

## Appendix B: Criteria for inclusion and exclusion applied to screening of publications retrieved in the literature search

The screening process of the papers retrieved by the literature search (see appendix A) was performed using an online collaborative tool (DistillerSR<sup>1</sup>). This tool is designed to support the conduct of systematic reviews which allows the traceability of all the references screened with the possibility of re-iterate the process at any step. The screening was performed by one reviewer in two steps: title and abstract (TiAb) and initial screening for relevance (full text).

In order to define the criteria to be applied to the screening process, the FAF Panel asked the ccWG Nano to advise on:

1. general exclusion criteria for biological and toxicological studies;
2. relevance of the retrieved studies based on the tested material.

Following this advice, at the TiAB screening, the following criteria for exclusion were applied:

- Non-biological, toxicological or genotoxicity studies (e.g. synthesis, photocatalytic performance, soil analysis)
- Studies on non-mammal species (e.g. fish, *Drosophila*, bees) or plants
- *In vivo* studies that have used a non-relevant route of administration (e.g. dermal, dental and bone implants).
- Studies performed only with coated TiO<sub>2</sub>
- Studies performed only with TiO<sub>2</sub> nanofibres, nanocomposites or nanotubes
- Reviews, editorials, letters to the editors, etc

As a general principle, in case of doubt or insufficient information in the abstract to draw a conclusion on possible exclusion, the approach taken has been to bring the publication to the following step, i.e. full- text screening.

As a first step, full text of the publications were screened to confirm relevance of the test material(s): E 171, TiO<sub>2</sub> on the microsize, TiO<sub>2</sub> containing a fraction of nanoparticles, TiO<sub>2</sub> NPs. At this step, publications with test material(s) not relevant for the assessment of E 171 were excluded (e.g. coated TiO<sub>2</sub>, TiO<sub>2</sub> nanofibers, TiO<sub>2</sub> brookite, etc).

At the same time, detailed information on the test material(s) was extracted:

1. Particle size of the test material; methodology used for the analysis
2. Shape of the test material
3. crystalline form
4. Purity of the test material

In a second step, the full-text publications were screened for relevance along with a classification of the studies according to the following areas of assessment:

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<sup>1</sup> <https://www.evidencepartners.com/products/distillersr-systematic-review-software>

- In vitro/in vivo/gut microbiota
- Aim of the study, e.g.
  - toxicokinetics
  - genotoxicity
  - local effect (e.g. inflammation, proliferation)
  - apical effects/ general toxicity
  - mechanisms of action (e.g. oxidative stress)
- test/measured endpoints

In addition, information on the study design was extracted from the publications (e.g. type of cells/animal species, doses tested, duration of the studies, etc).