Dear Colleagues,

I am honored and privileged to begin my term as President of the Regulatory and Safety Evaluation Specialty Section of SOT. I am excited to serve but also a little anxious—I’m following in the footsteps of some amazing individuals, including Dr. Marie Fortin, who (thankfully!) will remain on our executive committee as Past President. I am very fortunate to have a fantastic executive committee team with Amy Roe as Vice-President, Annette Koerner as VP-elect, Norm Kim as Secretary/Treasurer, Ryan Hamilton and Haitian Lu as Councilors, Lauren Walker as Postdoctoral Representative, and Jessica Jimenez as Graduate Student Representative. I would also like to thank Ed Ohanian (previous Past President) and April O’Connell (past Secretary/Treasurer) for all of their help—you will be missed!

As a specialty section, we seek to provide a forum for the interaction of SOT members to discuss the impact of regulations, guidelines, and guidance on the practice of toxicology and safety evaluation of environmental chemicals, consumer and household products, pharmaceuticals, food additives, and other products of concern. Our work embodies SOT’s mission to create a safer and healthier world by advancing defensible and supportable science and increasing the impact of toxicology.

The Annual Meeting gives us the opportunity to present what we have most recently discovered, learn from the accomplishments of others, recognize the worthy achievements of our colleagues and trainees, reconnect with long-time friends and colleagues, and do some networking. RSESS was well-represented in the meeting program as primary or other endorser on four CE Courses, two Informational Sessions, seven Symposium Sessions, five Workshop Sessions, and one Roundtable Session.

At the 2019 Annual Meeting in Baltimore, MD, RSESS activities were a success. Our annual reception was well-attended where Drs. Ryan Vandery (Johns Hopkins University School of Medicine) and Peter Pressman (Polyscience Consulting and The Daedalus Foundation) debated on the safety of marijuana (moderated by Dr. A. Wallace Hayes; University of Florida). Our best paper winner was Dr. Daniele Wikoff (ToxStrategies) for her publication entitled “Benefit-risk analysis for foods (BRAFO): Evaluation of exposure to dietary nitrates.” Two graduate students (Sarah Faure and Sarah Burnett) and two postdoctoral researchers (Drs. Wei-Chun Chou and Yi-Hsien Cheng)
were recognized for their contributions through our Graduate Student and Postdoc Excellence Awards.

Greg Smith and Brett Winters (2018-2019 RSESS Postdoc and Student Representatives, respectively) worked with the Risk Assessment Specialty Section (RASS) to coordinate a mentoring luncheon on the Wednesday of the 2019 SOT Annual Meeting (March 13). They and their Postdoc and Student counterparts from RASS have been very successful in finding a balance of volunteer mentors from both RASS and RSESS. We received great feedback on this event, and the attendees were grateful for the opportunity to speak with mentors. Thank you to all who served as a mentor for this event. We hope to hold another mentoring luncheon at the 2020 Annual Meeting.

I would also like to take this opportunity to thank Mary Ellen Cosenza and Angelique Braen for their outstanding work chairing our proposal review committee this year. Together with their team (Krisa Camargo, Matthew Taylor, Dave Allen, Brian Hughes, Santhini Ramasamy, and Claire Neilan) they reviewed and ranked a total of 37 proposals in a very short amount of time! In 2018 RSESS established a new endowment fund to encourage research and training, scientific progress, collaboration, and the modernization of the fields of safety evaluation and/or regulatory toxicology, primarily by supporting outstanding graduate students and/or postdocs with monetary awards based on the scientific excellence of their work. These awards can be issued once the fund has achieved the $50,000 threshold to become a permanent fund. Please consider supporting the RSESS Future of Regulatory and Safety Evaluation endowment and help us achieve the $50,000 threshold required for transition to permanent status. This will ensure that we establish a sustainable future for our activities (awards, mentoring activities, webinars, and our annual reception and debate).

