SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

REGULATORY & SAFETY EVALUATION Specialty Section

Summer 2025 Newsletter

Table of Context:

President's Message

Dear RSESS Members,

As I write this message, the RSESS Program Committee is actively reviewing proposals for sessions at the 2026 SOT Annual Meeting. This is one of my favorite times of the year, as we have the opportunity to help shape the scientific content of the meeting and gain an early look at some of the most exciting and innovative research emerging from across our discipline. I highly encourage anyone interested in expanding their perspective beyond their immediate sector to consider volunteering with this committee—it's a rewarding experience that offers both insight and inspiration.

Our Specialty Section has been busy over the past several months. In December, we hosted the webinar *"Opportunities to Harness AI and ML in Drug Discovery Toxicology"*, followed in May by a special session featuring presentations from our recent award recipients—first recognized at our annual meeting reception in March. These events showcase the breadth of talent and innovation within our community.

Continued on Page 2

President's Message (cont.)

Your RSESS Officers have also been working diligently to expand our impact through new initiatives. One of the most exciting developments is a new collaboration with the European Regulatory and Safety Sciences Specialty Section (ERASS) of EUROTOX. Starting this fall, we will launch a transatlantic seminar series focused on current toxicology topics, highlighting similarities and differences in regulatory approaches between our regions. This initiative is particularly timely given the FDA's recent announcement of its plan to phase out animal testing requirements for monoclonal antibodies and other pharmaceuticals.

Looking ahead, we're also thrilled to offer a September webinar titled *"An Overview of the Safety Evaluation of Veterinary Pharmaceuticals"*, presented by Samuel Fletcher, Head of the Human and Environmental Safety Team at the UK's Veterinary Medicines Directorate (VMD).

Supporting the next generation of toxicologists remains a top priority. We are committed to providing more opportunities for students and early-career professionals to explore career paths and build essential skills. If you have ideas or suggestions for how we can better serve our membership—especially in this area—we would love to hear from you.

Thank you for your continued engagement with RSESS. Your involvement is what drives our success.

Warm regards,

Claire Neilan, PhD DABT
President, RSESS

REGULATORY & SAFETY EVALUATION
Specialty Section

New Officer Introduction:

RSESS is excited to welcome and introduce the new RSESS officers!

April O'Connell – Vice President-Elect
April O'Connell is honored to serve the RSESS as the incoming VP-elect for 2025. April has worked in the pharmaceutical industry for the past 10 years and is currently a Scientific Associate Director at Amgen in Nonclinical Safety and Risk Assessment. Prior to Amgen she worked at Horizon Therapeutics and Gilead Sciences after completing postdoctoral studies at the EPA's Integrated Systems Toxicology Division as an ORISE participant (2014-15) and graduate studies at the University of Arizona in 2013.

Tim McGovern – Councilor
Tim McGovern is excited to begin his term as RSESS Councilor. He is currently the Co-Founder and Principal Consultant at White Oak Regulatory Tox, LLC following his recent retirement from the US Food and Drug Administration where he was an Associate Director for Pharmacology/Toxicology in the Office of New Drugs within the Center for Drug Evaluation and Research since 2013. Prior to that, Tim was a Managing Consultant at SciLucent, LLC, and a primary reviewer and Supervisor in the FDA's Division of Pulmonary and Allergy Drug Products.

New Officer Introduction (cont.):

Nikolaos Georgiadis – Program Committee Chair
Nikolaos Georgiadis is a toxicologist with experience in the field of international regulation linked to chemicals. He holds a PhD and an MSc in Toxicology, an MSc in Pharmacology, an MSc in Food Science, a university degree in Food Science and an MBA. Since 2010, Nikolaos has worked as Human Health Toxicologist with European Chemicals Agency (ECHA) and European Food Safety Authority (EFSA). In 2021, he was appointed as the Technically Qualified Member of the Board of Appeal of ECHA. He has published various articles and book chapters, as well as numerous scientific opinions, dealing with methodologies for risk assessment. He has been a member of SOT since 2016, and a member of the Finnish and Greek Societies of Toxicology and a Eurotox certified Toxicologist (ERT).

