# Maximum levels proposed for the addition of niacin to foods including food supplements

The accompanying main opinion "**Updated recommended maximum levels for the addition of vitamins and minerals to food supplements and conventional foods**" can be found here: https://www.bfr.bund.de/cm/349/updated-recommended-maximum-levels-for-the-addition-of-vitamins-and-minerals-to-food-supplements-and-conventional-foods.pdf

## 1 Results

The term "niacin" is used as a collective term for nicotinic acid and nicotinic (acid) amide (SCF, 2002). Both substances may be added to foods as sources of niacin. In food supplements, inositol hexanicotinate is permitted as an additional source of niacin. Due to substance-specific characteristics, separate maximum levels have been derived for the three niacin sources mentioned.

### 1.1 Nicotinamide (= nicotinic acid amide)

The German Federal Institute for Risk Assessment (BfR) recommends for the addition of nicotinamide to food supplements a maximum level of 160 milligrams (mg) per daily recommended dose of an individual product. For food supplements with daily recommended doses of more than 16 mg nicotinamide, a caution note is recommended that pregnant women should refrain from taking such products (including a justification, if applicable) (Table 1).

For the fortification of conventional foods, based on the assumption of a 'saturated' market of fortified foods (30 % of the daily energy intake comes from fortified foods), a maximum level of 37 mg per 100 grams (g) is recommended for solid foods and of 10 mg per 100 millilitres (ml) for beverages (Table 1).

**Table 1: Proposed maximum levels for nicotinamide**

| Food category | Maximum levels |
|---|---|
| Food supplements (per daily recommended dose of an individual product) | 160 mg** |
| Fortified solid foods (per 100 g) | 37 mg |
| Fortified beverages (per 100 ml) | 10 mg |

** For products with a daily recommended dose of more than 16 mg, an information note is recommended that pregnant women should refrain from taking such products (including a justification, if applicable).

### 1.2 Nicotinic acid

The BfR recommends for the addition of nicotinic acid to food supplements a maximum level of 4 mg per daily recommended dose of a food supplement. In the case of conventional foods, fortification with nicotinic acid should be avoided (Table 2).

**Table 2: Proposed maximum levels for nicotinic acid**

| Food category | Maximum levels |
|---|---|
| Food supplements (per daily recommended dose of an individual product) | 4 mg |
| Fortified conventional foods (per 100 g or 100 ml) | No addition |

### 1.3 Inosithexanicotinate (= inositol niacinate)

For the addition of inositol hexanicotinate to food supplements, the BfR recommends a maximum level of 4.4 mg per daily recommended dose of a food supplement. The use of inositol hexanicotinate as a source of niacin for the fortification of conventional foods is currently not permitted under European Union food law (Table 3).

**Table 3: Proposed maximum levels for inositol hexanicotinate**

| Food category | Maximum levels |
|---|---|
| Food supplements (per daily recommended dose of an individual product) | 4.4 mg |
| Fortified conventional foods (per 100 g or 100 ml) | No addition** |

** Inositol hexanicotinate is not listed in Annex 2 to Regulation (EC) No 1925/2006.

## 2 Rationale

### 2.1 Tolerable Upper Intake Level[1] (UL) and Dietary Reference Values

#### *2.1.1 Tolerable Upper Intake Level (UL)*

The term "niacin" comprises nicotinic acid and nicotinic (acid) amide. Both substances have different toxicity profiles. The former Scientific Committee on Food (SCF) of the European Commission derived a UL for nicotinic acid of 10 mg per day for adults and of 8 mg per day for adolescents aged 15 to 17 years. By contrast, for nicotinamide a UL of 900 mg per day was derived for adults and of 700 mg per day for 15- to 17-year-old adolescents (SCF, 2002; Table 4).

From the point of view of the BfR, differentiated maximum levels are therefore to be derived for both sources of niacin for the addition to foods including food supplements.

