PQRI Workshop:
TiO2 Use in Pharmaceuticals
Global Regulatory and Technical Challenges
June 13-14, 2023

FDA and other Regulator Perspective on TiO2 Safety – Current Global Status

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Multiple stakeholders; **one objective.**

INTERNATIONAL PHARMACEUTICAL EXCIPIENTS COUNCIL
IPEC AMERICAS

International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

Disclaimer

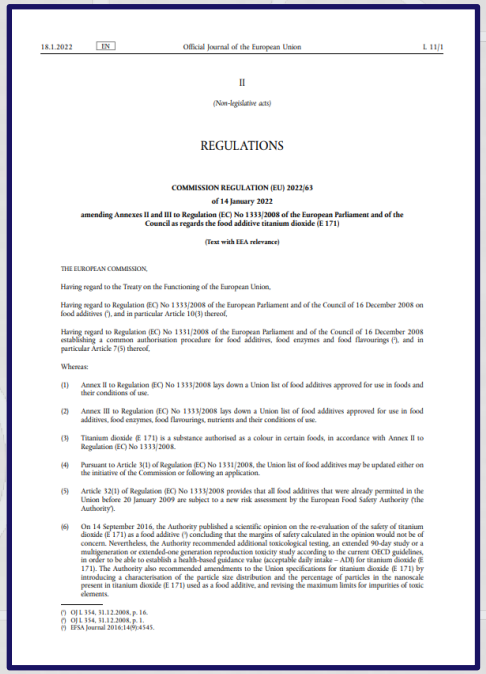
The views, thoughts and opinions expressed in the text belong solely to the authors, and should not be taken as being endorsed by any organization, committee, or other groups or individuals with whom the authors are associated.

EFSA E171 opinion: recap

- European Food Safety Authority (EFSA) concluded that TiO_2 can no longer be **considered safe** for use as the food additive E171, based on data gaps related to genotoxicity on nano grades of TiO_2

They DID NOT say that E171 is not safe!!

- Regardless of the lack of any true indication of a safety concern, the EU Commission (EC) and Parliament banned the use of E171 in food products using the **precautionary principle**.



18.1.2022 EN Official Journal of the European Union L 11/1

II

(Non-legislative acts)

REGULATIONS

COMMISSION REGULATION (EU) 2022/63

of 14 January 2022

amending Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards the food additive titanium dioxide (E 171)

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives (1), and in particular Article 10(3) thereof,

Having regard to Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings (2), and in particular Article 7(5) thereof,

Whereas:

(1) Annex II to Regulation (EC) No 1333/2008 lays down a Union list of food additives approved for use in foods and their conditions of use.

(2) Annex III to Regulation (EC) No 1333/2008 lays down a Union list of food additives approved for use in food additives, food enzymes, food flavourings, nutrients and their conditions of use.

(3) Titanium dioxide (E 171) is a substance authorised as a colour in certain foods, in accordance with Annex II to Regulation (EC) No 1333/2008.

(4) Pursuant to Article 3(1) of Regulation (EC) No 1331/2008, the Union list of food additives may be updated either on the initiative of the Commission or following an application.

(5) Article 32(1) of Regulation (EC) No 1333/2008 provides that all food additives that were already permitted in the Union before 20 January 2009 are subject to a new risk assessment by the European Food Safety Authority ('the Authority').

(6) On 14 September 2016, the Authority published a scientific opinion on the re-evaluation of the safety of titanium dioxide (E 171) as a food additive (3) concluding that the margins of safety calculated in the opinion would not be of concern. Nevertheless, the Authority recommended additional toxicological testing, an extended 90-day study or a multigeneration or extended-one generation reproduction toxicity study according to the current OECD guidelines, in order to be able to establish a health-based guidance value (acceptable daily intake – ADI) for titanium dioxide (E 171). The Authority also recommended amendments to the Union specifications for titanium dioxide (E 171) by introducing a characterisation of the particle size distribution and the percentage of particles in the nanoscale present in titanium dioxide (E 171) used as a food additive, and revising the maximum limits for impurities of toxic elements.

(1) OJ L 354, 31.12.2008, p. 16.
(2) OJ L 354, 31.12.2008, p. 1.
(3) EFSA Journal 2016;14(9):4545.

- Other global regulators also have re-assessed TiO_2 safety for food uses and come to different conclusions

Global Activities Related to TiO_2

New Information was considered by Global Regulators!

United States FDA (CFSAN)

- After the EFSA Opinion was published, FDA CFSAN put together an expert group of toxicologists, chemists and Nano experts to re-evaluate the safety of TiO2 for use in food
- FDA quickly realized that much of the data that EFSA reviewed was unpublished study data that had been supplied by TDMA and other industry organizations directly to EFSA
- Once the FDA's re-evaluation was initiated, the Titanium Dioxide Manufacturer's Association (TDMA) and other industry groups provided significant safety information to the FDA that included what was supplied to EFSA's call for data and more information never requested by EFSA.
- **Additional critical information was also provided to FDA in a report from Keller & Heckman's toxicologists that highlighted the many flaws in the EFSA Opinion and many of the studies which EFSA used to develop their Opinion**

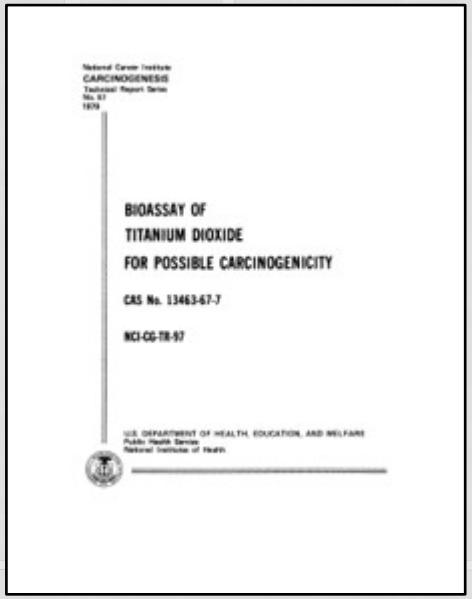
United States FDA (CFSAN)

Reviewed scientific data and information supplied by TDMA/TDSC, IACM, and IPEC as part of their re-evaluation.

- FDA discussed TiO_2 safety with Health Canada.
- Both FDA & Health Canada were interested in a large 1979 NTP Cancer study - SUMMARY:

> It is concluded that under the conditions of this bioassay, titanium dioxide was not carcinogenic by the oral route for Fischer 344 rats or B6C3F1 mice.