2024-2025 RSESS Leadership:

President:
Claire Neilan
(cneilan@ideayabio.com)

Secretary/Treasurer:
William D. Klaren
(wklaren@toxstrategies.com)

Senior Councilor:
Dahea You
(dhyou21@gmail.com)

Vice President:
Manoj Aggarwal
(manoj.aggarwal@merck.com)

Past President:
Senthil Perumal Kuppusamy
(senthilpk@gmail.com)

Postdoctoral Rep.:
Taylor Carter
(taylor.carter@uscmed.sc.edu)

Vice President-Elect:
April O'Connell
(aoconn02@amgen.com)

Junior Councilor:
Timothy McGovern
(timmcgovern7@gmail.com)

Grad Student Rep.:
Olivia Lampe
(liv.lampe@tamu.edu)

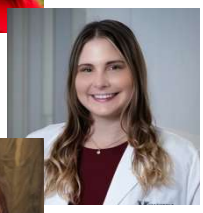
Appointed Officers:

Program Committee Chair:
Nikolaos Georgiadis
(nikolaos.georgiadis@echa.europa.eu)

Endowment Committee Chair
Madelyn Huang
(madelyn.huang@premierconsulting.com)

2024/2025 Award Winners:

At the RSESS Reception at the Annual Meeting earlier this year, multiple talented members were recognized for their outstanding work in the field of Toxicology. Below is the list of Award winners for 2024/2025. Many congratulations to all!



Graduate Student Excellence Award:

Ist Place: **Gabrielle Griffin*** (University of Louisville, Kentucky, KY)
Unraveling the Sex-Dependent Mechanisms of Hexavalent Chromium-Altered, Diet-Induced Metabolic-dysfunction Associated Steatotic Liver Disease

2nd Place: **Katie Clark** (Vanderbilt University, Nashville, TN)
Low-Level Manganese Exposure in Drinking Water Alters Brain Relaxometry Profiles: A Potential Biomarker for Environmental Metal Exposure

3rd Place: **Emma VanderMeulen** (University of Florida, Gainesville, FL)
Distribution and Environmental Impact of Pharmaceuticals and Personal Care Products (PPCPs) in the Lake Huron–Lake Erie Corridor

Postdoc Excellence Award:

Ist Place: **Li Xia** (National Center for Toxicological Research, FDA, Jefferson, AR)
Mechanistic exploration of mutagenicity of N-nitrosodiethylamine via the cII transgenic mutation assay, Duplex Sequencing and gene expression analysis of the liver and bone marrow samples in Big Blue rats

2nd Place: **M. Jakaria** (Purdue University, West Lafayette, IN)
The neuromelanin building block 5,6-dihydroxyindole increases sensitivity to ferroptotic toxicity

Best Paper of the Year Award:

Liquid application dosing alters the physiology of air-liquid interface (ALI) primary human bronchial epithelial cell/lung fibroblast co-cultures and in vitro testing relevant endpoints
Nicholas M. Mallek, Elizabeth M. Martin, Lisa A. Dailey, and Shaun D. McCullough
Front Toxicol. 2024 Jan 23;5:1264331.