RSESS is not only the largest Specialty Section (with over 800 members!), it is also at the intersection of nearly all other SOT Specialty Sections. We epitomize the ultimate goal of every scientist and toxicologist: making a difference. Because Specialty Section members strive to improve the safety evaluation and regulatory acceptance of the best approaches, through the course of the year, we will also foster relationships with other Sections in order to increase our awareness of the most recent advances in toxicology testing. I think I speak for the entire EC when I say we look forward to serving you and to continuing to advance our values and aspirations as a Specialty Section. Please do not hesitate to reach out to any of us with your thoughts and suggestions to help us achieve our goals.

Special thanks to Lauren Walker and Samantha Goodman for editing the newsletter!

Looking forward to a wonderful year!

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Calling All Volunteers!

NEWSLETTER COMMITTEE

• Now seeking editors and article contributors!
• Please indicate interest to Lauren Walker (Lauren.M.Walker@Rutgers.edu).

AWARDS COMMITTEE

• Now seeking volunteers to review annual RSESS award applications.
• The RSESS Awards Committee will convene between November and January.
• Interested individuals should contact Amy Roe (roe.al@pg.com) no later than November 15th.

ATTENTION TRAINEES (and mentors)!
Supplemental Training for Education Program (STEP)

Next Deadline: May 1, 2020
Doctoral students are encouraged to apply with a strong application that proposes participation in a workshop or event that enables professional or scientific training needed to achieve career goals, but that is outside the scope of their graduate program.

For more info:
http://www.toxicology.org/education/st/step.asp

New Experiences in Toxicology (NEXT) Program

Next Deadline: May 1, 2020
Outstanding postdoctoral trainees are encouraged to apply to the NEXT program. The NEXT award covers costs associated with additional training related to toxicology that will broaden a postdoc’s expertise and prepare them for the competitive job market. Applicants will identify professional development workshops, short courses, or activities that would provide training outside of their academic, governmental, or industrial postdoc.

For more info:
www.toxicology.org/awards/sot/awards.aspx?AwardID=290
Biosketches of Incoming Officers

Lauren is a Postdoctoral Researcher in the Environmental and Occupational Health Sciences Institute at Rutgers University, where she studies the impacts of placental toxicity on early development under the guidance of Lauren Aleksunes.

As a graduate student at the University of California, Riverside, Lauren studied the effects of gestational diabetes and harm-reduction tobacco products on early tissue development. She first presented her research at the 2014 SACNAS Annual Meeting. Since then, Lauren has presented at various local and international meetings and received several recognitions for her work, including the 2019 Teratology Society MARTA James C. Bradford Poster Award and 2016/2018 Society of Toxicology Southern California RC Student Travel Awards. To date, her graduate work has produced 2 peer-reviewed articles.

Lauren joined SOT in 2015. She has served on the Women in Toxicology Executive Committee (2016–2018) as the graduate student representative and the Graduate Student Leadership Committee (2017–2018, 2018–2019) as the Professional Development Committee Secretary and Chair, respectively.

Jessica is a PhD student in the Curriculum in Toxicology and Environmental Medicine at the University of North Carolina at Chapel Hill. She is interested in exploring the gene-environment interactions that can influence susceptibility to neurodevelopment and neurodegenerative disorders. As an undergraduate student at Oberlin College, Jessica began sharing her research on metal-induced neurotoxicity at the 2016 Annual Society of Toxicology Meeting and co-authored her work into 2 peer-reviewed articles. She has presented at numerous scientific meetings and received various awards for her work, including the 2016 SOT Committee on Diversity Undergraduate Full Travel Award and the 2019 SOT Perry J. Gehring Diversity Travel Award. Under the guidance of Dr. Mark Zylka, she is currently studying the influence of pesticides and other chemical exposures on Autism risk. Jessica has been a graduate student member of SOT since 2017.
Highlights from the 2019 SOT RSESS Reception

Congratulations to all of our award recipients!