  - Ref: TR-097: Titanium Dioxide (CASRN 13463-67-7) (nih.gov)
- FDA questioned TDMA, during an initial meeting, if the material in the NTP study (Trade Name: UNITANE) represents current material on the market.
- TDMA was able to locate samples of the UNITANE grade used

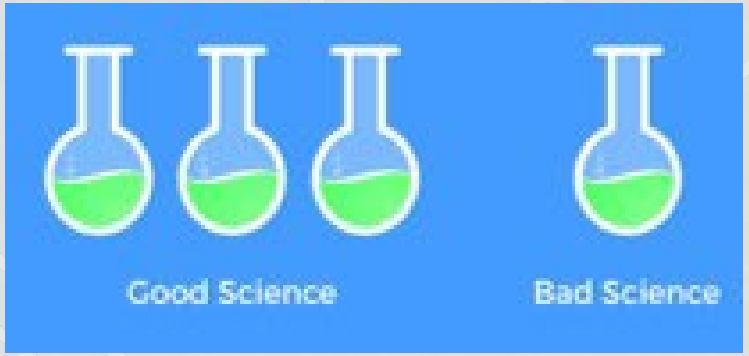

BIOASSAY OF
TITANIUM DIOXIDE
FOR POSSIBLE CARCINOGENICITY

CAS No. 13463-67-7

NCI-CG-TR-97

United States FDA (CFSAN)

- TDMA performed nanoparticle analysis showing the UNITANE grade used in the NTP study was representative of current commercial food grade TiO_2.
- Samples of UNITANE were sent by TDMA to FDA for their own nanoparticle analysis
- FDA's re-evaluation has been completed.
- FDA stated that they had no plans to publish a formal report summarizing their position unless a Citizen's Petition is filed since they felt TiO_2 was safe in the past and their re-evaluation did not change this position.
- **FDA has publicly stated that they do NOT have a safety concern with TiO_2 and do not plan to take any action to ban or restrict its use.**



United States FDA (CFSAN)

SYMPOSIUM

FDA NanoDay Symposium 2022

OCTOBER 11, 2022

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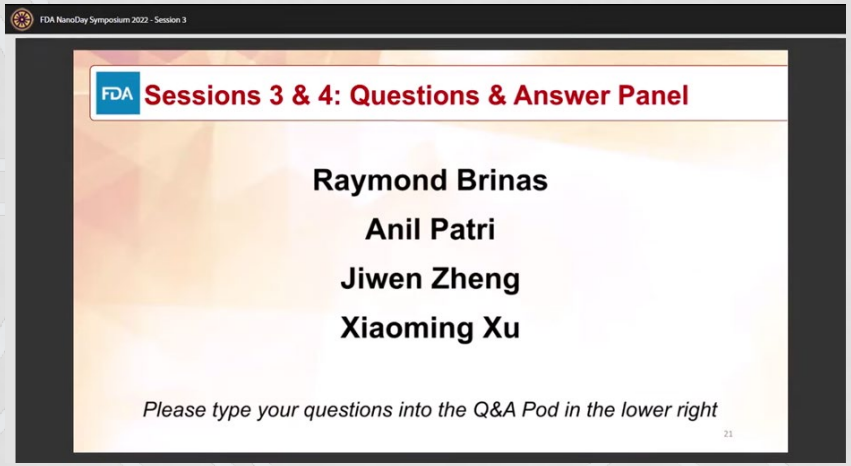
On This Page

- Meeting Information

Date: October 11, 2022

Time: 8:50 AM - 3:10 PM ET



Listen to the specific recording at: [FDA NanoDay 2022 Session 3 - YouTube]

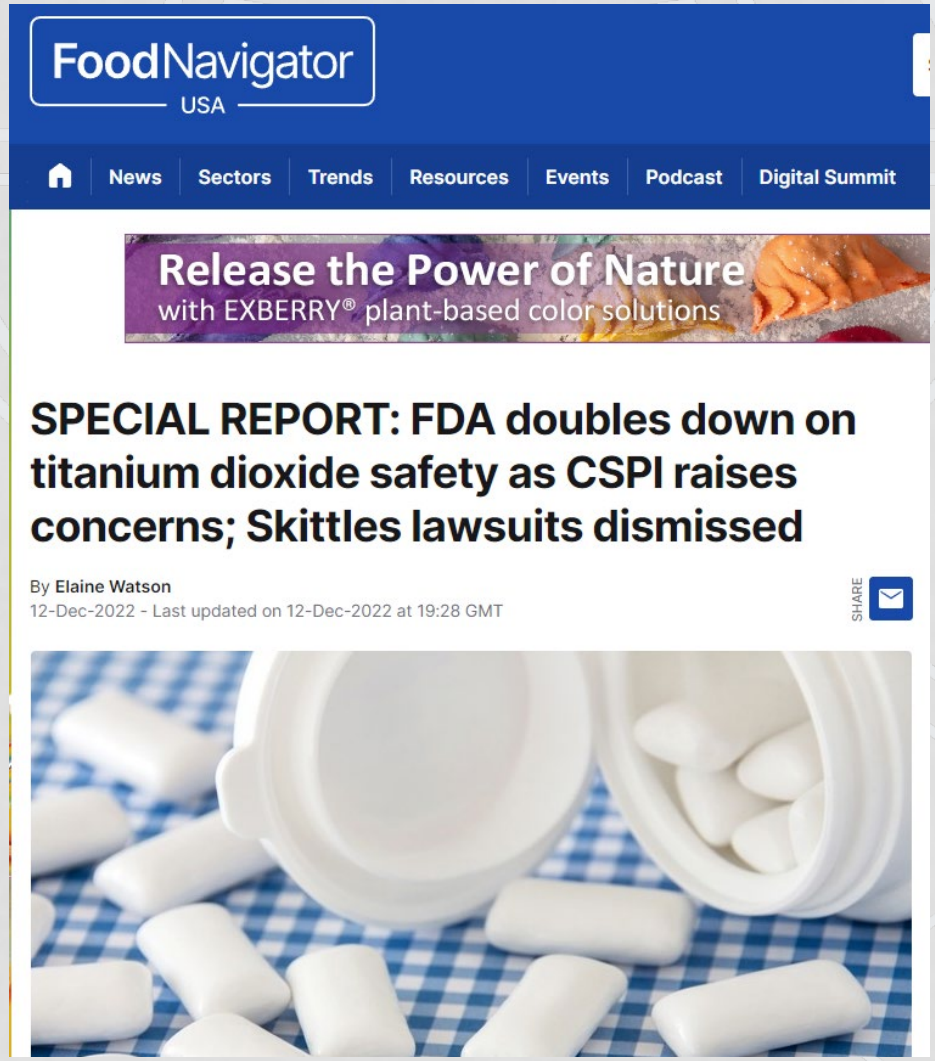
TiO2 Question about FDA's evaluation of the safety of TiO2:

>> Thank you! Let's go back to Ray. A person has an FCN question. Can you discuss FDA's current evaluation of the safety of standard pigment grade titanium dioxide containing fraction of nanomaterial that have been safely used in food and drugs for decades. Given the cautionary ban in foods as taking place in Europe, it's not based on a safety plan but a perceived gap on the nanomaterial themselves. Can you talking about our safe city evaluation of titanium dioxide. Thanks!

