

COT Overall Conclusion and References

In this guide

[In this guide](#)

1. [Introduction - \(E171\) Executive Summary](#)
2. [Characterisation and ADME considerations](#)
3. [Review of toxicity for the endpoints identified by the COT](#)
4. [Establishment of a Health-Based Guidance Value \(HBGV\)](#)
5. [Exposure Assessment - \(E171\) Executive Summary](#)
6. [Risk Characterisation - \(E171\) Executive Summary](#)
7. [COT Overall Conclusion and References](#)

Overall Conclusion

37. The COT concludes that it is unlikely that there would be a risk to health from current UK dietary exposures of E171 TiO₂.

COT

August 2024

References

Bettini, S., Boutet-Robinet, E., Cartier, C., Coméra, C., Gaultier, E., Dupuy, J., Naud, N., Taché, S., Grysan, P., Reguer, S., Thieriet, N., Réfrégiers, M., Thiaudière, D., Cravedi, J-P., Carrière, M., Audinot, J-N., Pierre, F. H., Guzylack-Piriou, L. & Houdeau, E. (2017). Food-grade TiO₂ impairs intestinal and systemic immune homeostasis, initiates preneoplastic lesions and promotes aberrant crypt

development in the rat colon. Scientific Reports: 7, 40373. [DOI: 10.1038/srep40373](https://doi.org/10.1038/srep40373).

Blevins, L. K., Crawford, R. B., Bach, A., Rizzo, M. D., Zhou, J., Henriquez, J. E., Khan, D. M. I. O., Sermet, S., Arnold, L. L., Karen L. Pennington, K. L., Souza, N. P., Cohen, S. M. and Kaminski, N. E. (2019). Evaluation of immunologic and intestinal effects in rats administered an E171-containing diet, a food grade titanium dioxide (TiO₂). Food and Chemical Toxicology: 133: 110793. [doi:10.1016/j.fct.2019.110793](https://doi.org/10.1016/j.fct.2019.110793).

COM. (2024a). Assessment of in vitro studies of TiO₂ genotoxicity. (not yet published).

COM. (2024b). Assessment of in vivo studies of TiO₂ genotoxicity. (not yet published)

Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT). 2022. Interim position paper on titanium dioxide. Available at: [TiO₂ COT Interim position paper \(food.gov.uk\)](https://www.food.gov.uk/publications-and-consultation/papers/papers/ti02-cot-interim-position-paper).

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrients Sources added to Food). 2016. Re-evaluation of titanium dioxide (E171) as a food additive. EFSA Journal 2016;14(9):4545, 83 pp.

EFSA FAF Panel (EFSA Panel on Food Additive and Flavourings), 2019. Scientific opinion on the proposed amendment of the EU specification for titanium dioxide (E171) with respect to the inclusion of additional parameters related to its particle size distribution. EFSA Journal 2019;17(7):5760, 23 pp.

EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings) (2021) Scientific Opinion on the safety assessment of titanium dioxide (E171) as a food additive. EFSA Journal 2021;19(5):6585, 130 pp.

FAO/WHO (Joint FAO/WHO Expert Committee on Food Additives). (2024). Evaluation of certain food additives: ninety-seventh report of the Joint FAO/WHO Expert Committee on Food Additives. WHO technical report series; 1051. Available at: [Evaluation of certain food additives: ninety-seventh report of the Joint FAO/WHO Expert Committee on Food Additives](https://www.who.int/publications/m/item/evaluation-of-certain-food-additives-ninety-seventh-report-of-the-joint-fao-who-expert-committee-on-food-additives).

Food Standards Australia New Zealand (FSANZ). (2022). Titanium Dioxide as a Food Additive. Available at: [FSANZ TiO₂ Assessment report.pdf \(foodstandards.gov.au\)](https://www.foodstandards.gov.au/food-additives/ti02-assessment-report).

Han, H.Y., Yang, M.J., Yoon, C., Lee, G.H., Kim, D.W., Kim, T.W., Kwak, M., Heo, M.B., Lee, T.G., Kim, S. and Oh, J.H. (2020). Toxicity of orally administered food-grade titanium dioxide nanoparticles. *Journal of Applied Toxicology*. 41 (7): 1127-1147. <https://doi.org/10.1002/jat.4099>.

