

Conclusions - Statement on the safety of Titanium Dioxide (E171) as a Food Additive

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298. 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. In engineered nano-TiO₂ all (100%) of the particles are less than 100 nm in diameter and it is colourless and would therefore be unsuitable for use as a pigment in food applications. Hence, there is a limit to the proportion of NP that can be present in food grade TiO₂ while retaining its utility as a food additive.

299. The Committee concluded that there is uncertainty over the toxicological effects of TiO₂ nanoparticles. 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.

300. 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.

301. The COT concluded that the physical form of TiO₂ will affect the absorption and distribution of TiO₂. The focus of the COT was on food-grade TiO₂ but 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 specific percentage for the absorption of TiO₂. However, the Committee considered that

absorption of food grade TiO₂ (E171) is very low.

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

303. 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 on TiO₂ NP that are OECD compliant, and this led to conflicting data and some uncertainty in the risk assessment for TiO₂. (COM, 2024b).

304. 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).

305. Overall, therefore, 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). Hence, the genotoxicity risk from dietary food grade E171 was considered to be low. (COM 2024b).

306. 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.

307. The Committee concluded that 1,000 mg/kg bw per day was a robust Point of Departure (POD). This was based on the EOGRT study findings as well as studies by Warheit, Donner and Brown, (2015) 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).

308. 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 per day. There is likely to be conservatism in the application of this uncertainty factor to the NOAEL of E171

because 1,000 mg/kg bw per day was the highest dose of TiO₂ tested and therefore the LOAEL (lowest observed adverse effect level) could actually be appreciably higher and, because there is no metabolism of TiO₂ particles, the inter-/intra-species kinetic differences are likely to be lower than the defaults.

309. 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. Ninety-fifth percentile estimates of exposure for infants, toddlers, children and adolescents are 1.3- to 2.6-fold higher than the HBGV. However, the HBGV is more conservative than would typically be the case as the POD was the highest dose tested, so toxicity might not occur until doses appreciably higher than the NOAEL, and the uncertainty factor used allowed for possible variability within and between species in metabolism but TiO₂ is not metabolised, with the result that an uncertainty factor of 100 would be more conservative than the usual default. In addition, exposure was estimated assuming that all food categories assessed contained E171 and that in every case this would be at the maximum reported level. These assumptions would lead to overestimation of exposure. Hence, an apparent exceedance of the HBGV by up to 2.6-fold in some 95th percentile consumers is unlikely to lead to adverse health effects.

310. 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.

311. The Committee concludes that it is unlikely that there would be a risk to health from exposures of E171 TiO₂ from the diet in any of the age groups or scenarios assessed.

COT October 2024

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