FDA's Answer to the Question:

>> Thank you, for that question. So for titanium dioxide, FDA has reviewed the findings of the 2021 opinion on titanium dioxide and we note that the opinion continued to confirm no general organ toxicity and no reproductive toxicity and this does not demonstrate safety concerns connected to the use of titanium dioxide as a color additive so FDA continues to allow for the safe use of titanium dioxide as a color additive in foods generally according to the specifications and conditions including the quantity of titanium dioxide that does not exceed 1% by way of food found in our regulation which is in 21, code of federal regulation, 73.575. Thank you!

United States FDA (CFSAN)



FDA: 'The available safety studies do not demonstrate safety concerns connected to the use of titanium dioxide as a color additive'

Asked whether the FDA has looked again at Ti02 following the EC's decision, a spokesman told FoodNavigator-USA: "*The FDA reviewed the findings of EFSA's 2021 Opinion on titanium dioxide and notes that EFSA's 2021 Opinion continued to confirm no general and organ toxicity, as well as no effects on reproductive and developmental toxicity.*

"In its 2021 Opinion, EFSA noted that it could not rule out genotoxicity and included genotoxicity tests on titanium dioxide nanomaterials. Some of the genotoxicity tests included test materials not representative of the color additive, and some tests included administration routes not relevant to human dietary exposure. The available safety studies do not demonstrate safety concerns connected to the use of titanium dioxide as a color additive."

The spokesperson added: *"The FDA continues to allow for the safe use of titanium dioxide as a color additive in foods generally according to the specifications and conditions, including that the quantity of titanium dioxide does not exceed 1% by weight of the food, found in FDA regulations at 21 CFR 73.575. "*

EFSA's position is not shared by FDA

U.S. FOOD & DRUG ADMINISTRATION

Latest from TDMA

US FDA confirms the safety of titanium dioxide as a food additive

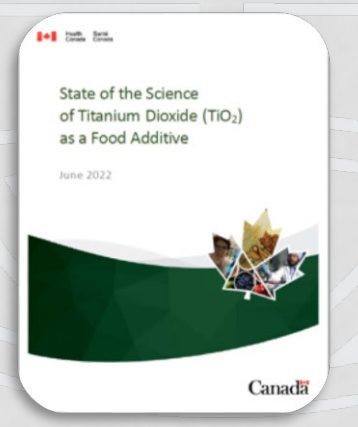
The United States Food and Drug Administration (FDA) communicated to the Titanium Dioxide Manufacturers Association (TDMA) its position on the

The FDA reviewed the findings of EFSA's 2021 Opinion on titanium dioxide. The FDA notes that EFSA's 2021 Opinion continued to confirm no general and organ toxicity, as well as no effects on reproductive and developmental toxicity. In its 2021 Opinion, EFSA noted that it could not rule out genotoxicity and included genotoxicity tests on titanium dioxide nanomaterials. Some of the genotoxicity tests included test materials not representative of the color additive, and some tests included administration routes not relevant to human dietary exposure. The available safety studies do not demonstrate safety concerns connected to the use of titanium dioxide as a color additive. The FDA continues to allow for the safe use of titanium dioxide as a color additive in foods generally according to the specifications and conditions, including that the quantity of titanium dioxide does not exceed 1% by weight of the food, found in FDA regulations at 21 CFR 73.575.

The U.S. FDA regulates food and color additives under the Federal Food, Drug, and Cosmetic Act. Under this statute, food additives and color additives, including color additives such as titanium dioxide, require pre-market review and approval by the FDA. Federal regulations require evidence that each substance is safe at its intended level of use before it may be added to foods. In the case of color additives, manufacturers submit data and information to the FDA as a petition requesting approval of the intended use. The FDA evaluates the petition, and if the data available demonstrates that the substance is safe under the proposed conditions of use, the agency issues a regulation authorizing the use of the color additive. Post-approval, our scientists continue to review relevant new information to determine whether there are safety questions and whether the use of such substance is no longer safe under the Federal Food, Drug, and Cosmetic Act. https://tdma.info/news/us-fda-confirms-the-safety-of-titanium-dioxide-as-a-food-additive/

EFSA's position is not shared by Global Regulatory Authorities

Several global regulatory authorities have carried out a critical review of the 2021 EFSA opinion on E171 considering available science relevant to food uses of TiO_2, incl. data generated after the EFSA opinion



Health Canada, June 2022

[Titanium dioxide (TiO2) as a food additive: Current science report - Canada.ca]

FOOD STANDARDS Australia New Zealand

Food Standards Australia New Zealand, Sept 2022

[Review of titanium dioxide as a food additive (foodstandards.gov.au)]

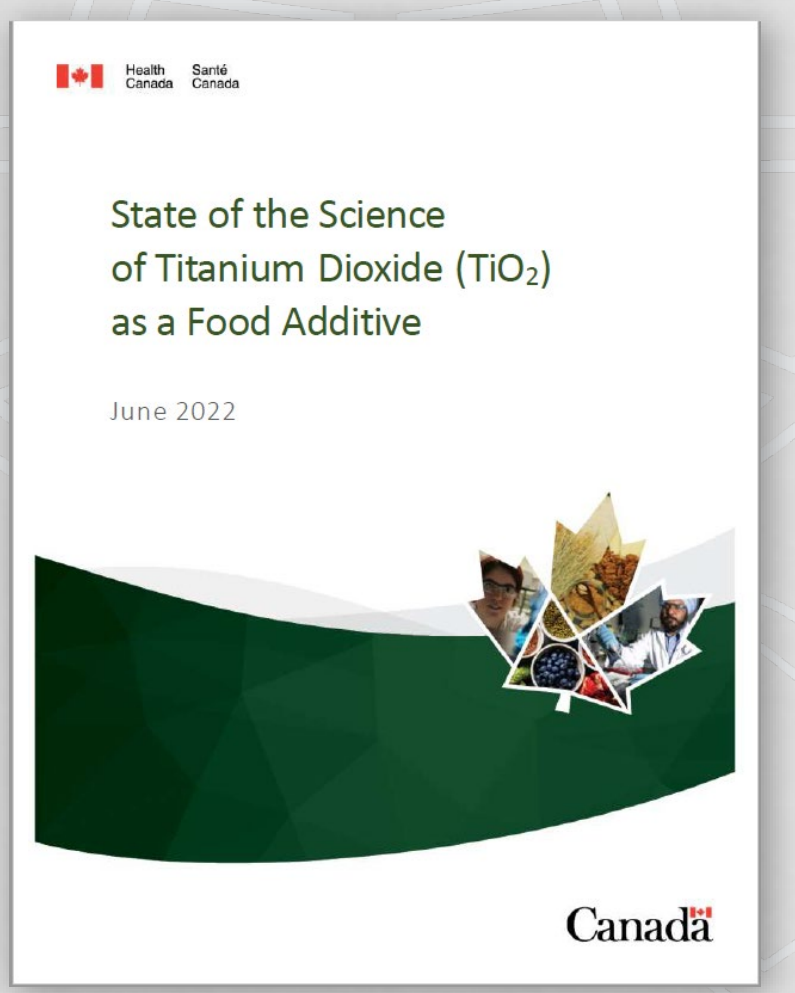
Food Standards Agency

UK Food Standards Agency, July 2021

[TOX/2021/46 TiO2 COT Interim position paper (food.gov.uk)]

