotoxic (JECFA 1995).

28. With respect to N-nitrosocompound formation in food, JECFA in 1995 emphasized the need for good manufacturing practice when nitrites and nitrates are used as food additives to ensure that that the minimum of these substances are used to achieve their functional purpose (JECFA 1995).

29. The Scientific Committee on Food (SCF) in 1995 concluded that dietary exposure to N-nitrosocompounds is very low, but that due to the genotoxic and carcinogenic nature of these substances, continued efforts should be done to reduce this dietary exposure (SCF 1995).

Endogenously generated N-nitrosocompounds

30. With respect to endogenously formed N-nitrosocompounds, JECFA in 1995 and 2002 observed that 'there are quantitative data only on those N-nitroso compounds that are readily formed endogenously, such as N-nitrosoproline, which is 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 precursors achievable in the diet, a quantitative risk assessment on the basis of endogenously formed N-Nitrosocompounds was not considered be appropriate.' (JECFA 1995, JECFA 2002).

31. IARC in 2002 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 N-nitroso compounds. 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.' 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 2002).

32. EFSA in 2010 referred to JECFA 1995.

Overview of nitrites evaluations

Acute effects

33. JECFA recommended at their 50th meeting in 2002 to review the acute effects of nitrite (methaemoglobinaemia) at a future meeting (JECFA 2002).

34. The WHO in 2011 in their 4th edition of the Guidelines for drinking water quality, derived a guideline value for nitrite in drinking water (3 mg nitrite ion/l) based on lowest level of the dose range associated with methaemoglobinaemia, i.e. 0.4 mg/kg body weight for bottle-fed infants. The WHO also mentioned that although clinically significant methaemoglobinaemia can occur as a result of extremely high nitrate intake in adults and children, the most familiar situation is its occurrence in bottle-fed infants. Gastrointestinal infection caused by nitrate-reducing bacteria may increase sensitivity towards methaemoglobinaemia. (WHO, 2011)

35. Food Standards Australia New Zealand (FSANZ) in 2013 concluded that an acute reference dose could not be established, but compared intakes with intakes known to cause methaemoglobinaemia (FSANZ 2013).

Chronic effects

36. JECFA evaluated nitrites in 1995 at their 44th meeting. As mentioned above under point 31, nitrite with and without nitrosatable precursors is genotoxic. As mentioned under point 34, JECFA considered a quantitative risk assessment based on endogenously formed N-nitrosocompounds not appropriate. JECFA therefore based the safety evaluation of nitrite on its direct chronic effects on heart and lungs in two-years study in rats and established an ADI of 0-0.06 mg/kg bw, expressed as nitrite ion (JECFA 1995).

37. JECFA at their 59th meeting in 2002, reconsidered the ADI of nitrite to be 0-0.07 mg/kg bw based on chronic effects on heart and lungs (JECFA 2002).

38. IARC in 2010 concluded that there is limited evidence in humans for the carcinogenicity of nitrite in food. Nitrite in food is associated with an increased incidence of stomach cancer. There is limited evidence in experimental animals for the carcinogenicity of nitrite per se (IARC 2010).

39. EFSA has set an ADI for nitrite comparable to JECFA (0.07 mg/kg bw/day; EFSA 2010).

40. Exceedance of the ADI may occur for nitrites (JECFA 2002, EFSA 2010). Currently, new European risk assessments performed by EFSA are ongoing and expected to be published by the end of 2016.

41. JECFA at their 59th meeting recommended that the Codex Committee on Food Additives and Contaminants reconsider the maximum level of nitrite in the *Codex General Standard for Food Additives* (GSFA), as the estimated intakes might exceed the ADI (JECFA 2002).

Overview of nitrates evaluations

42. JECFA evaluated nitrates in 1995 at their 44th meeting and concluded that nitrate itself has a relatively low toxicity and did not display genotoxic activity itself but toxicity should be seen in light of nitrite, which can be formed in the human body upon reduction of nitrate. JECFA based the safety evaluation of nitrate on its direct chronic effects on growth and established an ADI of 0-3.7 mg/kg bw, expressed as nitrate ion (JECFA 1995).

43. JECFA reconsidered nitrates in 2002 at their 59th meeting and concluded that the ADI of 0-3.7 mg/kg bw, expressed as nitrate ion, could be maintained (JECFA 2002).

44. IARC in 2010 concluded on ingested nitrate that there is inadequate evidence in humans for the carcinogenicity of nitrate in food and drinking water. There is inadequate evidence in experimental animals for the carcinogenicity of nitrate (IARC 2010).

