Exposure Estimation

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This is a draft statement for discussion. This does not represent the views of the Committee and should not be cited.

275. Exposure assessments were carried out for the following population groups: Infants, toddlers, other children, adolescents, adults and the elderly. There are two toddler groups. One group represents ages 1 - 1.5 years and the data used were from DNSIYC as this survey covers infants and young children aged 4 - 18 months (1.5 years). The other toddler group covers ages 1.5 - 3+ years and data were obtained from the NDNS, as this survey covers all age groups from 1.5 years. The mean and 95th percentile estimates are presented for each population group and food category in mg/kg bw/day in Table 2.

276. The reported data are consumer-based, meaning that only subgroups of the population that consumed these categories of food were considered. The mean and 95th percentile total exposures are derived from the combined exposure for each individual in the respective age group. The mean and 95th percentile total exposures have not been derived by adding up the mean and 95th percentile values respectively, for the food categories, as not all consumers will be exposed in each category. Total exposures were calculated to estimate exposures from the total diet in Table 8. These were calculated from a distribution of individual total exposure of any combination of food categories, rather than by summation of the respective mean/95th percentile consumption values for each of the food categories.

277. The mean calculated total exposures for TiO2 from foods ranged from 3.3 to 11 mg/kg bw/day. The 95th percentile total exposures for TiO2 ranged from 9.1 to 26 mg/kg bw/day. The 3 food groups that contribute the most to these exposures are: protein products; Decorations, coatings and fillings, except 4.2.4; and Sauces.

Table 7: Estimated mean and 95th percentile (P95) exposures (mg/kg bw/day)[a] to titanium dioxide E171 from its use as a food additive based on the maximum reported use level. The reported data are consumer-based.

	Infants (4 – 11 months)	**Toddlers** (1 - 1.5 years)	**Toddlers** (1.5 - 3 years)	**Children** (4 - 10 years)	**Adolescents** (11 - 18 years)	**Adults** (19 - 64 years)	**Elderly** (≥65 years)
Food group	**Mean (P95[b])**	**Mean (P95[b])**	**Mean (P95[b])**	**Mean (P95[b])**	**Mean (P95[b])**	**Mean (P95[b])**	**Mean (P95[b])**
1.4- Flavoured fermented milk products including heat-treated products	0.24 (0.6)	0.2 (0.49)	0.16 (0.4)	0.097 (0.23)	0.05 (0.12)	0.044 (0.11)	0.049 (0.11)
1.8. Dairy analogues and whitener	0.91 (1.9)	1.6 (5.6)	1.9 (5.7)	0.63 (2.3)	0.21 (0.78)	0.15 (0.47)	0.18 (0.75)
12.5. Soups and broths	0.45 (1.5)	0.53 (1.7)	0.55 (1.3)	0.37 (0.94)	0.23 (0.56)	0.21 (0.54)	0.24 (0.64)
12.6. Sauces	4 (14)	4 (12)	3.5 (11)	3.3 (9.2)	2.2 (6.1)	1.7 (5)	1.4 (3.8)

12.7. Salads and savoury based sandwich spreads	2.2 (9.4)	3 (12)	2.9 (9.2)	1.9 (4.6)	0.92 (2.7)	0.95 (2.7)	0.94 (2.9)
12.9. Protein products	14 (55)	27 (190)	38 (160)	11 (49)	5.3 (18)	5.3 (18)	7.6 (30)
14.1.4. Flavoured drinks	0.15 (0.53)	0.35 (1.1)	0.47 (1.4)	0.44 (1.2)	0.4 (1)	0.24 (0.73)	0.12 (0.32)
15.2. Processed nuts	1.3 (4.6)	2.1 (8.1)	2.8 (9.9)	2 (7.2)	1 (3.6)	1.2 (3.9)	1.2 (3.4)
16. Desserts excluding products covered in categories 1, 3 and 4	1.2 (3.2)	1 (2.6)	0.64 (1.8)	0.33 (0.85)	0.14 (0.38)	0.11 (0.28)	0.15 (0.4)
17.1. Food supplements supplied in a solid form, excluding for infants and young children	1.4 (3.3)	1.7 (2.7)	1.9 (4.2)	1.1 (2.6)	0.82 (1.3)	0.95 (2.1)	0.85 (2.2)

17.2. Food supplements in a liquid form, excluding for infants and young children	3.9 (16)	3.2 (12)	3.3 (11)	1.4 (4)	3.2 (9)	1.7 (5.6)	0.91 (2.3)
3. Edible ices	0.88 (2)	1.1 (3)	1.3 (3.3)	1 (2.5)	0.55 (1.5)	0.32 (0.74)	0.35 (0.84)
5.2. Confectionery and sweets	1.2 (2.9)	2.7 (6.9)	2.6 (7)	2.4 (7.6)	1.5 (4.7)	0.79 (2.9)	0.54 (1.8)
5.3. Chewing gum	0 (0)	1.5 (1.5)	0.73 (1.6)	0.6 (1.7)	0.57 (2.2)	0.41 (1.2)	0.63 (0.82)
5.4. Decorations, coatings and fillings, except 4.2.4	6 (16)	7.2 (19)	6.8 (17)	6.6 (18)	3.8 (10)	2.3 (6)	2.3 (6.3)
7.2. Fine bakery wares	0.3 (0.9)	0.5 (1.4)	0.6 (1.5)	0.55 (1.3)	0.3 (0.76)	0.21 (0.55)	0.23 (0.57)

*Estimates are rounded to 2 significant figures.