EFSA's position is not shared by Health Canada

Government of Canada

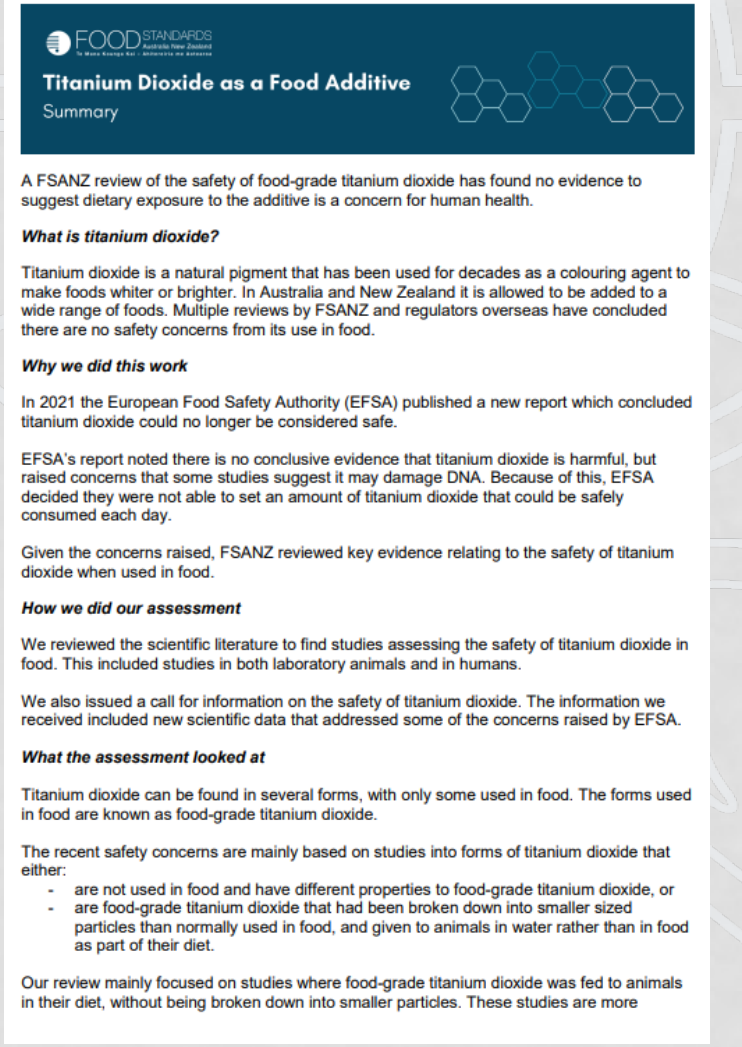


Key Outcomes

- No evidence of cancer or other adverse effects in mice and rats exposed to high concentrations of food-grade TiO_2.
- No changes to DNA in various animal studies.
- No adverse effects on reproduction, development, immune, gastrointestinal, nervous systems, or general health of rats.

In summary, the Food Directorate's position is that there is no conclusive scientific evidence that the food additive TiO_2 is a concern for human health.

EFSA's position is not shared by FSANZ in Australia/New Zealand



FOOD STANDARDS Australia New Zealand

Titanium Dioxide as a Food Additive

Summary

A FSANZ review of the safety of food-grade titanium dioxide has found no evidence to suggest dietary exposure to the additive is a concern for human health.

What is titanium dioxide?

Titanium dioxide is a natural pigment that has been used for decades as a colouring agent to make foods whiter or brighter. In Australia and New Zealand it is allowed to be added to a wide range of foods. Multiple reviews by FSANZ and regulators overseas have concluded there are no safety concerns from its use in food.

Why we did this work

In 2021 the European Food Safety Authority (EFSA) published a new report which concluded titanium dioxide could no longer be considered safe.

EFSA's report noted there is no conclusive evidence that titanium dioxide is harmful, but raised concerns that some studies suggest it may damage DNA. Because of this, EFSA decided they were not able to set an amount of titanium dioxide that could be safely consumed each day.

Given the concerns raised, FSANZ reviewed key evidence relating to the safety of titanium dioxide when used in food.

How we did our assessment

We reviewed the scientific literature to find studies assessing the safety of titanium dioxide in food. This included studies in both laboratory animals and in humans.

We also issued a call for information on the safety of titanium dioxide. The information we received included new scientific data that addressed some of the concerns raised by EFSA.

What the assessment looked at

Titanium dioxide can be found in several forms, with only some used in food. The forms used in food are known as food-grade titanium dioxide.

The recent safety concerns are mainly based on studies into forms of titanium dioxide that either:

- are not used in food and have different properties to food-grade titanium dioxide, or
- are food-grade titanium dioxide that had been broken down into smaller sized particles than normally used in food, and given to animals in water rather than in food as part of their diet.

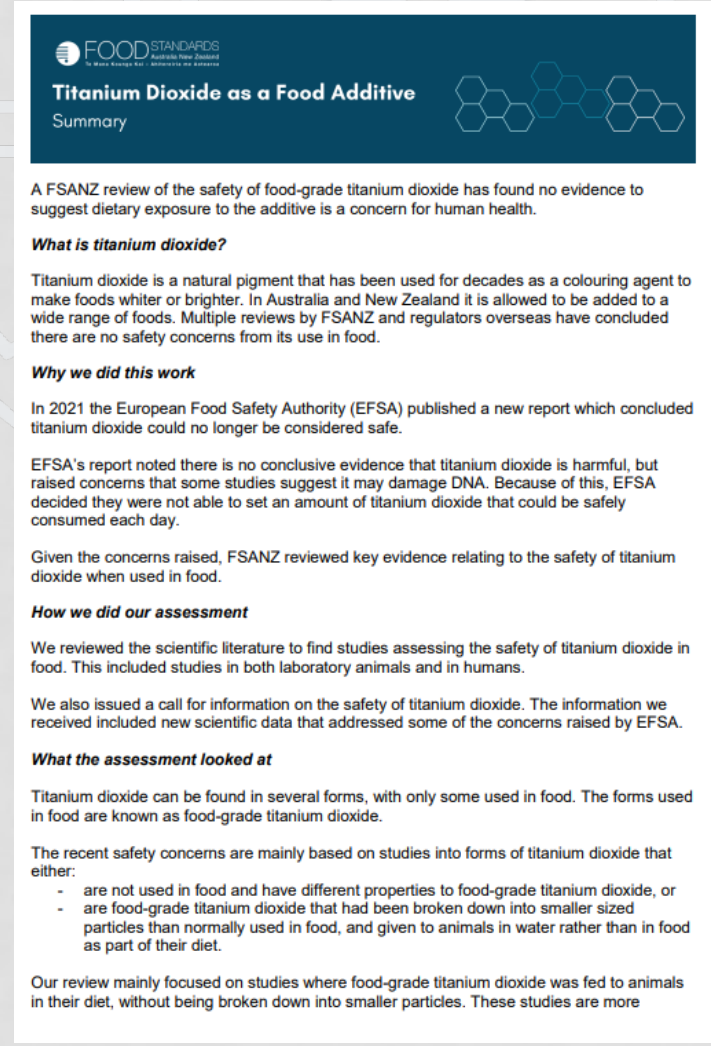
Our review mainly focused on studies where food-grade titanium dioxide was fed to animals in their diet, without being broken down into smaller particles. These studies are more

FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Key Outcomes

- No evidence food-grade TiO_2 is genotoxic;
- No evidence of toxicity or carcinogenicity or other effects observed at high levels of TiO_2 dietary concentrations in rats & mice

EFSA's position is not shared by FSANZ in Australia/New Zealand



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What we found

Absorption of food-grade titanium dioxide following ingestion in food is very low. Recent studies with food-grade titanium dioxide in rats suggest that less than 0.01% of the amount eaten is absorbed.

In animal studies there is no evidence of DNA damage from food-grade titanium dioxide. There is also no evidence of cancer or other harmful effects in studies with mice and rats fed diets containing very large concentrations of food-grade titanium dioxide over their lifetime.

Additional studies with food-grade titanium dioxide in rats found no evidence of general toxicity, and no harmful effects on reproduction, development or the gastrointestinal, immune and nervous systems.

What this tells us

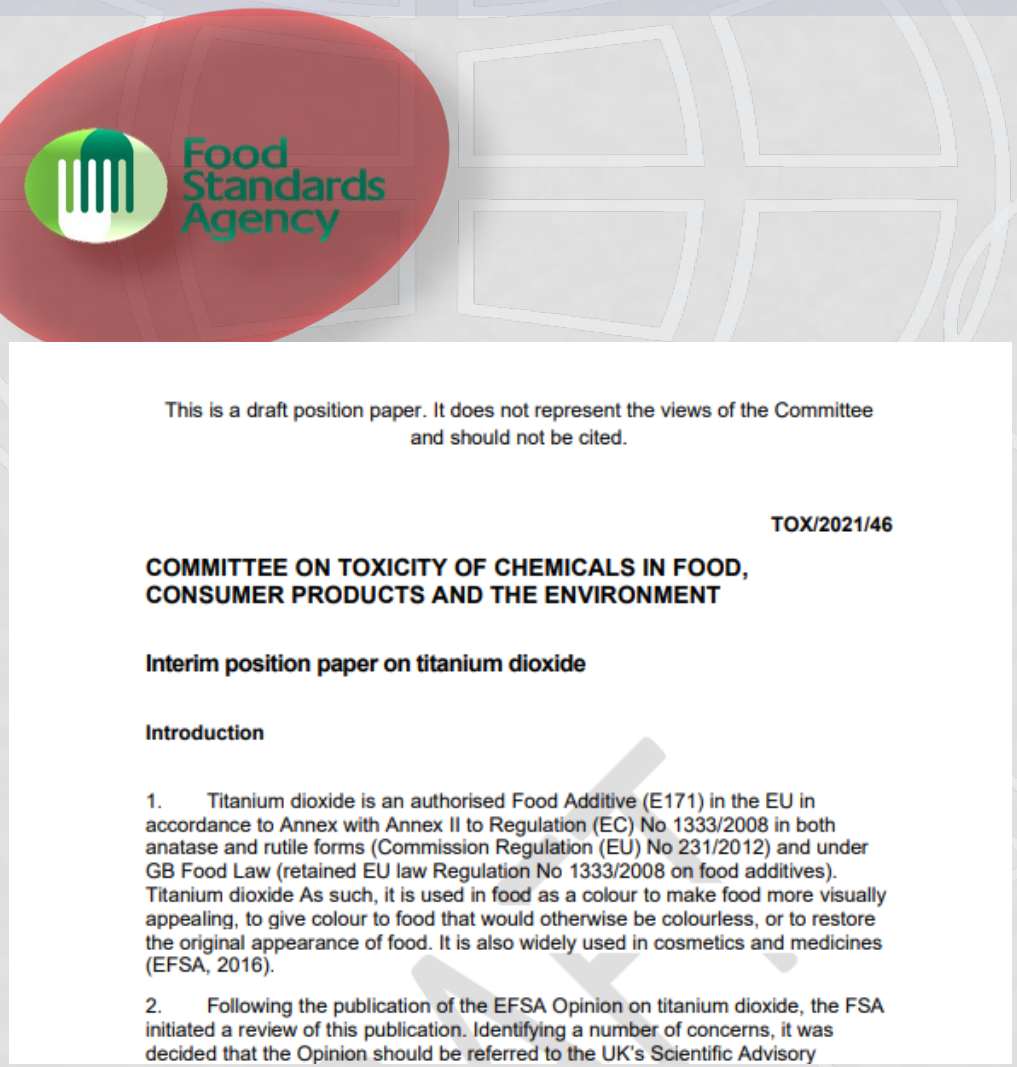
Currently, there is no evidence to suggest dietary exposure to food-grade titanium dioxide is a concern for human health.

Next steps

As no safety concerns were found, no action is required to review the current permissions for the use of titanium dioxide in food in Australia and New Zealand.

We will continue to monitor new information on the safety of titanium dioxide in food as it becomes available.

EFSA's position is not shared by the UK Food Standards Agency (FSA)



This is a draft position paper. It does not represent the views of the Committee and should not be cited.

TOX/2021/46

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Interim position paper on titanium dioxide

Introduction

1. Titanium dioxide is an authorised Food Additive (E171) in the EU in accordance to Annex with Annex II to Regulation (EC) No 1333/2008 in both anatase and rutile forms (Commission Regulation (EU) No 231/2012) and under GB Food Law (retained EU law Regulation No 1333/2008 on food additives). Titanium dioxide As such, it is used in food as a colour to make food more visually appealing, to give colour to food that would otherwise be colourless, or to restore the original appearance of food. It is also widely used in cosmetics and medicines (EFSA, 2016).

