# Annex A - Statement on the safety of Titanium Dioxide (E171) as a Food Additive

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## The search terms

1. A literature search was undertaken. The database Lit-fetch was used to search the following search terms between the dates 2021-01-01 to 2023-04-28. For the first 2 search strings, the numbers in brackets denote (number of hits; number of relevant hits), the 3rd search string just denotes number of hits. An updated search was also carried out for the first 2 search strings for 2023-04-28 to 2024-03-01, but only for in vivo studies.

- Search "In Vitro Techniques"[Mesh] OR "Caco-2 Cells"[Mesh] OR "Lysosomes"[Mesh] OR "Hypoxanthine Phosphoribosyltransferase"[Mesh] OR "Autopsy"[Mesh] OR "Micronucleus Tests"[Mesh] OR "Pathology"[Mesh] OR Autops*[tiab] OR histopath*[tiab] OR "in vivo"[tiab] OR "in vitro"[tiab] OR GALT[tiab] OR Caco 2 cell*[tiab] OR Colonic Epithelial Cell*[tiab] OR Colorectal epithelial cell*[tiab] OR Comet assay*[tiab] OR HPRT[tiab] OR "Hypoxanthine Phosphoribosyltransferase"[tiab] OR "hypoxanthin phosphoribosyl transferase"[tiab] OR Lysosom*[tiab] OR "M cell"[tiab] OR "M cells"[tiab] OR "Microfold cell"[tiab] OR "Microfold cells"[tiab] OR Micronucleus assay*[tiab] OR Micronucleus test*[tiab] OR "read across"[tiab] OR SCGE assay*[tiab] OR single-cell gel electrophoresis assay*[tiab] OR "xanthine guanine phosphoribosyl transferase"[tiab] OR "xanthine guanine phosphoribosyltransferase"[tiab] OR xprt[tiab] AND titanium dioxide (322; 19)
- Search "Aneugens"[Mesh] OR "Aneuploidy"[Mesh] OR"apoptosis"[Mesh] OR "Chromatids"[Mesh] OR "Chromosomes"[Mesh] OR "DNA Damage"[Mesh] OR "DNA Repair"[Mesh] OR "Mutagens" [Pharmacological Action] OR

"Mutagens"[Mesh] OR "Mutagenesis"[Mesh] OR "Oxidative Stress"[Mesh] OR Aneugen*[tiab] OR Aneuploid*[tiab] OR Chromatid*[tiab] OR Chromosome*[tiab] OR Clastogen*[tiab] OR "DNA binding"[tiab] OR DNA fragmentation*[tiab] OR DNA damage*[tiab] OR "DNA lesion"[tiab] OR "DNA lesions"[tiab] OR "DNA repair" [tiab] OR genotox*[tiab] OR mutagen*[tiab] OR Mutat*[tiab] OR oxidative stress*[tiab] AND titanium dioxide (209; 16)

- (Titanium dioxide AND Nanoparticles AND E171 AND toxicology) (1); (Titanium dioxide AND Nanoparticles AND E171 AND genotoxicity) (8); (Titanium dioxide AND Nanoparticles AND E171 AND human health) (13); (Titanium dioxide AND Nanoparticles AND E171 AND adverse effects) (7); (Titanium dioxide AND Nanoparticles AND E171 AND reproductive toxicity) (5); (Titanium dioxide AND Nanoparticles AND E171 AND developmental toxicity) (2); (Titanium dioxide AND Nanoparticles AND E171 AND Distribution) (8); (Titanium dioxide AND Nanoparticles AND E171 AND Metabolism) (4); (Titanium dioxide AND Nanoparticles AND E171 AND Excretion) (1); (Titanium dioxide AND Nanoparticles AND E171 AND ADME) (1); (Titanium dioxide AND Nanoparticles AND E171 AND immunotoxicology) (0); (Titanium dioxide AND Nanoparticles AND E171 AND neurotoxicology) (0).