Inositol hexanicotinate is a nicotinic acid derivative[2] and, as nicotinic acid can be released from it, is used as a source of niacin. The use of the substance for nutritional purposes as a source of niacin in food supplements was assessed by the European Food Safety Authority (EFSA) in 2009. The Authority considered such use to be safe provided that the levels of use comply with the UL derived for nicotinic acid (= 10 mg per day for adults)[3].

EFSA acknowledged that basing the UL derivation for nicotinic acid on the flushing effect, is considered as a conservative risk assessment approach for inositol hexanicotinate because of the slow release of nicotinic acid from inositol hexanicotinate. However, due to a lack of data, the Panel concluded that the UL derived for nicotinic acid should also be used in the risk assessment of inositol hexanicotinate (EFSA, 2009). Yet, it should be noted that this EFSA opinion focused primarily on the suitability of inositol hexanicotinate as a source of niacin rather than on the derivation of a UL for this substance.

[1] Tolerable Upper Intake Level = Maximum level of total chronic daily intake of a nutrient (from all sources) considered to be unlikely to pose a risk of adverse health effects to humans.

[2] Ester consisting of one molecule of inositol and six molecules of nicotinic acid

[3] An intake of 10 mg of nicotinic acid is equivalent to 11 mg of inositol hexanicotinate, and the UL derived for 15- to 17-year-olds of 8 mg of nicotinic acid per day is equivalent to 8.8 mg per day of inositol hexanicotinate.

**Table 4: Tolerable Upper Intake Level (UL) for nicotinamide and nicotinic acid**

| Age groups | UL (SCF, 2002) | |
|---|---|---|
| | Nicotinamide | Nicotinic acid |
| | mg/day | |
| 4 to 6 years | 220 | 3 |
| 7 to 10 years | 350 | 4 |
| 11 to 14 years | 500 | 6 |
| 15 to 17 years | 700 | 8 |
| Adults | 900 | 10 |

### *2.1.2 Dietary reference values*

The level of the daily niacin requirement depends on the level of the energy requirement. The D-A-CH societies[4] have derived a dietary recommended intake value of 6.6 mg niacin equivalents[5] per 1,000 kilocalories (kcal) (≈ 1.6 mg per MJ) for all age groups. Based on age- and gender-specific guidance values for energy intake at a physical activity level (PAL) of 1.4, this translates into recommended intake values of between 9 and 15 mg per day for children from 4 to under 15 years of age. For males and females aged 15 to under 19 years, intake recommendations are 17 mg per day and 13 mg per day, respectively. For men and women aged 19 years and older, age-dependent decreasing intakes between 16 to 14 mg per day and between 13 to 11 mg per day, respectively, are recommended (D-A-CH, 2019; Table 5). EFSA has also derived an energy-related intake recommendation of 1.6 mg per MJ, corresponding to approximately 6.6 mg niacin equivalents per 1,000 kcal, for all age groups (EFSA, 2014; Table 5).

**Table 5: Dietary reference values for niacin**

| Age groups | Recommended intake values* (D-A-CH, 2019**; EFSA, 2014) | |
|---|---|---|
| | male | female |
| | mg niacin equivalents[2]/day | |
| 4 to < 7 years | 9 | |
| 7 to < 10 years | 11 | 10 |
| 10 to < 13 years | 13 | 11 |
| 13 to < 15 years | 15 | 13 |
| 15 to < 19 years | 17 | 13 |
| Adults | 14–16 | 11–13 |
| Pregnant women | 14 (2nd trimenon); 16 (3rd trimenon) | |
| Lactating women | 16 | |

* Data are based on the energy-related intake recommendations of 6.6 mg niacin equivalent per 1,000 kcal and the age- and gender-specific guidance values for energy intake based on a PAL value of 1.4.

[4] German-Austrian-Swiss Nutrition Societies

[5] Niacin can also be formed from the amino acid tryptophan. The following conversion is applied: 1 mg niacin equivalents = 1 mg niacin = 60 mg tryptophan.