2. Following the publication of the EFSA Opinion on titanium dioxide, the FSA initiated a review of this publication. Identifying a number of concerns, it was decided that the Opinion should be referred to the UK's Scientific Advisory

Key Outcomes

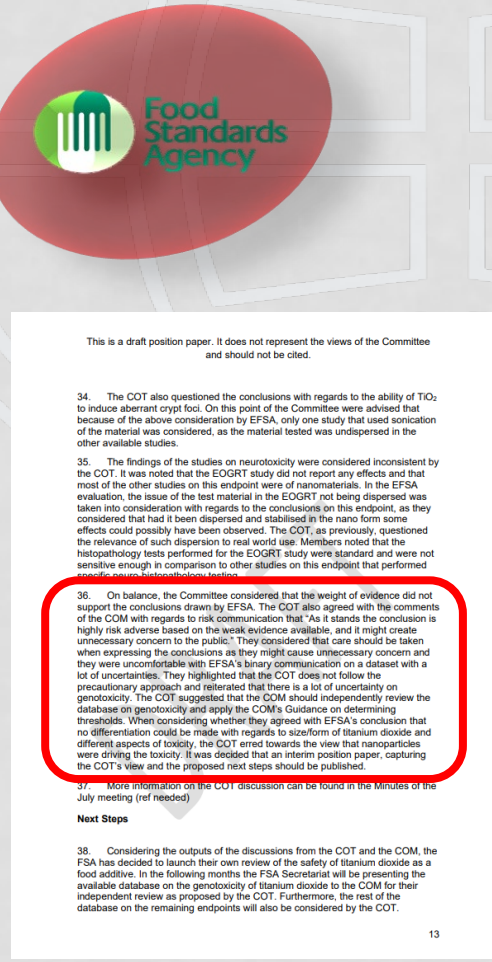
- The available evidence does not support the conclusions of EFSA

  (*interim opinion of Committee on Toxicology*)

- Formal position expected in July 2023

- Extremely critical of the EFSA Opinion

EFSA's position is not shared by the UK Food Standards Agency (FSA)



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34. The COT also questioned the conclusions with regards to the ability of TiO_2 to induce aberrant crypt foci. On this point of the Committee were advised that because of the above consideration by EFSA, only one study that used sonication of the material was considered, as the material tested was undispersed in the other available studies.

35. The findings of the studies on neurotoxicity were considered inconsistent by the COT. It was noted that the EOGRT study did not report any effects and that most of the other studies on this endpoint were of nanomaterials. In the EFSA evaluation, the issue of the test material in the EOGRT not being dispersed was taken into consideration with regards to the conclusions on this endpoint, as they considered that had it been dispersed and stabilised in the nano form some effects could possibly have been observed. The COT, as previously, questioned the relevance of such dispersion to real world use. Members noted that the histopathology tests performed for the EOGRT study were standard and were not sensitive enough in comparison to other studies on this endpoint that performed specific neuro-histopathology testing.

36. On balance, the Committee considered that the weight of evidence did not support the conclusions drawn by EFSA. The COT also agreed with the comments of the COM with regards to risk communication that "As it stands the conclusion is highly risk adverse based on the weak evidence available, and it might create unnecessary concern to the public." They considered that care should be taken when expressing the conclusions as they might cause unnecessary concern and they were uncomfortable with EFSA's binary communication on a dataset with a lot of uncertainties. They highlighted that the COT does not follow the precautionary approach and reiterated that there is a lot of uncertainty on genotoxicity. The COT suggested that the COM should independently review the database on genotoxicity and apply the COM's Guidance on determining thresholds. When considering whether they agreed with EFSA's conclusion that no differentiation could be made with regards to size/form of titanium dioxide and different aspects of toxicity, the COT erred towards the view that nanoparticles were driving the toxicity. It was decided that an interim position paper, capturing the COT's view and the proposed next steps should be published.

37. More information on the COT discussion can be found in the Minutes of the July meeting (ref needed)

Next Steps

38. Considering the outputs of the discussions from the COT and the COM, the FSA has decided to launch their own review of the safety of titanium dioxide as a food additive. In the following months the FSA Secretariat will be presenting the available database on the genotoxicity of titanium dioxide to the COM for their independent review as proposed by the COT. Furthermore, the rest of the database on the remaining endpoints will also be considered by the COT.

13

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JECFA Review of TiO2 Safety

- The Joint FAO-WHO Expert Committee on Food Additives (JECFA) will review TiO_2
- Global food additive safety coordinator made up of world-class toxicologists from around the world
- November 2022 – Issued a call for data for TiO_2
- February 2023 – TDMA submitted a comprehensive dossier to JECFA
- TDMA widely shared this dossier to many authorities
- JECFA Opinion expected in 2024
- **Will be key for food additives and important in other areas**

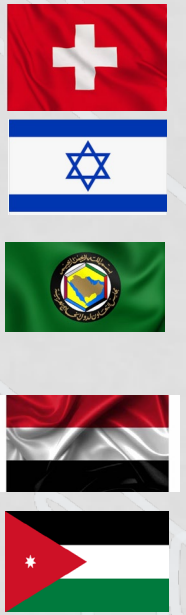
Regions following the EU

Brazil

- Initially indicated an intention to follow the EU and propose ban to MERCOSUR countries, but ANVISA is still evaluating new information.
- TDMA/TDSC and IACM is continuing to provide additional supporting information to ANVISA.

Already banned in Foods

- Switzerland: 15 September 2022
- Israel: 31 October 2022
- GCC / Saudi Arabia: 21 October 2022
  Some indications they may delay implementation until JECFA Opinion
- Yemen: 25 September 2022
- Jordan: 8 June 2022