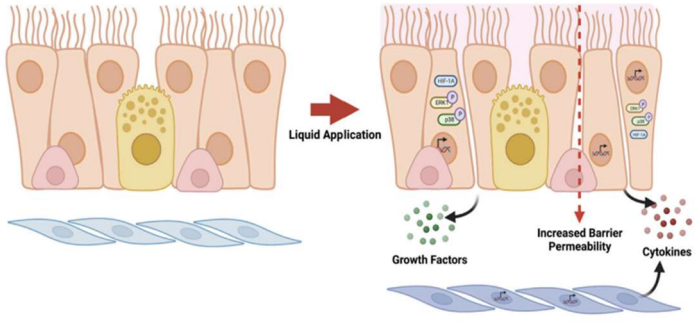
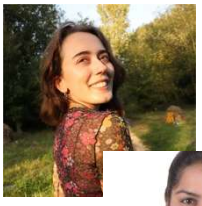


FIGURE 8
Summary of effects caused by liquid application to dpHBEC-ALI cultures. The application of 250 µL ALI medium induces the alternative regulation of transcripts, the activation of stress-responsive protein signaling pathways, the secretion of pro-inflammatory cytokines and growth factors, and the breakdown of epithelial barrier integrity. Figure made with BioRender.com.

Submitted by Shaun McCullough, RTI International

2024/2025 Award Winners: (cont.)



Elsevier Award: 3-Minute Thesis (TMT):
1st Place: **Emma Hailwood*** (UK HSA, Oxford, UK; University College London, London, UK.)

Understanding how blending renewable fuels with diesel changes the in vitro toxic potential effects within the lungs and influences lung cancer mechanisms.

2nd Place: **Dhruthi Mutyala** (Southern University and A&M College, Baton Rouge, LA)

Lipid Raft Disruption by E-Cigarette Exposure: Insights into Proteasomal Dysfunction and Inflammatory Pathways.

ISRTP (International Society of Regulatory Toxicology and Pharmacology) Awards:
Graduate Award - **Gabrielle Griffin**
Postdoc Award - **Li Xia**

RSESS Travel Award:
Sandeep Kondakala* (US FDA)

University of Arizona Trainee Award:
Daniel Wurm

Sex-dependent elevation of hepatic acylcarnitine species due to myocardial infarction

*Also, get to know some of the award winners better with a feature created by our Endowment Chair, **Madelyn "Mimi" Huang**, below in this newsletter!

Do not forget to apply for currently available SOT awards!! These awards cover a range of career and education levels and are open to many. Please visit the SOT website for more details, https://sot.toxicology.org/award.

A huge thank you to our RSESS members who collaborated with our current board members to review the applications: April O'Connell, Kevin French, and Kenjie Amemiya. If you are interested in reviewing applications later this year (2025/2026 awards) please email Claire Neilan or Manoj Aggarwal.

International Collaboration:

Over the years, the Society of Toxicology's Regulatory and Safety Evaluation Specialty Section (SOT-RSESS) has collaborated with various specialty sections within SOT. Now, SOT-RSESS and the European Society of Toxicology's European Regulatory Affairs and Safety Specialty Section (EUROTOX-ERASS) are taking the next step to establish a collaborative strategic partnership, creating a vital bridge in international toxicological research and regulatory science. This collaboration facilitates the exchange of scientific knowledge, regulatory perspectives, and emerging methodologies across continental boundaries, supporting harmonization of approaches for safety evaluation and risk assessments on a global scale. By jointly organizing workshops, webinars, and other initiatives, these specialty sections highlight global challenges in regulatory toxicology while providing valuable professional development opportunities for their members. The cooperation between SOT-RSESS and EUROTOX ERASS exemplifies how scientific societies can overcome geographical limitations to advance the field of regulatory toxicology and ultimately enhance human health protection.

SOT-RSESS: Regulatory and Safety Evaluation Specialty Section
EUROTOX-ERASS: Risk Assessment (ERASS) - Eurotox

Upcoming Webinar Announcement:

An Overview of the Safety Evaluation of Veterinary Pharmaceuticals

Wednesday, September 24, 2025
10:00 AM to 11:30 AM (US EDT, UTC -4)

Register free HERE!!!
https://aim-hq.zoom.us/webinar/register/WN_0ASzsD49Rna6rO7flfC0aA

Hosted by: The Regulatory and Safety Evaluation (RSESS) and Comparative Toxicology, Pathology, and Veterinary Toxicology (CTPVSS) Specialty Sections

