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International Association of Color Manufacturers

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Saudi Food and Drug Authority
SFDA – 4904 North Ring road Hitteen Unit (1) – Riyadh 13513 – 7148
Via E-mail: SPSEP.Food!@sfda.gov.sa

Re: G/SPS/N/ARE/206/Add.1; G/SPS/N/BHR/214/Add.1; G/SPS/N/KWT/79/Add.1; G/SPS/N/OMN/111/Add.1; G/SPS/N/QAT/115/Add.1; G/SPS/N/SAU/436/Add.1; G/SPS/N/YEM/56/Add.1

To whom it may concern:

The International Association of Color Manufacturers (IACM) is the trade association representing the global color industry, which comprises manufacturers and end-users of natural and synthetic coloring substances used in foods, drugs, and cosmetics. We are writing to provide information on titanium dioxide when used as a coloring agent in response to Saudi Arabia's proposal to modify the GCC Technical Regulation for "Additives Permitted for Use in Food Stuffs" to remove the food additive titanium dioxide (INS 171).

IACM urges Saudi Arabia to reconsider the proposed action to remove authorization of INS 171 as a food additive. While we understand this action is being taken primarily in response to recent activity by the European Union, there is no actual demonstrated safety concern to justify the proposed action. As described further in our letter, the opinion of the European Food Safety Authority (EFSA) was based on safety data for titanium dioxide that is not representative of the material on the market approved for use as a food color. Additionally, two other highly regarded food agencies from the United Kingdom and Canada have more recently reviewed the data supporting the safe use of titanium dioxide as a food colorant and determined it to support its continued safe use. Finally, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) has not yet completed its re-evaluation of titanium dioxide, and IACM urges Saudi Arabia to wait until the JECFA process is complete before finalizing any decision.

Titanium Dioxide as a Food Color

Titanium dioxide (TiO_2) is a naturally occurring crystalline solid that exists in three fundamental crystal forms: rutile, anatase, and brookite. Its bright white color, high refractive index, and resistance to discoloration have historically made it versatile in many applications as a pigment. The anatase and rutile forms, resulting in white and slightly off-white powder, respectively, are permitted to produce pigment-grade material approved as a food colorant.[1] TiO_2 may be coated with small amounts of alumina and silica to improve technological properties, such as mixing and dispersion properties in various matrices.

For TiO_2 to act as a pigment, the particles must be large enough to scatter visible light. For pigment-grade TiO_2 to function as a color additive optimally a significant number of particles

[1] Kuznesof and Rao. 2006. Titanium dioxide. Chemical and Technical Assessment. Accessed on March 22, 2013. http://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/67/cta_tio2.pdf

larger than 200 nm are required. Particles of this size are capable of refracting light. As the particle size decreases, the material loses its color and becomes transparent. Therefore, manufacturers produce pigment-grade TiO_2 to maximize the number of particles in the size range between 200 and 350 nanometers.

According to prior characterization of pigment grade TiO_2, the maximum refraction occurs around a particle size of 272 nm (range 180 – 300 nm). The light refraction decreases abruptly below this threshold and gradually above it. The narrower the size distribution, the better the light refractive properties of the pigment and the poorer they become as the size distribution widens or agglomeration occurs.[2,3] It is documented that optimum pigment characteristics are lost below the 100 nm threshold that generally defines nanomaterials. Thus, nanoscale TiO_2 has a different refractive index than pigment grade TiO_2 that renders it transparent.

Although useful in other applications, the loss of (white) color eliminates its utility as a color additive, and therefore it is not added directly to food for that purpose. Instead, the predominant food application for TiO_2 involves the use of pigment-grade material for use as a colorant. Exposure to nanoscale TiO_2 through food is limited to its inadvertent presence in small amounts in pigment-grade material or in other limited non-colorant applications. It should be stressed that particles below 100 nm are not deliberately manufactured in pigmentary food-grade TiO_2 and are present only as part of the overall particle size distribution.

EFSA Opinion

The EFSA Expert Panel on Food Additives and Flavorings published an opinion in 2021 regarding E171[4] stating that EFSA could not rule out concern for genotoxicity from ingestion of the material based on a perceived gap in data on this risk, which serves as the basis for Saudi Arabia's proposed action.