** last revised in 2015

## 2.2 Exposure

In the second National Food Consumption Survey (NFCS) II, median intakes of niacin equivalents of 36.1 mg per day (m) and of 25.2 mg per day (f) were recorded in male and female adolescents aged 14 to 18 years, respectively; the 95th intake percentiles of this age group was at 79.5 mg (m) and 59.7 mg (f) per day. In adult men (19 to 80 years), median intakes ranged from 31.5 to 39.9 mg per day and the 95th intake percentiles ranged from 50.3 to 83.1 mg per day, depending on age group. Women 19 years and older had median intakes between 24.7 and 27.9 mg per day and the 95th percentile intakes ranged between 39.7 and 54.6 mg per day (MRI, 2008).

In the EsKiMo study (nutrition module in KiGGS[6]), median intakes of niacin equivalents in 6- to 14-year-old boys ranged from 19.5 to 36.4 mg and in the 95th percentiles of this age group from 30.2 to 76.0 mg per day. In 6- to 14-year-old girls, median intakes ranged from 17.9 to 27.3 mg and in the 95th percentiles, from 25.6 to 68.2 mg (all these data do not include niacin intake via food supplements) (Mensink et al., 2007).

## 2.3 Maximum levels for niacin (nicotinamide, nicotinic acid and inositol hexanicotinate) in food supplements and conventional foods

### 2.3.1 Maximum levels for nicotinamide

#### *2.3.1.1 Maximum levels for nicotinamide in food supplements*

Applying the derivation procedure proposed by the BfR, based on the 95th intake percentile of niacin equivalents in 14- to 18-year-old male adolescents of 80 mg per day, the resulting residual amount of 620 mg per day is divided equally between food supplements and conventional foods.

$$\text{Residual amount} = UL_{\text{15-to 17-year-olds}} - P_{\text{95Nutrition}}$$

$$\text{Residual amount} = 700 \text{ mg/day} - 80 \text{ mg/day} = 620 \text{ mg/day}.$$

Accordingly, an amount of 310 mg of nicotinamide per day is available for each of the two categories.

Since a multiple intake of several nicotinamide-containing food supplements cannot be excluded (Römer and Heuer, 2017), an uncertainty factor of 2 is taken into account, which results, on the basis of the available data, in a maximum level for the addition of nicotinamide to food supplements of 155 mg or, rounded up, of 160 mg per daily recommended dose of a food supplement (310 mg per day ÷ 2 = 155 mg per day; rounded to 160 mg per day).

The SCF (2002) pointed out that the UL (derived for adults) is not applicable to pregnant and lactating women because there were insufficient data on the safety of nicotinamide (or nicotinic acid) for these population groups. However, the SCF (2002) did not see evidence that nicotinamide, at the levels commonly ingested in Europe via (fortified) foods, is associated with health risks for pregnant or lactating women, and according to one study, an additional intake of 15 mg per day was not associated with adverse pregnancy outcomes (MRC Vitamin

[6] German Health Interview and Examination Survey for Children and Adolescents

Study Research Group, 1991 cited in: SCF, 2002). In view of the existing data gaps on the health effects of additional intake of nicotinamide from supplements in pregnant women, for the time being it is recommended to limit the addition of nicotinamide to food supplements for pregnant women to the level of the dietary reference value derived by the D-A-CH Societies for pregnant women in the 3rd trimester of 16 mg nicotinamide per day, and to label food supplements with more than 16 mg nicotinamide per daily recommended dose with a note stating that pregnant women should refrain from taking such products (including a justification, if applicable).

The BfR recommends a maximum amount of 160 mg per daily recommended dose of a product for the addition of nicotinamide to food supplements. Food supplements with a daily dose of more than 16 mg nicotinamide should bear a note stating that pregnant women should refrain from taking such products (including a justification, if applicable).

