~ WELCOME ~
Society Of Toxicology
Ocular Toxicology Specialty Section
Virtual Reception

Program Starts at 4:15 pm EST
Send Questions to Ocular.SOT@gmail.com
2021 OTSS Virtual Reception Agenda

Time (EST)
4:15 pm  General Welcome and Thank You to our Sponsors
4:20 pm  Introduction of Current OTSS Executive Committee Officers and Updates
4:35 pm  Japanese Society of Comparative and Veterinary Ophthalmology (JSCVO) Update
4:45 pm  Awards & Award Presentations
5:05 pm  Passing of the Mallet and
          Introduction of Incoming OTSS Executive Committee Officers
5:10 pm  Social Networking: Chat in a breakout room. Bring your own beverage!
5:35 pm  Closing
Welcome!

Our Generous Sponsors: Thank You!
Current Executive Committee Officers (2020-2021)

<table>
<thead>
<tr>
<th>President</th>
<th>Vice President</th>
<th>Vice President-Elect</th>
<th>Treasurer</th>
<th>Communication</th>
<th>Councilor</th>
<th>Councilor</th>
<th>Past President</th>
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<td>Vlad Bantseev</td>
<td>Neera Tewari-Singh</td>
<td>Chris Steele</td>
<td>Andrea Rodrigues</td>
<td>Chris Schuetz</td>
<td>Kathleen Krenzer</td>
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<td>ToxStrategies</td>
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<td>iuvo BioScience</td>
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Contact [Ocular.sot@gmail.com](mailto:Ocular.sot@gmail.com) if you know someone interested in these positions!
OTSS Committee Updates

1. Program Committee - Qihong Huang

2. Communication Committee - Chris Steele

3. Treasurer Report - Neera Tewari-Singh

4. Membership Committee - Vlad Bantseev
1. Program Committee: Members
by Qihong Huang

Chairperson: Qihong Huang, *Boehringer-Ingeheilm Pharmaceuticals, Ridgefield, CT*

Members:
- Vlad Bantseev, *Genentech, South San Francisco, CA*
- Hiromi Hosako, *Alcon, Fort Worth, TX*
- Mercedes Salvador-Silva, *Alcon, Fort Worth, TX*
- Ken Schafer, *Greenfield Pathology Services, Greenfield, IN*
- Brenda Smith, *Vir Biotechnology, San Francisco, CA*
- Evan Thackaberry, *Vigil Neuroscience Inc., Cambridge, MA*

We are looking for more OTSS members who can join our program committee. Contact OTSS (Ocular.SOT@gmail.com) today or contact any member of the executive committee.
1. Program Committee: Activities by Qihong Huang

- **2020: SOT Continuing Education AM03: “Developing Therapeutics for Ocular Indications: A 20/20 View”**
  1. The Spectrum of Ocular Anatomy and Physiology in Animals. Seth Eaton, University of Wisconsin
  2. Clinical Evaluation Techniques for Ophthalmic Toxicology. Joshua Bartoe, Charles River
  3. Evolving Strategies for Histopathological Assessment of Ocular Tissues. Helen Booler, Genentech

  1. Toxicokinetic modeling approaches to informing dose selection for intravitreal biotherapeutics. Seung-Wook Chung, Boehringer Ingelheim
  2. Ocular inflammation in nonclinical intravitreal toxicity studies with biologics: types, timing and translatability. Helen Booler, Roche
  4. Pre-clinical pearls for successful gene therapy development, Past and Future. Daniel Chung
  5. Nonclinical Toxicology Strategies for Development of Novel Ocular Biotherapeutics. Theresa Chen, FDA
2. Communication Committee

by Chris Steele

- Newsletters: 2020 Summer Newsletter Issued
- Websites: https://www.toxicology.org/groups/ss/otss/
- LinkedIn
  - Follow “SOT OTSS Student/Post-Docs Outreach Group,” a new group page to support and connect with students and post-docs.
3. Treasury Report
by Neera Tewari-Singh

- Balance from beginning June 2020: $78,865
- Balance Ending November 2020: $80,365
  - Contributions: $1,500
  - Net Gain: $1,500
4. Membership Committee
by Vlad Bantseev