45. EFSA has set ADIs for nitrate comparable to JECFA (3.7 mg/kg bw/day for nitrate ions, respectively; EFSA 2010).

46. Exceedance of the ADI may occur (JECFA 2002). Intake of nitrates from natural sources is a more important contributor to exposure than intake of nitrates via food additives (JECFA 2002). Currently, new European risk assessments performed by EFSA are ongoing and expected to be published by the end of 2016.

47. JECFA in 2002 recommended that the Codex Committee on Food Additives and Contaminants reconsider the maximum levels of nitrate in the GSFA, as the estimated intakes of nitrate might exceed the ADI (JECFA 2002).

Estimation of the safety aspects of the proposed Maximum Use Levels for nitrites and nitrates

48. Annex A to the GSFA depicts guidelines for the use of food additives with numerical ADIs, thus also including nitrates and nitrites. According to these guidelines, the following calculations should be performed (CODEX STAN 192-1995, guidelines 5-9):

a. FS*ADI*40

b. FS*ADI*80

c. FS*ADI*160

d. FS*ADI*320,

With FS being the fraction for use in solid food (equal to 1 when the additive is only used in solid food, as is the case for nitrites and nitrates).

Table 2 shows these calculations for nitrates and nitrites together with their acceptability.

Table 2. Calculated reference values for maximum levels according to Annex A to the GSFA and their acceptability (CODEX STAN 192-1995, guidelines 5-9).

Calculations	**Nitrite (mg/kg as NO_2 ion)**	**Nitrate (mg/kg as NO_3 ion)**	**Acceptability**
FS*ADI*40	2.8	148	When proposed levels are lower than this value, provision suitable in food in general.
FS*ADI*80	5.6	296	When proposed levels are below this value, use is acceptable provided the daily consumption of the food containing the additive will usually not exceed half of the assumed maximum solid food intake (i.e. 12.5 g solid food/kg bw/day).
FS*ADI*160	11.2	592	When proposed levels are below this value, use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food/kg bw/day).
FS*ADI*320	22.4	1184	When proposed levels are below this value, use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one eighth of the assumed maximum solid food intake (i.e. 3.13 g solid food/kg bw/day); If proposed use levels are higher than this value, the use should only be accepted for products where calculation of potential intake from all proposed uses will show that exceeding the ADI is unlikely, or if estimation of the intake of the additive based on more exact intake estimates methods show that the use levels are acceptable.

Proposed provisions and their corresponding maximum levels

49. Table 3 and 4 summarises the proposed provisions for nitrites for nitrites of CX/FA 16/48/7, respectively.

Table 3. Provisions for nitrites proposed for inclusion in the GSFA as contained in CX/FA 16/48/7, together with their acceptability based on the guidelines of Annex A of the GFSA and the calculated amount of food to be eaten by a child weighing 20 kg and an adult weighing 60 kg to equal or exceed the acceptable daily intake (ADI) for the requested maximum level (ML)

Food Categories	**INS Functional Class**	**ML (mg/kg)**	**Notes[1]**	**Acceptability Guidelines Annex A GSFA**	**Calculated intake to reach or exceed the ADI**
01.6.1 Unripened cheese 01.6.2 Ripened cheese	Colour Retention Agent, Preservative	discontinued			
01.6.4 Processed cheese 01.6.5 Cheese analogues	Colour Retention Agent, Preservative	20	32	Use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one eighth of the assumed maximum solid food intake (i.e. 3.13 g solid food/kg bw/day);	A 20 kg child would need to eat 70 g food to equal the ADI, for 60 kg adult, this would be 210 g.
08.1.1 Fresh meat, poultry, and game, whole pieces or cuts 08.1.2 Fresh meat, poultry, and game, comminuted	Colour Retention Agent, Preservative	130		Use should only be accepted for products where calculation of potential intake from all proposed uses will show that exceeding the ADI is unlikely, or if estimation of the intake of the additive based on more exact intake	A 20 kg child would need to eat 11 g food to exceed the ADI, for 60 kg adult, this would be 33 g.
08.2.1.1 Cured (including salted) non-heat treated processed meat, poultry, and game products in whole pieces or cuts	Colour Retention Agent, Preservative	Requested: 420 eWG: adopt at 250			At the ML of 250 mg/kg, a 20 kg child would need to eat 6 g food to exceed the ADI, for 60 kg adult, this would be 18 g.
08.2.1.2 Cured	Colour	Requested: 300			