#### *2.3.1.2 Maximum levels for nicotinamide in conventional foods*

For the fortification of conventional foods, an amount of 310 mg per day (residual amount$_{FF}$) is available for nicotinamide. Allocating this amount to the estimated daily energy intake from fortified foods and assuming that 15 % to a maximum of 30 % of the daily energy is consumed from fortified foods, this results in age-dependent maximum levels of between 22.0 and 103.3 mg nicotinamide per 100 kcal (Table 6).

**Table 6: Daily energy intakes (95th percentile, P95) and nicotinamide levels, assuming that 15% or 30% of the ingested energy comes from fortified foods**

| Age groups | Energy intake* | Fortification of 15 % of daily energy intake | | Fortification of 30 % of daily energy intake | |
|---|---|---|---|---|---|
| | | 15 % of daily energy intake | Nicotinamide** | 30 % of daily energy intake | Nicotinamide** |
| | kcal/day | kcal | mg/100 kcal | kcal | mg/100 kcal |
| 4 to 6 years | 2,000 | 300 | 103.3 | 600 | 51.7 |
| 7 to 9 years | 2,400 | 360 | 86.1 | 720 | 43.1 |
| 10 to 11 years | 2,550 | 383 | 80.9 | 765 | 40.5 |
| 12 years | 3,900 | 585 | 53.0 | 1,170 | 26.5 |
| 13 to < 15 years | 3,900 | 585 | 53.0 | 1,170 | 26.5 |
| 15 to < 17 years | 4,700 | 705 | 44.0 | 1,410 | 22.0 |
| Adults | 3,500 | 525 | 59.0 | 1,050 | 29.5 |

* P95 of energy intake: adults from NFCS II (MRI, 2008); children and adolescents aged 4-18 years age-dependent from VELS/EsKiMo/NVS II (Heseker et al., 2003; Mensink et al., 2007; MRI, 2008).

** if the residual amount of 310 mg per day is allocated to 100 kcal portions.

To ensure that the addition of nicotinamide to fortified foods does not cause any of the age groups to exceed the residual amount$_{FF}$ of 310 mg per day, the lowest level of nicotinamide resulting from the calculations is proposed as the maximum level for the whole population, i.e.: 22.0 mg per 100 kcal assuming that the market of fortified foods is "saturated" (30% of the daily energy comes from fortified foods) and 44.0 mg per 100 kcal assuming that a smaller part of the fortifiable foods is actually fortified or consumed (15 % of the energy comes from fortified foods) (Table 6).

➔ *Conversion of energy-based into maximum levels per 100 g of solid foods or per 100 ml of beverages*

The conversion of energy-based maximum levels into maximum amounts per 100 g of solid foods or per 100 ml of beverages was performed using data from Schusdziarra et al. (2010) and Bechthold (2014).

Taking into account the average energy densities (170 kcal per 100 g for solid foods and 45 kcal per 100 ml for energy-containing beverages such as juices and soft drinks), the maximum levels for nicotinamide by weight and by volume for the addition to conventional foods are given in the following table (Table 7) .

**Table 7: Conversion of energy-based to weight- and volume-based maximum levels for nicotinamide**

| **Nicotinamide per 100 kcal** | **Nicotinamide per 100 g or ml** | |
|---|---|---|
| | **Solid foods** (energy density 170 kcal/100g) | **Beverages** (energy density 45 kcal/100ml) |
| 44.0 mg* | 74.8 mg | 19.8 mg |
| 22.0 mg** | 37.4 mg | 9.9 mg |

* assuming that 15 % of the energy comes from consumption of fortified foods

** assuming that 30 % of the energy comes from consumption of fortified foods

If an additional criterion in setting maximum levels is that the amounts of vitamins added to a food should be significant in order to be allowed to be claimed on the product according to the current EU regulation[7], then according to Regulation (EU) No. 1169/2011 (Annex XIII: "Reference amounts"), at least 15 % of the respective reference value for labelling (NRV) should be contained in solid foods (per 100 g) and at least 7.5 % in beverages (per 100 ml). In that Regulation, a NRV of 16 mg is set for niacin. Accordingly, additions of niacin ≥ 2.4 mg per 100 g (equal to at least 15 % of the NRV in solid foods) and ≥ 1.2 mg/ per 100 ml (equal to at least 7.5 % of the NRV in beverages) would be considered significant. The maximum levels calculated in Table 7 meet these criteria for any labelling and claiming of added nicotinamide.