The 2021 opinion diverges from the previous EFSA opinions on the safety of E171, including its 2016 opinion,[5] that the use of TiO_2 as a food additive does not raise a genotoxic concern. EFSA's subsequent opinions in 2018[6] and 2019[7] reaffirmed this conclusion of lack of genotoxic concern. It is worth noting that the 2021 opinion continues to confirm no general and organ toxicity, no effects on reproductive and developmental toxicity and only noted that it could not

[2] Johnson, R. W., Thiele, E. S. and French, R. H. 1997. Light-scattering efficiency of white pigments: an analysis of model core–shell pigments vs. optimized rutile TiO. TAPPI Journal. 80(11):233-39.
[3] Thiele, E. S. and French, R. H. 1998. Light-Scattering Properties of Representative, Morphological Rutile Titania Particles Studied Using a Finite-Element Method. Journal of the American Ceramic Society. 81(3):469-79. https://doi.org/10.1111/j.1151-2916.1998.tb02364.x
[4] EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings), 2021. Safety assessment of titanium dioxide (E171) as a food additive. EFSA Journal 2021;19(5):6585, 130 pp. https://doi.org/10.2903/j.efsa.2021.6585
[5] EFSA ANS Panel (EFSA Panel on Food Additives and Nutrients Sources added to Food), 2016. Re-evaluation of titanium dioxide (E 171) as a food additive. EFSA Journal 2016;14(9):4545, 83 pp. https://doi.org/10.2903/j.efsa.2016.4545
[6] EFSA ANS Panel (EFSA Panel on Food Additives and Nutrients Sources added to Food), 2018. Evaluation of four new studies on the potential toxicity of titanium dioxide used as a food additive (E 171). EFSA Journal 2018;16(7):5366, 27 pp. https://doi.org/10.2903/j.efsa.2018.5366
[7] EFSA FAF Panel (EFSA Panel on Food Additive and Flavourings), 2019. Scientific opinion on the proposed amendment of the EU specification for titanium dioxide (E 171) with respect to the inclusion of additional parameters related to its particle size distribution. EFSA Journal 2019;17(7):5760, 23 pp. https://doi.org/10.2903/j.efsa.2019.5760

rule out genotoxicity due to insufficient data to define threshold exposures below which genotoxicity will not occur. Additionally, the 2021 opinion is based on genotoxicity tests using TiO_2 nanomaterials not representative of titanium dioxide (E171) and exposure methods not representative of human exposures. The 2021 opinion showed no consideration of differences between E171 and TiO_2 nanomaterials and disregarded the most relevant studies, including those conducted by industry in response to EFSA's request.

The 2016 opinion considered that E171 contains at most 50% of particles in the range of less than 100 nm and the 2021 opinion is the first time the 2018 EFSA Scientific Committee Guidance on Nanotechnology[8] has been applied to the safety assessment of a food additive. However, in its 2021 opinion, EFSA did not adhere to its own guidance for assessing nanomaterials, which indicate that tests must be performed with representative material as used in the food market and in compliance with the specifications. Additionally, EFSA did not base its opinion on all relevant data concerning the safety of E171. Previous opinions had already considered TiO_2 particle distribution including the fraction less than 100 nm as provided by industry via the Titanium Dioxide Manufacturers Association (TDMA). The 2021 opinion did not justify grouping TiO_2 nanomaterials with E171. Therefore, the TiO_2 nanomaterials subjected to genotoxicity testing on which EFSA relied in its 2021 opinion are not representative of E171 as used in foods and present in the marketplace due to the inability of the nanomaterials to provide the white color necessitating its use.

The 2021 opinion also differs from EFSA's previous position that a food additive should be investigated by the dietary route of exposure in a food matrix and focuses on conditions unrealistic to dietary intake. Additionally, the 2021 opinion gave undue weight to results of *in vitro* genotoxicity studies that do not represent dietary intake of E171 and did not give appropriate weight to results of compelling *in vivo* genotoxicity studies. Considering both the application of the guidance and exclusion of specific important components of the scientific dataset for E171 that show no adverse impacts, the conclusions reached by the 2021 opinion are based on an entirely novel, untested approach to risk assessment rather than any new safety concerns. To state that E171 can no longer be considered safe when used as a food additive is not supported by the data reviewed by EFSA over the last six years, and to remove a food additive from the market that has demonstrated no safety concerns is a mistake and unwarranted.

<u>Other Jurisdictions Diverge From EFSA</u>

However, the United Kingdom has taken a divergent approach, whereby two expert committees of the Food Standards Agency (FSA) have provided opinions indicating no safety concerns for TiO_2 when used as a food additive. Therefore, the FSA, along with Food Standards Scotland (FSS) are finalizing a risk assessment expected to be published early next year that will determine the evidence supporting the European Union's decision is not conclusive, and as such, make no amendments to the existing TiO_2 regulations.