Speaker: Samuel Fletcher, Head of the Human and Environmental Safety Team at Veterinary Medicines Directorate (VMD), UK

This webinar will provide an overview of non-clinical safety data requirements for veterinary drugs, including 'Novel Therapies', in the UK, incorporating VICH requirements. Participants will gain insights into the distinct regulatory considerations for both companion animals and food-producing species, exploring the nuanced safety evaluation approaches required for each category. Additionally, the webinar will highlight some of the emerging opportunities to incorporate New Approach Methodologies (NAMs) and apply the 3Rs principles (Replacement, Reduction, Refinement) in veterinary drug development. This informative presentation is designed for toxicologists, regulatory professionals, researchers, and others involved in veterinary pharmaceutical development seeking to navigate the complex global regulatory landscape effectively.

Program Committee Update:

A total of 24 session proposals for the 2026 Annual Meeting were received for review and endorsement by the RSESS, while a total of 21 session proposals were received for pre-review.

Many thanks to our volunteers who participated in the review of 2026 proposals – Nikolaos Georgiadis (Chair), Claire Neilan, Leah Zorilla, Matt Taylor, Sherleen Adamson, Mimi Huang, Ashley Brinkman, Kevin French, Manoj Aggarwal, Nicholas Drury and Deidre Dalmas-Wilk. If you have any interest in participating on this committee or if you simply have any questions, please contact Claire Neilan cneilan@ideayabio.com or Nikolaos Georgiadis nikolaos.georgiadis@echa.europa.eu

---

Graduate Student and Post-Doc Update:

Hi everyone! It was a pleasure meeting many of you at the annual meeting. We would like to extend a warm welcome to new RSESS trainees especially. We had a lot of amazing trainees receive RSESS student awards, and we always encourage you to apply for awards if you are planning to submit an abstract at SOT next year. As your graduate and postdoctoral student representatives, we want to make sure your voices are heard. If you have any trainee networking ideas or additional topics you'd like brought up, feel free to reach out—we're always happy to advocate on your behalf!

Happy Spring!

Olivia Lampe
RSESS Graduate Student Representative

Taylor Carter, PhD
RSESS Postdoctoral Representative

Regulatory Guidance Subcommittee Update:

Dahea You, PharmD, PhD, DABT --- Stephene Ford, BS, MBM --- Jessica Sapiro, PhD, DABT

The regulatory guidance subcommittee was formed in the fall of 2022 to alert RSESS membership of new and updated guidances as well as impactful articles in the field of regulatory and safety evaluation.

RSESS is seeking new members to begin serving on this Regulatory Guidance Subcommittee beginning May 1, 2025. In particular, we are looking for individuals with expertise in working in or supporting drug development/pharmaceuticals, environmental, in vitro/alternatives, consumer products, pesticides, and medical devices. The commitment will be 1-year and the expectation is to share and provide text for a communication for at least 1 newly released or recently updated regulatory guidance or impactful research article to the regulatory and safety evaluation field.

Seeking New Members!

Please contact Dahea You (dhyou21@gmail.com) if you are interested.

Folders have been created on ToXchange in which new and recently updated guidance and articles of interest are stored. *RSESS Guidances and Articles (Remember to log in on the SOT site to get full access.)*

Recent additions include:

- **Artificial Intelligence (AI) in Drug and Biological Product Development:** The FDA distributed a new draft guidance, "Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products," in January 2025. AI model selection, credibility assessment, and performance are key considerations. A framework consisting of 7 steps is provided to perform a risk-based credibility assessment of the AI model to help ensure that the model is objective, dependable, accurate, and robust for its intended application. Performance should be continually assessed, looking for data drift and updating the AI model as needed as new data inputs are introduced over the drug product life cycle. Documentation of this performance review, along with the initial system credibility assessment, continue to validate the model's on-going credibility. Early engagement with the FDA is encouraged to set expectations regarding appropriate risk and credibility assessments, identify potential challenges, and discuss possible solutions to challenges. FDA Commissioner Robert M. Califf, M.D. commented: "With the appropriate safeguards in place, artificial intelligence has transformative potential to advance clinical research and accelerate medical product development to improve patient care."