Graduate Student Excellence Award
Sarah Burnett

Graduate Student Excellence Award
Sarah Faure

Postdoctoral Fellow Excellence Award
Yi-Hsien Cheng, PhD

Postdoctoral Fellow Excellence Award
Wei-Chun Chou, PhD

Best Paper
Daniele Wikoff, PhD
In the United States, most states have legalized the medical use of cannabis products and a number of states have legalized recreational cannabis use. With many divergent thoughts in the society and by scientists, RSESS sponsored the annual Great Debate on this topic during the RSESS reception at the 2019 SOT Annual Meeting in Baltimore.

A. Wallace Hayes, PhD moderated the session with debaters, Ryan Vandrey, PhD (Johns Hopkins University) and Peter Pressman, MD. (The Daedalus Foundation and PolyScience Consulting), who presented the pro and con perspectives, respectively. Vastly differing opinions were presented and well received by the audience. RSESS would like to specially thank Wally, Ryan and Peter for making time to prepare in advance to educate many on the key issues of cannabis use.
When the executive board came together for the first time after the last annual meeting, ideas sparked surrounding what to focus on in the coming year. But do we really know how our section is composed? What is the key background of our members and might there be other interests and needs not currently addressed by the group? As good scientists we tackled these questions with some data mining in our membership repository to understand where our future focus should be centered. Some things may not surprise us at all while others should make us reflect on future improvements.

We are the largest specialty section of SOT with currently 849 members. Not surprisingly, most of our members are US citizens (89%), with smaller groups from Europe (5%) and Asia (~3%). The gender distribution is well-balanced with 55% male and 45% female members to date. We were very satisfied to see that RSESS is a place where employees from different professions come together: Industry (61%), Consultancy (16%), Government (8%) and Contract Research (5%). There is an impressive depth of experience with 74% of RSESS colleagues having more than 10 years, and almost 50% have even more than 20 years of experience within the professional field of regulatory safety evaluation and risk assessment. About 80% hold a PhD and 45% a DABT certifying the highest standards of scientific and toxicological education in the field.

While all of this is an excellent foundation of a lively, scientifically sound and well-balanced specialty section, we should also look into what we can improve to hold these achievements alive and even build on them as we move into the future. In particular, it should be of major interest to engage with the younger generation of scientists, toxicology specialists, and our colleagues from academia more closely. Currently, there is an alarmingly low percentage of students (12, <1%) and members from research institutions (12, <1%) and academia (36, 4%)—which make academic research a minority in our section. That’s why we believe it is so important that we continue with our mentoring luncheons at the annual meetings. At the same time, we should seriously consider leveraging the wealth of experiences to provide learning opportunities for the younger generation and other professionals in the field.

(Continued on page 8)
Although representation from US citizens is naturally the majority, we may benefit from a more global outreach inviting colleagues from all over the world including not only Europe and Asia, but also South America and Africa. I truly believe we can learn a lot from our different global perspectives and realities both in science and society.

Now it is up to you to give us your feedback. Please send us your thoughts, proposals and contribute to our membership survey (https://bit.ly/2JFwehA). We would like to engage with you in an open dialog on where your key interests are, how you see the future of our specialty section, and what we can already do today to be an even more active and valuable community of safety evaluation and risk assessment professionals in the future.

### Future of Regulatory & Safety Evaluation Endowment Fund

Marie C. Fortin, PhD, DABT, ERT

Established in September 2018, this fund encourages research and training, scientific progress, collaboration, and the modernization of the fields of safety evaluation and/or regulatory toxicology. The fund, aligned with the Regulatory and Safety Evaluation Specialty Section, will be used primarily to provide a monetary award(s) to graduate students and/or postdocs based on scientific excellence and scientific progress toward novel, better, and fit for purpose, modern approaches to safety evaluation and/or regulatory toxicology. It can also be used to help provide support for Society of Toxicology programs that help foster sharing of knowledge related to scientific progress in the fields of safety evaluation and/or regulatory toxicology. This Endowment Fund is intended to recognize and disseminate the value of new approaches that represent the future of safety evaluation and regulatory decision-making.