**Calculated from a distribution of individual total exposure of any combination of food categories rather than by summation of the respective mean/95th percentile consumption values for each of the food categories.

a Exposure per bodyweight was calculated for each individual before calculating the mean and P97.5 exposure. The mean and 95th percentile estimates are presented for each population group and food category in mg/kg bw/day in Table 2. The estimates are based on individual bodyweights and not the average for the population group. However, for context, the average bodyweights of the population groups are 9.11 kg for infants; 10.9 kg for 12-18 months old; 14.6 kg for 1.5 -3 years; 27.1 kg for 4-10 years; 58.9kg fo r 11-18 years; 78.6 kg for 19-64 years; and 70. 6kg for the elderly.

b 95th percentile exposures have been reported for the UK to aid the comparison with data reported by EFSA.

Table 8: Estimated mean and 95th percentile (P95) total exposures (mg/kg bw/day)[a] to titanium dioxide E171 from its use as a food additive based on the maximum reported use level.

	Infants (4 – 11 months)	**Toddlers** (1 - 1.5 years)	**Toddlers** (1.5 - 3 years)	**Children** (4 - 10 years)	**Adolescents** (11 - 18 years)	**Adults** (19 - 64 years)	**Elderly** (≥65 years)
	Mean (P95b)	**Mean (P95b)**	**Mean (P95b)**	**Mean (P95b)**	**Mean (P95b)**	**Mean (P95b)**	**Mean (P95b)**
Total exposure**	3.9 (14)	6.9 (19)	11 (26)	9.5 (24)	5 (13)	3.7 (10)	3.3 (9.1)

a Exposure per bodyweight was calculated for each individual before calculating the mean and P97.5 exposure. The mean and 95th percentile estimates are presented for each population group and food category in mg/kg bw/day in Table 2. The estimates are based on individual bodyweights and not the average for the population group. However, for context, the average bodyweights of the population groups are 9.11 kg for infants; 10.9 kg for 12-18 months old; 14.6 kg

for 1.5 -3 years; 27.1 kg for 4-10 years; 58.9kg for 11-18 years; 78.6 kg for 19-64 years; and 70. 6kg for the elderly.

[b] 95th percentile exposures have been reported for the UK to aid the comparison with data reported by EFSA.

** The total exposure includes all of the following food groups:

1.4- Flavoured fermented milk products including heat-treated products.

1.8. Dairy analogues and whitener.

12.5. Soups and broths.

12.6. Sauces.

12.7. Salads and savoury based sandwich spreads.

12.9. Protein products.

14.1.4. Flavoured drinks.

15.2. Processed nuts.

16. Desserts excluding products covered in categories 1, 3 and 4.

17.1. Food supplements supplied in a solid form, excluding for infants and young children.

17.2. Food supplements in a liquid form, excluding for infants and young children.

3. Edible ices.

5.2. Confectionery and sweets.

5.3. Chewing gum.

5.4. Decorations, coatings and fillings, except 4.2.4.

7.2. Fine bakery wares.

Assumptions and uncertainties

Evidence base

278. To be updated.

Exposure assessment

279. The exposure assessment takes into account use levels in only sixteen food groups whereas, E171 is approved in more categories (forty-eight). This may introduce underestimations for exposures. However, not all foods within the categories assessed will contain E171, which means exposure in those categories may be overestimated. In addition, the assessments are based on the assumption that all food in these categories contain E171 at the maximum reported levels. It is unlikely that all foods in each category assessed will contain E171 and at the maximum reported levels. This assumption may overestimate exposure.

280. There are differences between the granularity of food groups used by EFSA for the purposes of their exposure assessment, and those used here for the UK population. This could introduce uncertainties about the comparability of the data.

281. The European Union (EU) banned the use of titanium dioxide as a food additive in 2022. This followed EFSA's update on the safety of the food additive and taking into account uncertainties around genotoxicity concerns (Commission Regulation (EU) 2022/63). Titanium dioxide has not been banned in the UK. However, the EU ban on titanium dioxide may lead to a decline in its use by industry, even for foods consumed in the UK. Given these reasons, the exposure estimates derived may overestimate current and future exposure to titanium dioxide in the UK population.

282. The exposure estimates do not account for exposures from medicines, toothpaste and other non-food sources. Exposure may be higher if these other sources are considered.