Food Categories	INS Functional Class	ML (mg/kg)	Notes[1]	Acceptability Guidelines Annex A GSFA	Calculated intake to reach or exceed the ADI
(including salted) and dried non-heat treated processed meat, poultry, and game products in whole pieces or cuts	Retention Agent, Preservative	eWG: adopt at 250		estimates methods show that the use levels are acceptable.	
08.2.1.3 Fermented non-heat treated processed meat, poultry, and game products in whole pieces or cuts	Colour Retention Agent, Preservative	Requested: 130 eWG: adopt at 150			At the ML of 150 mg/kg, a 20 kg child would need to eat 10 g food to exceed the ADI, for 60 kg adult, this would be 30 g.
08.2.3 Frozen processed meat, poultry and game products in whole pieces or cuts	Colour Retention Agent, Preservative	Requested: 170 eWG: adopt at 150			
08.4 Edible casings (e.g. sausage casings	Colour Retention Agent, Preservative	Requested: 130 eWG: adopt at 250			At the ML of 250 mg/kg, a 20 kg child would need to eat 6 g food to exceed the ADI, for 60 kg adult, this would be 18 g.
09.2.4.1 Cooked fish and fish products		100	32	Use should only be accepted for products where calculation of potential intake from all proposed uses will show that exceeding the ADI is unlikely, or if estimation of the intake of the additive based on more exact intake estimates methods show that the use levels are acceptable.	At the ML of 100 mg/kg, a 20 kg child would need to eat 15 g food to exceed the ADI, for 60 kg adult, this would be 45 g.
09.2.5 Smoked, dried, fermented, and/or salted fish and fish products, including mollusks, crustaceans, and echinoderms		130		Use should only be accepted for products where calculation of potential intake from all proposed uses will show that exceeding the ADI is unlikely, or if estimation of the intake of the additive based on more exact intake estimates methods show that the use levels are acceptable.	At the ML of 130 mg/kg, a 20 kg child would need to eat 11 g food to exceed the ADI, for 60 kg adult, this would be 33 g.
09.3.3 Salmon substitutes, caviar, and other fish roe products		5		Use is acceptable provided the daily consumption of the food containing the additive will usually not exceed half of the assumed	At the ML of 5 mg/kg, a 20 kg child would need to eat 280 g food to exceed the ADI, for 60 kg adult, this would be 840 g.

Food Categories	INS Functional Class	ML (mg/kg)	Notes[1]	Acceptability Guidelines Annex A GSFA	Calculated intake to reach or exceed the ADI
				maximum solid food intake (i.e. 12.5 g solid food/kg bw/day).	

[1]Notes

- **32**: As residual NO2 ion

Table 4. Provisions for nitrates proposed for inclusion in the GSFA as contained in CX/FA 16/48/7, together with their acceptability based on the guidelines of Annex A of the GFSA and the calculated amount of food to be eaten by a child weighing 20 kg and an adult weighing 60 kg to equal or exceed the acceptable daily intake (ADI) for the requested maximum level (ML)

Food Category	INS Functional Class	ML (mg/kg)	Notes[1]	Acceptability Guidelines Annex A GSFA	Calculated intake to equal or exceed the ADI
01.6.1 Unripened cheese	Colour Retention Agent, Preservative	40 eWG: discontinue	30	Provision suitable in food in general	At a ML of 40, a 20 kg child would need to eat 1850 g food to equal the ADI (3.7 mg/kw bw/day), for 60 kg adult, this would be 5550 g
01.6.2 Ripened cheese	Colour Retention Agent, Preservative	Requested: 40 eWG: Adopt at 50 mg/kg with 2 notes "excluding soft cheeses as defined in Codex Stan 283-1978" and "excluding products conforming to the standard for cheese in brine (Codex Stan 208-1999)		Provision suitable in food in general	At a ML of 50, A 20 kg child would need to eat 1480 g food to equal the ADI, for 60 kg adult, this would be 4440 g
01.6.4 Processed cheese 01.6.5 Cheese analogues	Colour Retention Agent, Preservative	Requested: 40 eWG: Adopt at 50 mg/kg			
08.1.1 Fresh meat, poultry, and game, whole pieces or cuts	Colour Retention Agent, Preservative	Requested: 150		ML 150: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed half of the assumed maximum solid food intake (i.e. 12.5 g solid food/kg bw/day)	A 20 kg child would need to eat 500 g food to exceed the ADI, for 60 kg adult, this would be 1500 g
08.1.2 (Fresh meat, poultry, and game, comminuted)	Colour Retention Agent, Preservative	Requested: 150 eWG: adopt at 300		ML 300: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food/kg bw/day)	At a ML of 300, a 20 kg child would need to eat 250 g food to exceed the ADI, for 60 kg adult, this would be 750 g
08.2.1.1 (Cured (including salted) non-heat treated processed meat, poultry, and game products in whole	Colour Retention Agent, Preservative	Requested: 1600 eWG: adopt at 500		ML 500: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the	At a ML of 500, a 20 kg child would need to eat 250 g food to exceed the ADI, for 60 kg adult, this would