Please use the online giving system or download the **Donation Form** to make a gift to the Future of Regulatory and Safety Evaluation Endowment Fund today!

https://www.toxicology.org/endowment/

![Years in Profession](https://bit.ly/years-in-profession)
The China drug regulatory authority, NMPA (National Medical Products Administration, formal CFDA), has implemented major changes on drug review and approval policies since 2015 to encourage innovation and speed up new drug development. The regulatory environmental improvement significantly streamlined IND/NDA processes, increased review/approval transparency, and enhanced international harmonization.

In August 2015, China State Council issued the “Opinion on reforming the review and approval system of drugs and medical devices”, which identified the challenges and inconsistencies to the global standards for new drug and device registration. It initiated the regulatory reforms and led to the revision/approval of a series of policies to accelerate the new drug development in China.

In June 2017, NMPA joined ICH as a new Regulatory Member. The agency committed to promote adaptation of all ICH technical guidelines in China. The implementation is under-going now. The guidelines from US FDA and EMA were also largely adopted. Previous restrictions on new drug review and approval process have been removed. The global harmonized IND/NDA packages according to ICH requirement are generally accepted by China healthy authority.

In July 2018, NMPA issued an “Adjustment of review and approval procedures for drug clinical trial” according to China State Council’s “Opinion on deepening review and approval system reform to encourage the innovation on drugs and medical devices” on October 2017. With this, a new 60 working day IND review procedure was announced. The Agency shall, within 60 working days from the date of the IND application fee received, decide whether the approval is offered and notify the sponsor. In case the sponsor is not notified within the stipulated period, the application shall be deemed approved. Following this new policy, the IND review and approval process is substantially shortened (from average of 2 years to 3 months). Pre-IND meetings are also officially offered. Although not mandatory, the agency strongly recommends the sponsor to have a pre-IND meeting with the agency. It provides a best opportunity to communicate with the agency to interpret the data, discuss the development program and clinical trial designs. It is also no longer required to submit applications to the NMPA provincial offices for the format and reliability check before the formal review by NMPA CDE (Center of Drug Evaluation). The process became much simpler.

In the same month, NMPA also announced to accept the foreign clinical data for NDA in China based on the outcome of assessment of the quality of oversea clinical data, the efficacy, safety, and racial sensitivity. This new policy will allow patients to get innovative therapies as early as possible by avoiding non-necessary repetitive clinical studies in China.

In addition to these changes, the new “Drug administration law of China” approved in August 2019 also indicated that conditional approval is accepted for drug used for treatment of serious life-threatening diseases for which there is no effective treatment, as well as drug urgently needed for public health, as long as its clinical trial data shows efficacy and predictable clinical value.
The China regulatory environmental reform smoothed the road to the new drug approval. More and more innovative drug INDs/NDAs have been submitted to NMPA than ever. More and more China local drug development programs met the international standards. Even more thorough alignment of China’s regulatory environment to global standards can be expected.

About the Author. Until just recently, Jack Xie was the Site Head of Pharmaceutical Sciences at the F. Hoffmann-La Roche Innovation Center Shanghai with the executive responsibilities of multiple functions including general and regulatory Toxicology, DMPK, Investigative Safety, Bioanalysis, Biomarker, and Clinical Pharmacology. He joined SOT in 2004 and is also a council member of the Chinese Society of Toxicology (CSOT). Prior to joining F. Hoffmann-La Roche in Shanghai, Jack served as a regulatory toxicologist from 2006 to 2013 in Targacept, Inc (Winston Salem, North Carolina) and a study director at Toxickon Corp. (Bedford, Massachusetts).

Hot Topics Read: The CBD Conundrum

Bradley J. Lampe, BS, MPH

The dietary supplements industry is no stranger to the field of regulatory toxicology, where toxicological uncertainties pertaining to a single high-profile substance or ingredient “du jour” can stir years of debate and cause friction between industry and regulators. In the world of dietary supplements, perhaps no other ingredient has demonstrated this phenomenon more completely than cannabidiol (CBD).