- **Hybridization-Dependent Off-Target Risk Assessment for Oligonucleotide Therapeutics**: The Oligonucleotide Safety Working Group published the updated industry recommendations for assessing off-target risk of oligonucleotide therapeutics (ONTs). The paper reviews (1) the mechanism of the off-target toxicity by ONTs; (2) class-wide and class-specific (for steric blocking oligonucleotides and siRNAs) considerations in assessing the off-target risk of ONTs; and (3) proposed workflow and decision tree in assessment of hybridization-dependent off-target risks of ONTs. The 5-step assessment approach consists of two phases: (1) screening phase which involves in silico prediction and transcriptomic analysis; and (2) in-depth assessment phase which involves further in silico characterizations of potential off-targets, experimental verification in relevant in vitro models, and assessment and mitigation of off-target risks. This paper serves as a valuable resource complementing the recent FDA guidance on Nonclinical Safety Assessment of ONTs.

  The Utility of NAMs for Regulatory Decision Making (Please find below)

- **The Agency Review on Genotoxicity of Titanium Dioxide** (Please find below)

Previous additions over the past year include:

- Publications on nonclinical safety assessment of oligonucleotide therapeutics, including the new FDA guidance, and industry recommendations on gene tox and carcinogenicity testing
- Novel Foods guidance from EFSA (European Food Safety Authority)
- FDA draft guidance on Ames Positive follow-up
- FDA draft guidance on Gene/Cell therapy development
- EMA draft guidance on Gene therapy development
- EMA guidance on environmental risk assessment
- Revised FDA guidance on the control of nitrosamine impurities in human drugs
- Publications by ICH S1B(R1) Expert Working Group reviewing the framework and outcomes of the weight of evidence (WoE) approach for carcinogenicity risk assessment
- Enzyme Containing Cleaning Products Risk Assessment
- FDA guidance on Development of Chimeric Antigen Receptor T Cell Products
- FDA guidance on Human User Safety in Animal Drug Applications
- EMA concept paper on Nanoparticle Safety in Veterinary Medicine

As a reminder, all RSESS members must be logged into ToXchange to view guidances and articles.

RSESS would like to thank the 11 subcommittee members with additional ad-hoc contributors across several sectors and areas of the globe for their contributions over the last year!!

Jessica Sapiro (Chair)
Dahea You (Co-Chair)
Kevin French
Pramila Singh
Logeswari Ponnusamy
Jossie Garthoff
Gina Hilton
Erik Pacyniak
Stephene Ford
Francis Kruszewski
James Kim

FDA Introduces a Paradigm Shift for Regulatory Animal Testing Requirements:

As a direct result of the sulfanilamide and thalidomide tragedies, the Federal Food, Drug and Cosmetic Act (FD&C Act) of 1938 and the Kefauver-Harris amendment in 1962 were enacted to give FDA authority to oversee the safety of food, drugs and cosmetics for sponsors of clinical trials to submit data from "preclinical tests (including tests on animals)" in order to demonstrate that safety prior to testing in humans. However, the high rate of attrition for drug candidates associated with traditional animal testing suggests alternative methods to support clinical development should be considered.