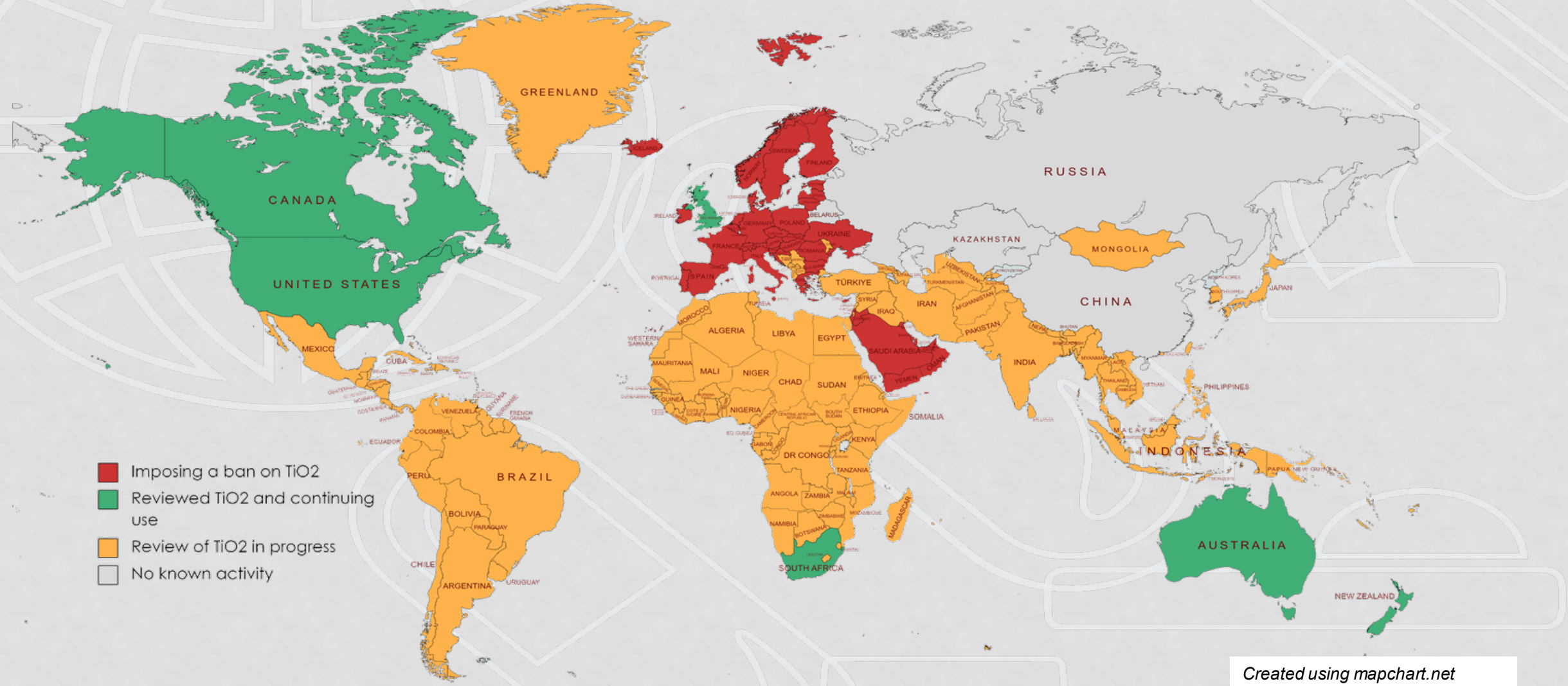


WTO and the US Gov't. getting involved due to trade implications

Other Countries Considering a Ban

Argentina	Evaluating, no position yet.
Mercosur Countries	Evaluating, no position yet.
Colombia	Evaluating, no position yet.
Japan	Evaluating, no formal position yet. Recent indications are that they have no safety concerns. Japanese Ministry to start formal review of E171 in July 2023
South Korea	WTO notification to ban E171 in food sent out on 31 January 2023. Deadline for comments was 1 April 2023. Entry into force date TBD
Russia & Turkey	No plans to take action at this time; following what happens in the EU
Thailand	Neutral and awaiting JECFA

Status of TiO2 for use in Food



Information collated from various sources, January 2023

Potential Impact of a TiO2 (E171) Ban in Pharmaceuticals

Pharmaceutical Company Initiatives

- **What products will Pharma really reformulate??**
  - Will **>91000** current drug products in the EU market be reformulated?
  - Probably **NOT** !!
  - Reformulation costs will be extremely high! (**est. 1 to 1.5 million Euros)** per product.
  - ***Could be >31 billion Euros to reformulate all products***
  - Who will end up paying for this reformulation cost?
    - ***The patients or industry??***

Pharmaceutical Company Initiatives

- **Many companies may only reformulate recently launched products and ones which are highly profitable, if TiO2 remains approved in most other countries**
  - No business case to reformulate older, low-margin products or products for niche/orphan
  - This could leave European patients without many of the drug products they need for their health which will create a **REAL safety problem**!!
- **Did EMA and EC consider that this would be the result of a TiO2 ban in pharma?**

IPEC Initiatives

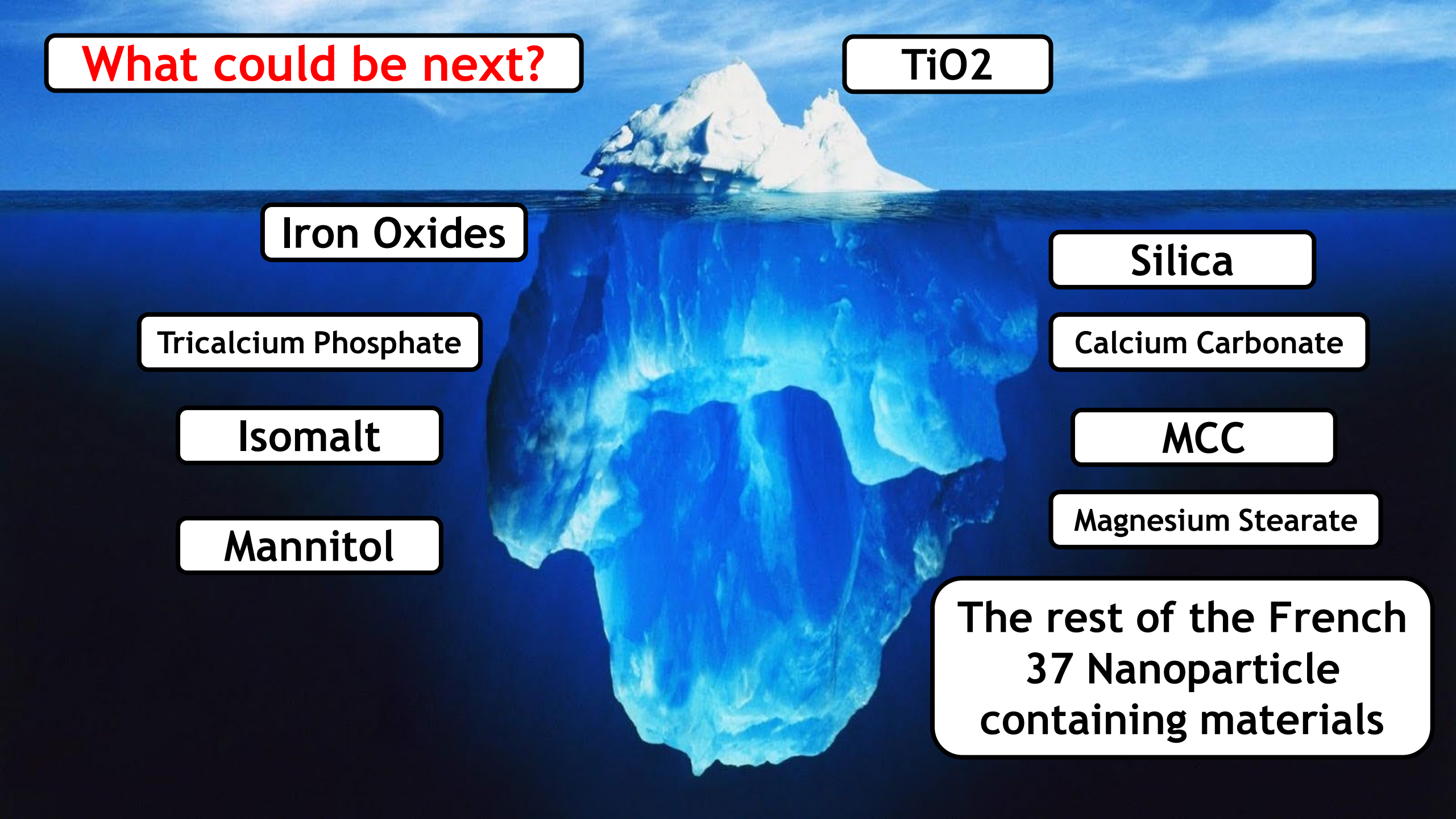
IPEC has prioritized these developing issues with TiO2

- **Collaboration established between IA/IE and the IQ Consortium**
- *Collaborations with AAPS, PQRI and various other trade associations have been initiated – publications, workshops, data collection on challenges to provide to EMA – (ex; PQRI Workshop in Washington DC, June 13-14, 2023)*
- *IQ Consortium and others have published papers on pharma impact of a ban and the challenges with using E171 alternatives (see references)*

IPEC is monitoring all issues related to Nanotechnology, including the presence of nanoparticles in other excipients and will advocate as needed

- French list of 37 additives that contain nanoparticles includes many common excipients which could be the next targets (i.e., iron oxides, silica, many TiO2 alternatives, etc.)