CBD is a phytocannabinoid derived from the hemp cultivar of the Cannabis sativa plant. Anyone who has shopped at a health products retailer recently is likely familiar with the fast pace of CBD products (including CBD oil, capsules, tinctures, gummies, cream, and the like) entering the market bearing various analgesic or antipsychotic claims. The US CBD market was reported as $1.9 billion in 2018, with a compound annual growth rate of 101%, and with an estimated 6% of the total CBD market share currently occupied by dietary supplements. However, the US FDA has maintained that the marketing of CBD-containing dietary supplements is unlawful, questioning the safety of CBD and has emphasized the need for more toxicological data to address critical data gaps. Therefore, despite skyrocketing demand for CBD products, the dietary supplements industry faces significant regulatory uncertainty related to CBD.

Central to US FDA’s position on CBD is the current use of the substance in an approved drug (Epidiolex®): according to the Dietary Substance Heath and Education Act (DSHEA), any substance that has been the subject of substantial clinical trials is excluded from the definition of a dietary ingredient. Therefore, no regulatory pathways are available for CBD-containing dietary supplements unless the US FDA issues new rulemaking, a process that could take several years. Furthermore, the US FDA has not committed to issuing any new rulemaking unless the dietary supplements industry conducts additional safety studies to address critical data gaps. On the other side, the dietary supplements industry argues that (in part) since estimated daily intake levels of...
CBD associated with dietary supplement use will be orders of magnitude less than the maintenance dose of its approved drug use, the US FDA should treat CBD like any other new dietary ingredient, and to allow manufacturers the opportunity to submit a new dietary ingredient notification (NDIN), which is a regulatory requirement for new dietary ingredients that includes a comprehensive safety evaluation. The dietary supplements industry also emphasizes that there is little incentive to invest millions of dollars in new safety studies if the US FDA will not commit to providing a regulatory pathway for their products.

Despite the impasse between regulators and industry, new safety studies on CBD have been published recently. Most importantly, the results of several Epidiolex® clinical trials have been published in peer-reviewed journals, providing limited insight on potential adverse effects of CBD in human subjects. However, toxicological assessment in the clinical trials were mostly limited to self-reported effects, along with a limited evaluation of liver enzyme activities; thus, additional studies in animals are needed in which all relevant toxicological parameters can be evaluated. Fortunately, in 2018, the results of a guideline-compliant 90-day subchronic toxicity study in rats as well as critical genotoxicity assays (mutagenicity and clastogenicity) were published, an important first step. Despite these recent publications, critical data gaps remain. For example, the dataset lacks a chronic study to evaluate the potential effects of lifetime exposure to CBD, as well as data to evaluate reproductive and developmental effects in mammals. Comparative toxicokinetic data in humans and rats at comparable dose levels will also be critical for extrapolating the dose levels tested in the animal studies to human equivalent doses.

Recently, the industry has reached out to Congress in further efforts to resolve the regulatory situation. In September 2019, Senate Majority Leader Mitch McConnell (R-KY) has introduced language into a Senate appropriations bill that would require US FDA provide Congress with a report on how it will evaluate CBD for use in US FDA-regulated products within 90 days of the bill's passage. If passed, the bill may expedite the US FDA’s rulemaking process, substantially raising the incentive for the industry to invest in new safety studies. In the meantime, a plethora of CBD products continue to be marketed unlawfully with no regulatory or industry-based assurance that these products are safe at intended use levels. Therefore, in the interest of both consumers and in the continued viability of the market for CBD-based dietary supplements, any developments encouraging the US FDA and the dietary supplements industry to find common ground are most welcome.

About the Author. Bradley J. Lampe is a research toxicologist at NSF International with an MPH degree in Environmental Health from the University of Michigan. He has over ten years of experience in evaluating food contact regulations in the US and Europe, and also has six years of experience in chemical risk assessment.