The FDA Modernization Act 2.0 passed in 2022 formally recognized the use of new approach methods (NAMs) to support investigation of the safety and efficacy of human pharmaceuticals. A subsequent amendment to the 2022 legislation, known as FDA Modernization Act 3.0 (2024), directed FDA to establish approaches to support the development, qualification, and implementation of NAMs for regulatory use to align with principals of the 3Rs to improve the speed and predictivity of nonclinical testing.
Progress has been made towards the adoption and implementation for the use of NAMs in regulatory decision making. Monoclonal antibodies (mAbs) represent a promising modality to treat a wide range of diseases, however nonclinical safety assessment of mAbs is recognized to be complex, expensive and time intensive. As such FDA published a strategic roadmap which outlined examples and regulatory expectations for the application of NAMs for nonclinical development of mAbs (FDA 2025). Examples of NAMs with the potential to facilitate mAb development included, but are not necessarily limited to systems biology (e.g., cell- and tissue-based assays to evaluate whole organism responses), engineered tissues (e.g., scaffolds and cells to form biologically active tissues), omics and computer modelling strategies (computational modeling, artificial intelligence, machine learning) and microphysiological systems (e.g., organs-on-chips). FDA recommend sponsors apply NAMs in an integrated (combinatory) approach to adequately address potential gaps in animal data and enhance human relevance (e.g., human organ chip for toxicity; physiologically based pharmacokinetic model for PK; AI immunogenicity predictor). Of note, the use of NAMs (e.g., organoids) have been used to support biologic submissions to FDA particularly when monoclonal antibodies are not cross-reactive in animal models.

To support the 3-year timeframe for implementation of their strategic framework to reduce animal testing FDA will also be considering investigate international clinical safety data, working to reduce routine toxicology testing timeframes, develop an open-access toxicity database, and validate NAMs through retrospective and prospective analyses. Additionally, FDA will work to update its guidelines to allow consideration of data from these new methods and offer, on a case-by-case basis, streamlined reviews in an attempt to incentivize investment in modernized testing platforms. For the long-term, FDA expectations are to establish animal studies as the exception rather than the norm, with a comprehensive NAM toolbox becoming the new standard for safety assessment.

Broad utilization and adoption of NAMs in support of regulatory submissions will likely require involvement across stakeholders most notably public/private pharmaceutical developers. Carratt et al. (2025) provided an industry perspective on considerations, challenges and opportunities for when including NAMs data as part of regulatory submissions.

- Recommend regulatory health authorities create a "safe harbor" submission of supplementary NAMs data in advanced of qualified nonclinical methodologies
- Sponsors should provide detailed rationale and justification on the

purpose and use for how NAMs data effectively replaces (supplements) traditional animal data

- Recognition that clinical translation of NAMs data likely to exceed timeframe for nonclinical method qualification
- Acceptance of nonclinical safety assessment packages using validated NAMs by regulatory health authorities will be critical to maintain momentum for their adoption in drug development
- The pharmacological target(s), mechanism of action, and the modality are critical to determine the appropriateness and value of any given NAM
- Given potential metabolism-based off-target effects observed with small molecules sponsors are encouraged to leverage non-animal NAM assays to supplement traditional animal data
- Implement available 3R approaches for nonclinical safety assessment programs including avoiding repetitive studies unlikely to identify novel toxicities, eliminating recovery groups (when appropriate), eliminate chronic toxicity studies (when appropriate), select the most appropriate, lowest order species, consider the use of virtual control groups
- Enrich computational toxicology prediction models to enable a "proof of safety" risk assessment score to support clinical trial design, dose level selection and confirmation of an appropriate safety monitoring strategy
- Sponsors urged to contribute to the evolution of NAMs through consortia participation and peer-reviewed publications and document the reduction of animals in studies/programs

It is recognized that NAMs intended to reduce animal tests are still in various stages of development. Significant research investment from regulatory authorities and sponsors alike will be required to validate the efficiency and translatability of these nonclinical data as replacements for animal testing to inform regulatory decision-making. The FDA's roadmap signifies a paradigm shift in drug development, moving away from animal testing towards more reliable and ethical alternatives. This initiative not only addresses the limitations of animal models but also aims to enhance drug safety, reduce research and development costs, and improve the efficiency of the drug development process.

