Issued on 24 November 2023

JECFA's risk assessment of titanium dioxide risk released – background information

Assessment of the health impacts of the food colour additive titanium dioxide (TiO2) has been released by the and the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) Joint Expert Committee on Food Additives (JECFA) on 24 November 2023.

Titanium dioxide (also called INS171[1] in The International Numbering System for Food Additives (INS)) is a widely used food additive. It is mainly used as whitening and brightening agent in a wide range of products such as chewing gum, mayonnaise, soy milk, candies, pastries, coffee creamers, chocolates, and cake decorations.

JECFA noted that INS171 was poorly absorbed from the gastrointestinal tract and that the oral bioavailability of TiO2 in humans is very low. JECFA furthermore considered that no evidence for carcinogenic, reproductive or developmental toxicity effects after long term exposure in animals have been identified. JECFA also noted that there are currently no epidemiological studies that allow any conclusions to be drawn with respect to any association between dietary exposure to INS171 and human health effects.

After reviewing the available scientific literature JECFA noted limitations in the available evidence for genotoxicity. JECFA emphasizes that the OECD guidelines for investigating genotoxicity have been developed and validated for chemicals, and that they may not be easily applicable without adaptations for testing poorly soluble particulate matter such as TiO2. Recognizing the limitations and some equivocal findings in the available data on genotoxicity JECFA noted that the available data did not provide convincing evidence of genotoxicity for INS171.

"JECFA reviewed all available research on genotoxicity risk and determined that the evidence is insufficient, owing mostly to the lack of suitable testing methodologies for nanoparticles," said Dr Moez Sanaa, WHO's Head of the Standards and Scientific Advice on Food and Nutrition Unit. "We need more research to address the current uncertainty about the distribution of TiO2 particle sizes in food and to develop genotoxicity tests that are more appropriate for nanoparticles".

In light of the very low oral absorption of INS171, and in the absence of any identifiable hazard associated with INS171 in the diet, the JECFA reaffirmed the ADI "not specified" established in 1969.

[1] INS171 consists of uncoated TiO2 particles including a minor fraction of nano size particles. In the European Union (EU), food-grade TiO2 is identified and labelled as E171. INS171 and E171 are equivalent except that INS171 does not include the TiO2 coating of pearlescent pigments (INS 176).

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JECFA has previously evaluated titanium dioxide back in 1969, when JECFA concluded that the use of INS 171 as a food additive does not pose as safety concern and therefore allocated an ADI "not specified" under conditions of Good Manufacturing Practices (GMP).

Titanium dioxide has since then been classified by the International Agency for Research on Cancer (IARC) as possibly carcinogenic to humans (IARC Group 2B) based on "limited evidence" that when humans are exposed to TiO2 dust through inhalation ultrafine particles can cause cancer. The IARC assessment only includes inhalation of TiO2 and does not include exposure to TiO2 from oral sources such as when it's used as a food additive.

In recent years several regional and national food safety authorities have evaluated the safety of TiO2 when used as food additive. The outcome of these evaluations have provided equivocal results going from no safety concerns to a recent safety assessment by the European Food safety Authority (EFSA) from 2020 when it was concluded that TiO2 (E 171) can no longer be considered safe as a food additive. A critical element in reaching this conclusion is that EFSA could not exclude genotoxicity concerns after consumption of E171 nanoparticles.

JECFA in its new updated safety assessment considered additional toxicological studies relevant to the safety assessment of INS171. The new assessment included data on toxicokinetics, acute toxicity, short-term toxicity, long-term toxicity and carcinogenicity, genotoxicity, and reproductive and developmental toxicity, as well as special studies addressing the short-term initiation/promotion potential for colon cancer.

JECFA identified a number of TiO2 test materials that were considered representative of INS171. Further, JECFA recognized that a large number of toxicological studies have been conducted using test materials, including nanoparticles, having size distributions and physico-chemical properties not comparable to INS 171. These studies on non-representative materials were evaluated by JECFA, but it was concluded that they were not relevant to the safety assessment of INS 171.