Nano Concerns in France on ALL ingredients containing nanoparticles


What could be next?
TiO2
Iron Oxides
Tricalcium Phosphate
Isomalt
Mannitol
Silica
Calcium Carbonate
MCC
Magnesium Stearate
The rest of the French 37 Nanoparticle containing materials

Consumer Activist Activity in the U.S.

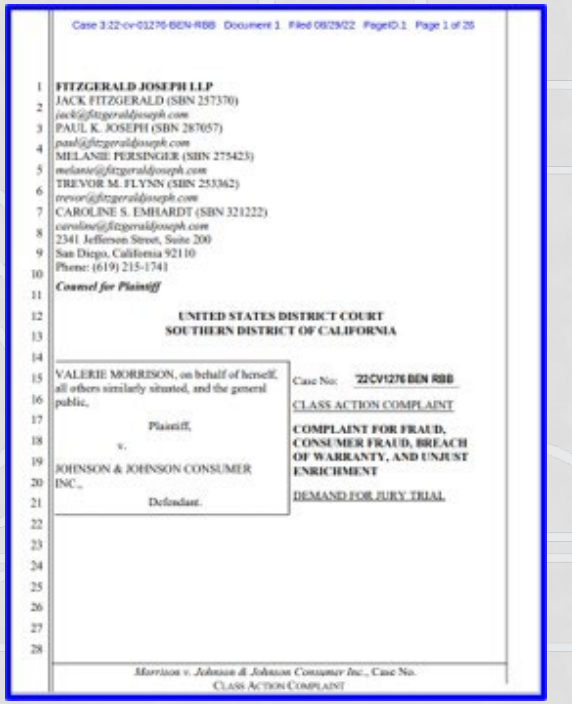
Lawsuit against Mars, Inc. - Skittles

- July 2022, class action lawsuit was filed against Mars, Inc., the maker of Skittles candies.
- The plaintiff alleges that Skittles "are unfit for human consumption because they contain TiO2." a "known toxin"
- Garnered significant media attention: *"Are Skittles Toxic from Titanium Dioxide?"*
- Lawsuit is not based on science
  - We must get the facts into the public domain
  - TDMA, other groups and individuals are working to do this.
- Dr. Lyle Burgoon, independent expert toxicologist: "4,080 Skittles per Day, DNA Damage and the Law - The Toxic Truth Blog"
  - Calculations show that people would have to eat 4080 Skittles a day, every day for over 9 years before having any safety risk assuming that all the EFSA study data evaluated was accurate

Lawsuit against J&J - Tylenol

- **August 30, 2022 - Lawsuit claims J&J failed to warn consumers that some Tylenol contains titanium dioxide.**
  - Consumer class action lawsuit filed in California southern district court over J&J's labeling of Tylenol.
  - Accuses the company failed to warn consumers that certain varieties of Tylenol contain titanium dioxide, a metal which can accumulate and cause harm inside the body.
  - Similar to claims seen in the Skittles lawsuit.
  - **This lawsuit more directly brings the issue into the pharma world and shows that consumer groups are now attacking pharma as well as food uses of TiO_2.**

Thuocdactri247.com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UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

VALERIE MORRISON, on behalf of herself, all others similarly situated, and the general public,
Plaintiff,
v.
JOHNSON & JOHNSON CONSUMER INC.,
Defendant.

Case No: '22CV1276 BEN RBB
CLASS ACTION COMPLAINT
COMPLAINT FOR FRAUD, CONSUMER FRAUD, BREACH OF WARRANTY, AND UNJUST ENRICHMENT
DEMAND FOR JURY TRIAL

Morrison v. Johnson & Johnson Consumer Inc., Case No.
CLASS ACTION COMPLAINT

How Many Pills/Capsules Would It Take to Reach the Alleged Genotoxic Dose?

- To understand pharma exposure potential after the Tylenol lawsuit, IPEC asked Dr. Burgoon to perform a statistical analysis (similar to the Skittles example) showing how many tablets or capsules need to be ingested daily to reach the genotoxic dose described by EFSA (80mg/L)

- The worst-case scenario showed it would take 681 tablets, taken every 6 hr. (or 4 times a day), every day for about 8.5 years to reach the genotoxic dose

  - ~2 tablets per minute for 8.5 years

  - Or…275,000 tablets every 6 hours for one day.

Recent NGO Activity on TiO2 in the U.S.

February 2023 - California

- Assembly Bill 418 seeks to prohibit the manufacture, sale or distribution of food products in California containing 5 additives including TiO_2
- If passed, the bill would go into effect on 1 January 2025

- **Similar Bills have been filed in New York and New Jersey**

- **Petition has been filed to the FDA by a group of NGOs to repeal approval of TiO2 use in foods**

- **TiO_2 industry and food groups in the US are vigorously defending the safety of TiO_2 - Jay West from TDSC will provide further details on this**

Conclusions

- **Advocacy is needed to address the spread of the non-scientific precautionary decisions from negatively impacting patients and consumers around the world!**
- Progress is being made in conducting evaluations to address uncertainties/gaps in current data.
- Industry groups will continue to engage with the EU Commission and global scientific authorities (incl. EFSA and EMA) to support further evaluation of E171 using new science-based information as it becomes available.
- **TiO_2 is just the tip of the Iceberg! Many other commonly used food additives are also at risk!**

Recently Published Papers and Studies

- The Role of Titanium Dioxide (E171) and the Requirements for Replacement Materials in Oral Solid Dosage Forms: An IQ Consortium Working Group Review - Journal of Pharmaceutical Sciences (jpharmsci.org)
- A weight of evidence review of the genotoxicity of titanium dioxide (TiO2) – ScienceDirect
- Everyday Toxicology – Exposure to Ingredients: Titanium Dioxide - Center for Research on Ingredient Safety (msu.edu)
- Why would the EU want to ban titanium dioxide in pharmaceutical products? What would be the potential impact on patients? | Published in Journal of Excipients and Food Chemicals (scholasticahq.com)
- How Banning TiO2 Might Impact Pharma (pharmtech.com)

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Questions??