Prepared by: Erik K. Pacyniak, PhD, DABT

References

Carratt SA, Zuch de Zafra CL, Oziolor E, Rana P, Vansell NR, Mangipudy R, Vaidya VS. An industry perspective on the FDA Modernization Act 2.0/3.0: potential next steps for sponsors to reduce animal use in drug development. Toxicological Sciences, 2025, 203(1), 28–34.

FDA 2025. Roadmap to Reducing Animal Testing in Preclinical Safety Studies. Available at: https://www.fda.gov/media/186092/download

Update on Titanium Dioxide: Global Regulatory Bodies Reaffirm Safety of Titanium Dioxide (TiO_2) as a Food Additive:

The European Food Safety Authority (EFSA) raised concerns in 2021 about the potential genotoxicity of titanium dioxide (TiO_2), particularly in its nanoparticle form, when used as a food additive (E171). This prompted a series of reviews and reassessments by various global regulatory bodies to evaluate the safety of TiO_2 who reinforced the scientific consensus regarding the safety of TiO_2 in food (***TDMA***). Details are outlined below. There is a growing international consensus that existing scientific evidence suggests E171 is safe as a food additive.

European Union (EU)

Cosmetics: The **Scientific Committee on Consumer Safety (**SCCS) concluded that the available evidence is insufficient to exclude the genotoxicity potential of most TiO2 grades in oral cosmetic products, except for two nano grades (RM09 and RM11), which show no genotoxicity concern. More data is needed on the potential uptake and cellular effects of these nano grades in the oral mucosa to consider them safe for oral-care products.

Medicines: The EMA concluded (in 2021) that replacing TiO2 in medicines cannot be achieved without a negative impact on the quality and quantity of medicines in the EU. It has highlighted the essential role of TiO2 in medicines, including its use in protective coatings to preserve the efficacy of medicines over time and its role in ensuring color consistency for patient safety. No viable alternatives are available for Pharmaceutical use thus far. The EU will re-evaluate the use of TiO2 in medicines by February 2025.

United Kingdom (UK)

The UK Committee on Mutagenicity (COM) reviewed studies referenced by the European Food Safety Authority (EFSA) and additional literature from 2021 to 2023 and found "little evidence" of health concerns related to TiO_2 in nanoform, noting that study results have not been consistently replicated across different laboratories. Additionally, E171 (food-grade TiO_2) does not fall under the definition of a nanomaterial, as less than 50% of its particles are in nanoform.

United States

The U.S. Food and Drug Administration (FDA) has confirmed the safety of TiO_2 as a food additive, referencing recent conclusions from the World Health Organization (WHO) and the Food and Agriculture Organization (FAO), which found no conclusive evidence to support concerns raised by the EFSA in 2021. The FDA allows the use of TiO_2 as a color additive in foods, provided the quantity does not exceed 1% by weight of the food, as specified in FDA regulations (21 CFR 73.575).

Canada

Health Canada's Food Directorate's comprehensive "state of the science" report confirms the safety of TiO2 as a food additive in Canada and internationally, despite recent analyses indicating a significant portion of particles may be within the nanoscale. Health Canada conducted its own review of potential genotoxic risk of TiO2 nanoparticles and found no conclusive evidence of cancer or other adverse effects from food-grade TiO_2. Health Canada will continue to monitor emerging science on the safety of TiO_2 as a food additive and may revisit their position if new information becomes available.

Australia and New Zealand

Food Standards Australia New Zealand (FSANZ) found no evidence suggesting human health concerns of dietary exposure to food-grade TiO_2. TiO_2 has been used for decades as a coloring agent in foods without reports of adverse effects. Although the EFSA raised concerns in 2021 about potential DNA damage from TiO_2, they found no conclusive evidence of harm.

China

A new study (***Liang C et al. (2024***) from the Chinese National Centre for Food Safety Risk Assessment confirmed the safety of food-grade TiO_2 (E171), finding no adverse effects on human health.