Risk Characterisation

283.Exposures for all population groups for the mean total diet are below or very close to the derived HBGV of 10 mg/kg bw/day. Adverse health effects would not be expected for any of these populations.

284. Exposures calculated for the 95^{th} percentile total diet range from 9.1 to 26 mg/kg bw/day. The exposures for adults (18 +) and the elderly are below the derived HBGV and adverse health effects would not be expected. The remaining

exposures are 1.3- to 2.6-fold the HBGV. However, for reasons discussed in the assumptions and uncertainties section, exposures are likely to be lower than calculated. Therefore, it is unlikely that there would be a risk to health from exposures of E171 TiO2 from the diet.

Conclusions

285. Specifically in food, the primary function of TiO2 is as an opacifier and white pigment. To achieve this function, it is critical that food grade TiO2 (E171) exists as an aggregate of smaller primary particles with a median particle size of 200 – 300 nm. Engineered nano-TiO2 have all (100%) of their particles less than 100 nm in diameter and are colourless and would therefore be unsuitable for use as a pigment in food applications.

286. The Committee concluded that there is uncertainty over the effect that TiO2 nanoparticles have on toxicity. The Committee therefore considered that if animals and/or humans are exposed to test substances which contain higher levels of NPs than normally found in food-grade TiO2, that could change the toxicological profile and potentially the risk but it is unclear by how much or in what way.

287. This statement has separated the assessment of the engineered nano form and the food grade TiO2. The focus and conclusions of the statement are based on food grade TiO2.

288. The COT concluded that the physical form of TiO2 will affect the absorption and distribution of TiO2. The wide variance of test materials used (nano, micro and mixtures of nano and micro) was noted. Due to this large variability, as well as the potential impact of the matrix of administration, the Committee could not ascribe a percentage for the absorption of TiO2. However, the Committee considered that absorption of food grade TiO2 (E171) is low, based on the available evidence.

289. The COM reviewed a number of studies to assess the genotoxicity of TiO2.

290. The COM stated that a definitive assessment of the safety of food grade E171 was difficult when there were no high-quality OECD-compliant studies that adequately incorporate the study design considerations and characterisation of the nanoparticulate fraction present in E171. It was also noted that there is a lack of high-quality data sets that are OECD compliant, and this led to conflicting data and uncertainty in the risk assessment for TiO2. (COM, 2024b).

291. The COM opinion is that there is little evidence that TiO2 micro-sized or nanoparticles are genotoxic in vitro or in vivo based on data from well conducted studies. There is also a lack of replication of study outcomes using the same nanoparticle in different labs. (COM, 2024a).

292. Overall, however, the COM concluded that there was little evidence in the literature to suggest that there was a health concern related to genotoxicity induction by TiO2, particularly via the oral route and especially the micro sized TiO2 fraction (most studies in the literature used nano-sized material) (COM 2024b).

293. The Committee considered that the data from the relevant studies available indicated that TiO2 did not induce ACF, nor were there significant effects from studies that assessed inflammation and immunotoxicity, reproductive and developmental toxicity, and neurotoxicity. On balance, the COT considered that the NOAEL of 1,000 mg/kg bw per day was robust.

294. The Committee concluded that on the basis of the available evidence, 1,000 mg/kg bw/day was a robust Point of Departure (POD). This was based on the EOGRT study findings as well as studies by Warheit et al., 2015b and Lee et al., 2019 that reported no effects up to the same dose. There was variability noted in the other studies, but nothing which would alter the proposed POD for food grade TiO2 (E171).

295. A standard uncertainty factor of 100 (10 for inter species variability and 10 for individual variability) was agreed by Members and applied to the POD which results in a HBGV of 10 mg/kg bw/day. There is likely to be additional conservatism in the application of this uncertainty factor to the NOAEL of E171 due to the low absorption of TiO2 and because there is no metabolism of TiO2 particles.

296. Titanium dioxide (E171) can be found in a number of food categories. The exposures calculated and considered in this assessment are only for food and were for infants, toddlers, children, adolescents, adults, and the elderly using food consumption data from UK surveys. Maximum occurrence levels of titanium dioxide for specific food items, reported by EFSA (2021), were also used in the estimation of exposure. All mean total dietary exposures were below or very close to the HBGV and would not be expected to lead to adverse health effects. Although exposures for infants, toddlers, children and adolescents are 1.3- to 2.6-fold higher than the HBGV the conservatism built into the calculated HBGV is likely to exceed that of the uncertainty factor of 100 and the calculated exposures

are likely to be lower than calculated.

297. Based on the uncertainties and assumptions of the exposure assessment as mentioned, the exposure estimates derived probably overestimate the current and future exposure to titanium dioxide in the UK population. It is therefore unlikely that there would be a risk to health from exposures of E171 TiO2 in the diet.

298. In conclusion, based on the current available data and the derived HBGV, it is unlikely that there would be a risk to health from current dietary exposures of E171 TiO2 from the diet.

COT Secretariat

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