For the fortification of conventional foods, assuming a "saturated" market of fortified foods (30 % of the daily energy intake comes from fortified foods), a maximum level of 37.4 mg/100 g, rounded down to 37 mg/100 g, is recommended for solid foods and a maximum level of 9.9 mg/100 ml, rounded up to 10 mg/100 ml, for beverages.
Assuming that only a smaller portion of fortifiable foods is actually fortified or consumed (15% of energy intake from fortified foods), higher maximum levels of 74.8 mg/100 g, rounded up to 75 mg/100 g, would be possible for solid foods and 19.8 mg/100 ml, rounded up to 20 mg/100 ml, for beverages (Table 7).

[7] Conditions for claiming products with the claim "source of..." or "rich in...", according to EU Regulation 1924/2006 (Health Claim Regulation)

### 2.3.2 Maximum levels for nicotinic acid

#### *2.3.2.1 Maximum levels for nicotinic acid in food supplements*

When considering maximum recommended levels for nicotinic acid, niacin intake from the usual diet can be disregarded as the toxicological endpoint used for the UL derivation for nicotinic acid (occurrence of flushing) has only been observed in relation with isolated nicotinic acid or nicotinic acid added to foods, but not with foods naturally containing niacin.

Due to the low UL for nicotinic acid of 8 mg per day for adolescents aged 15 years and older, it is recommended that the total tolerable intake level of 8 mg per day be set as maximum level for food supplements. Applying the above-mentioned uncertainty factor of 2 to account for possible multiple consumption results in a maximum level of 4 mg for the addition of nicotinic acid to food supplements, per daily recommended dose of an individual product (8 mg per day ÷ 2 = 4 mg per daily dose.

For the addition of nicotinic acid to food supplements, the BfR recommends a maximum level of 4 mg per daily recommended dose of a product.

#### *2.3.2.2 Maximum levels for nicotinic acid in conventional foods*

Since the total tolerable daily intake of nicotinic acid has already been exhausted in the derivation of maximum levels for food supplements, it is recommended to refrain from fortifying conventional foods with nicotinic acid.

### 2.3.3 Maximum levels for inositol hexanicotinate

#### *2.3.3.1 Maximum levels for inositol hexanicotinate in food supplements*

As no UL has been derived for inositol hexanicotinate so far and EFSA (2009) recommended that there are no safety concerns when using inositol hexanicotinate as a source of niacin in supplements as long as the UL derived for nicotinic acid is not exceeded, the BfR proposes to provisionally proceed analogously to nicotinic acid in deriving the maximum level for inositol hexanicotinate, i.e. to set a maximum level corresponding to an intake of 4 mg nicotinic acid per daily recommended dose of a product. Since 4.4 mg of inositol hexanicotinate corresponds to 4 mg of nicotinic acid, this amount is proposed as the maximum level for inositol hexanicotinate per daily recommended dose of a food supplement.

#### *2.3.3.2 Maximum levels for inositol hexanicotinate in conventional foods*

Inositol hexanicotinate is not listed in Annex 2 of Regulation (EC) No 1925/2006. The addition of inositol hexanicotinate as a source of niacin to conventional foods is therefore currently not permitted in Europe. Maximum levels for the fortification of conventional foods are therefore not required.

**Further information on the BfR website on the subject of minerals**

Topic page on the assessment of vitamins and minerals in foods:
https://www.bfr.bund.de/en/vitamins_and_minerals-54417.html

"Opinions-App" of the BfR

## 3 References

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