Japan

The Ministry of Health, Labour and Welfare of Japan (MHLW) reaffirmed the safety of TiO_2 as a food additive. A 90-day study by the Japanese National Institute of Health Sciences (NIHS) showed extremely low absorption and no adverse effects from oral ingestion of TiO_2. Japan will continue to allow TiO_2 as a food additive, with no further action required.

Brazil

The Brazilian Health Regulatory Agency (ANVISA) concluded that existing scientific evidence does not indicate safety concerns about using food-grade TiO_2. ANVISA noted that the EFSA 2021 opinion was based on studies that did not reflect the actual use of food-grade TiO_2 in food and did not confirm a concrete risk.

WHO JECFA

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) found no safety concerns of TiO2 as a food additive (E171) due to its low oral absorption and lack of identifiable hazards. The acceptable daily intake (ADI) for E171 remains "not specified," indicating no required limits on its consumption.

Recent Publications:

A study by ***Battersby RV et al, 2024***, indicates that TiO_2 does not affect the reproductive system. This research was commissioned by the Titanium Dioxide Manufacturers Association (TDMA) in response to a request from the European Commission to fill knowledge gaps identified by the European Food Safety Authority (EFSA) in their 2016 opinion.

A critical review paper updated the analysis of TiO_2's genotoxic potential, focusing on in vitro comet assays, mode of action, and cellular uptake studies. However, the paper found inconsistencies in the data quality (Kirkland, D et al.***, 2024***).

Prepared by: Logeswari Ponnusamy, DMV

Reference:

1. TDMA news. News Archive - TDMA
2. Liang C *et al.* (2024). Genotoxicity evaluation of food additive titanium dioxide using a battery of standard in vivo tests. *Regulatory Toxicology and Pharmacology* **148:** 105586. doi: 10.1016/j.yrtph.2024.105586
3. Battersby RV, Adam J, Williams AL, DeSesso JM. Extended one-generation reproductive toxicity study of food-grade titanium dioxide E171 with emphasis on reproductive and endocrine endpoints. Reprod Toxicol. 2024 Dec;130:108687. doi: 10.1016/j.reprotox.2024.108687. Epub 2024 Aug 20. PMID: 39173974.
4. Kirkland, D., Burzlaff, A., Czich, A., Doak, S. H., Fowler, P., Pfuhler, S., & Stankowski, L. F. (2024). Updated assessment of the genotoxic potential of titanium dioxide based on reviews of in vitro comet, mode of action and cellular uptake studies, and recent publications. *Regulatory Toxicology and Pharmacology*, 105734.

Endowment Committee Update:

Congratulations to the 2025 RSESS awardees!

Get to know some of them here…

	 **Emma Hailwood (1st place 3MT Winner)**	 **Gabby Griffin (RSESS and ISRTP Graduate Student Award)**	 **Sandeep Kondakala (RSESS 2025 Travel Award)**
What is your favorite chemical?	*Benzo[a]pyrene- a classic toxicant!*	*Gold- I like what it symbolizes, and it looks best with my skin.*	*Ethanol- if you spill it, you don't have to clean it up!*
What has been an interesting session/poster at this year's SOT meeting?	*ADME/TK sessions, particularly ones that talk about BaP metabolism.*	*The metals poster session, its always interesting to learn about all the different kinds of metals.*	*I was able to visit my old mentor's poster and reconnect with them and the lab.*
What are some of your hobbies?	*Rock climbing! I enjoy bouldering primarily and have gone to places all around the UK and Europe.*	*Drawing (mostly pencil), going to concerts, trying new things!*	*Cricket- I am an all-around player.*

Brought to you by the RSESS Endowment Committee.
Your donation to the RSESS endowment fund makes these awards possible!

Scan to donate!

SOT 64TH ANNUAL MEETING & ToxExpo • March 16–20, 2025 ORLANDO, FLORIDA

REGULATORY & SAFETY EVALUATION Specialty Section

GREAT TO SEE EVERYONE!!!