[8] EFSA Scientific Committee, 2018a. Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: part 1, human and animal health. EFSA Journal 2018;16(7):5327, 95 pp. https://doi.org/10.2903/j.efsa.2018.5327

Just last month, Health Canada's Food Directorate completed its comprehensive "state of the science" report on TiO_2 as a food additive[9]. The report concluded there is no direct scientific evidence that food-grade titanium dioxide, when used as a food additive, is a concern for human health. In reaching this conclusion, Health Canada evaluated new scientific data that addressed some of the uncertainties identified by EFSA in its 2021 opinion that were not available at the time of EFSA's review. Additionally, Health Canada's report notes that many studies that raised concern about the safety of TiO_2, including EFSA's concern for genotoxicity, used forms of TiO_2 that are not considered acceptable for use in food and have different properties than food-grade TiO_2. Overall, Health Canada's Food Directorate's comprehensive review of the available science of TiO2 as a food additive showed no evidence of cancer or other adverse effects in mice and rats exposed to high concentrations of food-grade TiO_2 (long-term or lifetime study), no changes to DNA in various animal studies, and no adverse effects on reproduction, development, immune, gastrointestinal, or nervous systems, or general health when rats were exposed from pre-conception to adulthood.

Trade Impact

Titanium dioxide has a long history of safe use as a color additive. JECFA)[10] has evaluated titanium dioxide (INS 171) and established an acceptable daily intake (ADI) of "not limited." In response to the 2021 EFSA opinion, the JECFA Secretariat signaled its intent to issue a call for data for purposes of conducting its own re-evaluation. While new specifications for TiO_2 were established by JECFA in 2012[11], the last toxicological assessment was conducted in 1969.

During the 52nd Codex Committee on Food Additives (CCFA) meeting, held virtually September 1-10, 2021, the CCFA agreed with JECFA's proposal to add the re-evaluation of TiO_2 to its priority list. This action was taken to minimize any further disruption to international trade that is expected to be caused by the actions of the European Commission, and which would be further exacerbated by the proposed action by Saudi Arabia. [12]

Additionally, there are currently no substances that can match the whitening color or opacity of TiO_2 when used as a food coloring agent while not imparting unwanted flavors, requiring significantly higher usage rates, or affecting the texture in food products. TiO_2 is exceptionally stable across a wide variety of applications, including in coatings, where it provides a smooth surface covering.

While there may be some applications where alternatives can be used to provide a similar white shade, removing INS 171 as an approved food additive will have an impact on the ability of global food and beverage companies to provide consumers with the following food products that most frequently contain titanium dioxide: extruded snacks, tortilla chips, potato chips, granola bars, macaroni and cheese, confectionery goods including chewing gum and those that contain compound coatings, bakery products, dairy products, cheeses, icing and decorations, frozen

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[9] https://www.canada.ca/en/health-canada/services/food-nutrition/reports-publications/titanium-dioxide-food-additive-science-report.html

[10] Joint FAO/WHO Expert Committee on Food Additives (JECFA), 1969. Titanium dioxide. FAO Nutrition Meetings Report Series 46a. https://inchem.org/documents/jecfa/jecmono/v46aje19.htm.

[11] http://www.fao.org/fileadmin/user_upload/jecfa_additives/docs/monograph13/additive-466-m13.pdf

[12] http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FMeetings%252FCX-711-52%252FCRDs%252Ffa52_CRD06.pdf

desserts, nondairy creamers, soups (including dried soups), beverages, plant-based meat alternatives (meat analogues), non-alcoholic drink mixers, popcorn, nuts and seeds, and dietary supplements.

Therefore, IACM urges Saudi Arabia to reconsider its proposed action to remove INS 171 authorization as a food additive due to the lack of safety concern for INS 171 when used as a pigment to provide color in food. IACM also encourages Saudi Arabia to consider the outcome of other safety reviews, including the recent Health Canada report and the forthcoming FSA and JECFA re-evaluations of TiO_2 prior to finalizing any risk management actions, to minimize any disruption to international trade. Finally, an implementation grace period of no less than 18-24 months is needed to allow producers enough time to transition and fully comply with any change to the regulation.

IACM appreciates the opportunity to provide this information.

Sincerely,

Sarah A. Codrea

Sarah Codrea
Executive Director