Food Category	INS Functional Class	ML (mg/kg)	Notes[1]	Acceptability Guidelines Annex A GSFA	Calculated intake to equal or exceed the ADI
pieces or cuts)				assumed maximum solid food intake (i.e. 6.25 g solid food/kg bw/day)	be 450 g
08.2.1.2 (Cured (including salted) and dried non-heat treated processed meat, poultry, and game products in whole pieces or cuts	Colour Retention Agent, Preservative	Requested: 450 eWG: adopt at 500 mg/kg			
08.2.1.3 (Fermented non-heat treated processed meat, poultry, and game products in whole pieces or cuts)	Colour Retention Agent, Preservative	Requested: 450 eWG: adopt at 300		ML 300: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food/kg bw/day)	At a ML of 300, a 20 kg child would need to eat 250 g food to exceed the ADI, for 60 kg adult, this would be 750 g
08.2.2 (Heat-treated processed meat, poultry, and game products in whole pieces or cuts)	Colour Retention Agent, Preservative	Requested: 365 eWG: Adopt at 300 mg/kg with note excluding CS 96-1981 and 97-1981			
08.2.3 (Frozen processed meat, poultry and game products in whole pieces or cuts)	Colour Retention Agent, Preservative	Requested: 220 eWG: adopt at 300			
08.3.1.1 (Cured (including salted) non-heat treated processed comminuted meat, poultry, and game products)	Colour Retention Agent, Preservative	Requested: 1250 eWG: adopt at 500		ML 500: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food intake/kg bw/day)	At a ML of 500, a 20 kg child would need to eat 250 g food to exceed the ADI, for 60 kg adult, this would be 450 g
08.3.1.2 (Cured (including salted) and dried non-heat treated processed comminuted meat, poultry, and game products)	Colour Retention Agent, Preservative	Requested: 365 eWG: adopt at 500 mg/kg			
08.3.1.3 (Fermented non-heat treated processed comminuted meat, poultry, and game products)	Colour Retention Agent, Preservative	Requested: 365 eWG: adopt at 500 mg/kg			
08.3.2 (Heat-treated processed comminuted meat, poultry, and game products)	Colour Retention Agent, Preservative	Requested: 365 eWG: adopt at 300 mg/kg with note excluding CS 88-1981, 89-1981, and 98-1981	30	ML 300: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food intake/kg bw/day	At a ML of 300, a 20 kg child would need to eat 250 g food to exceed the ADI, for 60 kg adult, this would be 750 g
08.3.3 (Frozen processed comminuted meat, poultry, and game products)	Colour Retention Agent, Preservative	Requested: 365 eWG: adopt at 300 mg/kg			
08.4 (Edible casings (e.g. sausage casings))	Colour Retention Agent, Preservative	Requested: 150 eWG: adopt at 250		ML 250: use is acceptable provided the daily consumption of the food containing the additive	At a ML of 300, a 20 kg child would need to eat 300 g food to exceed the ADI, for 60 kg

Food Category	INS Functional Class	ML (mg/kg)	Notes[1]	Acceptability Guidelines Annex A GSFA	Calculated intake to equal or exceed the ADI
				will usually not exceed half of the assumed maximum solid food intake (i.e. 12.5 g solid food/kg bw/day)	adult, this would be 900 g
09.2.1 Frozen fish, fish fillets, and fish products, including mollusks, crustaceans, and echinoderms		150	30	ML 150: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed half of the assumed maximum solid food intake (i.e. 12.5 g solid food/kg bw/day)	A 20 kg child would need to eat 500 g food to exceed the ADI, for 60 kg adult, this would be 1500 g
09.2.5 Smoked, dried, fermented, and/or salted fish and fish products, including mollusks, crustaceans, and echinoderms		365	30	ML 365: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed one fourth of the assumed maximum solid food intake (i.e. 6.25 g solid food/kg bw/day).	A 20 kg child would need to eat 203 g food to exceed the ADI, for 60 kg adult, this would be 608 g
09.3 Semi-preserved fish and fish products, including mollusks, crustaceans, and echinoderms		220	30	ML 220: use is acceptable provided the daily consumption of the food containing the additive will usually not exceed half of the assumed maximum solid food intake (i.e. 12.5 g solid food/kg bw/day).	A 20 kg child would need to eat 336 g food to exceed the ADI, for 60 kg adult, this would be 1010 g
14.2.4 Wines (other than grape)		70	30 31	Provision suitable in food in general.	A 60 kg adult would need to consume 3175 g food to exceed the ADI.

[1]Note 30: As residual NO3 ion

Note 31: on the mash used basis

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