Health Canada. (2022). State of the Science of Titanium Dioxide (TiO₂) as a Food Additive. Available at: [H164-341-2022-eng.pdf \(publications.gc.ca\)](https://www150.com/eng/164-341-2022-eng.pdf).

Lee, J., Jeong, J-S., Kim, S. Y., Park, M-K., Choi, S-D., Kim, U-J., Park, K., Jeong, E. J., Nam, S-Y. and Yu, W-J. (2019). Titanium dioxide nanoparticles oral exposure to pregnant rats and its distribution. *Particle and Fibre Toxicology*. 16:31 <https://doi.org/10.1186/s12989-019-0313-5>.

Leuschner. (2020). Extended One-Generation Reproductive Toxicity study of titanium dioxide E171 in rats by oral administration via the diet. (Unpublished report).

Mortensen, N. P., Caffaro, M. M., Aravamudhan, S., Beeravalli, L., Prattipati, S., Snyder, R. W., Watson, S. L., Patel, P. R., Weber, F. X., Montgomery, S. A., Sumner, S. J. and Fennell, T. R. (2021). Simulated Gastric Digestion and In Vivo Intestinal Uptake of Orally Administered CuO Nanoparticles and TiO₂ E171 in Male and Female Rat Pups. *Nanomaterials*. 11: 1487. <https://doi.org/10.3390/nano11061487>.

National Cancer Institute. (1979). Bioassay of Titanium Dioxide for Possible Carcinogenicity. *Carcinogenicity*. 97, [Online]: https://ntp.niehs.nih.gov/sites/default/files/ntp/htdocs/lt_rpts/tr097.pdf.

Pinget, G., Tan, J., Janac, B., Kaakoush, N.O., Angelatos, A.S., O'Sullivan, J., Koay, Y.C., Sierro, F., Davis, J., Divakarla, S.K. and Khanal, D. Moore, R. J., Stanley, D., Wojciech Chrzanowski, W. and Macia, L. (2019). Impact of the food additive titanium dioxide (E171) on gut microbiota-host interaction. *Frontiers in Nutrition*. 6:57. doi: [10.3389/fnut.2019.00057](https://doi.org/10.3389/fnut.2019.00057).

Riedle, S., Wills, J. W., Minitier, M., Otter, D. E., Singh, H., Brown, A. P., Micklethwaite, S., Rees, P., Jugdaohsingh, R., Roy, N. C., Hewitt, R. E. and Powell, J. J. (2020). A murine oral-exposure model for nano- and micro-particulates: demonstrating human relevance with food-grade titanium dioxide. *Nano-Micro Small*, 16, 2000486. DOI: [10.1002/sml.202000486](https://doi.org/10.1002/sml.202000486).

Talamini, L., Gimondi, S., Violatto, M.B., Fiordaliso, F., Pedica, F., Tran, N.L., Sitia, G., Aureli, F., Raggi, A., Nelissen, I., Cubadda, F., Bigini, P. and Diomedede L. (2019).

Repeated administration of the food additive E171 to mice results in accumulation in intestine and liver and promotes an inflammatory status. *Nanotoxicology*. 13(8): 1087-1101. [DOI: 10.1080/17435390.2019.1640910](https://doi.org/10.1080/17435390.2019.1640910).

TDMA (Titanium Dioxide Manufacturer's Association). (2022). Comparison of current food grade titanium dioxide (E171) with historical samples of Unitane O-220. Unpublished draft TDMA|1175b dated 12 April 2022 provided to the FSA by the TDMA.

Warheit, D. B., Boatman, R. and Brown, S. C. (2015a). Developmental toxicity studies with 6 forms of titanium dioxide test materials (3 pigment-different grade & 3 nanoscale) demonstrate an absence of effects in orally-exposed rats. *Regulatory Toxicology and Pharmacology*. 73: 887-896. <http://dx.doi.org/10.1016/j.yrtph.2015.09.032>.

Warheit, D.B., Brown, S.C., and Donner, E.M. (2015b). Acute and subchronic oral toxicity studies in rats with nanoscale and pigment grade titanium dioxide particles. *Food and Chemical Toxicology*. 84: 208-224. <http://dx.doi.org/10.1016/j.fct.2015.08.026>.