# of current members: 90-100 members

Demographics by Sector
- Pharma/Biotech: 48%
- Consulting: 12%
- Academic: 10%
- Government: 6%
- CPI: 19%
- Others: 4%

Demographics by Year
- 5-10 years: 45%
- 1-2 years: 26%
- 3-5 years: 16%
- 6-12 years: 13%
- 1-2 years: 26%
- Others: 4%
- CPI: 19%
Japanese Society of Comparative and Veterinary Ophthalmology

- **Mission**: Execution of leadership in animal ophthalmology
- **Foundation**: In 1991 following small group discussions started in 1981
- **President**: Dr. Shoji Sasaki, Alexion GK
- **Membership**: 530 members
- **Diploma**: JCVO for veterinarians and JCFO for researchers
- **Activities**: Annual meeting, journal (Animal Eye Research), three-day training course, case discussion forum
- **Collaborations**: OTSS, JSOT, ACVO, ECVO, etc.
Japanese Society of Comparative and Veterinary Ophthalmology

- **2020 Performance**
  - **Special Lecture at 40th Basic Seminar**
    Current status and future issues of gene therapy with channelrhodopsin by Dr. Hiroshi Tomita

- **2020 41st JSOT Fundamental Seminar (December 19, Online)**
  - Education Lecture; Dr. Akiko Maeda, “Development of Readthrough Drug for Retinitis Pigmentosa, Current Status and Future Issues.”

- **2021 42nd JSOT Fundamental Seminar in JSCVO Annual Conference (July 2-3, Online/F2F in Okinawa)**
  - Not decided yet; Basic research-related topics (under planning)

- **2021 43rd JSOT Fundamental Seminar (December, Online)**
  - Not decided yet; Basic research-related topics (under planning)
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Award Announcements
by Andrea Rodrigues & Chris Schuetz

- **2019 Award Acknowledgements**
  - Taylor and Francis “Paper of the Year” Award *presented by Wallace Hayes*
  - OTSS Best Poster Award *presented by Andrea Rodrigues*

- **2020 Award Announcements**
  - Taylor and Francis “Paper of the Year” Award *presented by Wallace Hayes*
  - OTSS Best Poster Award *presented by Chris Schuetz*
  - OTSS Career Achievement Award *presented by Chris Schuetz*
  - OTSS I² Award *presented by Ted Ira, Biomere*
Winning Paper

Investigation of comet assays under conditions mimicking ocular instillation administration in a three-dimensional reconstructed human corneal epithelial model

Haruna Tahara¹, Kazuyo Sadamoto¹, Yoshinori Yamagiwa¹, Shingo Nemoto¹ & Masaaki Kurata¹


¹Research and Development Division, Senju Pharmaceutical Co., Ltd., Kobe, Hyogo, Japan.
OTSS Best Poster Award, 2019

Winner

Sairum Bellum

Optical Coherence Tomography (OCT)
In Vivo Imaging Tool to Monitor Retina in Preclinical Species

S. Bellum1*, B. Bennett3, S. Born1, W. Cook1, C. Lazarus1, B. Mattson1, N. Muniappa2, M. Viola1, A. Galijatovic-Idrizbegovic1, G. Wollenberg2

1Department of Toxicological Sciences, Safety Assessment and Laboratory Animal Resources, Merck & Co., Inc., West Point, PA, USA
2Department of Pathology, Safety Assessment and Laboratory Animal Resources, Merck & Co., Inc., West Point, PA, USA
3Department of Toxicology and Biodistribution, Voyager Therapeutics, Cambridge, USA

* Presenting Author/ Awardee
The Taylor & Francis Award is presented to the best paper in ocular toxicology published in *Cutaneous and Ocular Toxicology*

**Winning Paper**

**Validation of the OptiSafe™ eye irritation test**

Neepa Choksi¹, Stewart Lebrun², Minh Nguyen², Amber Daniel¹, George DeGeorge³, Jamin Willoughby⁴, Adrienne Layton⁵, Donnie Lowther⁶, Jill Merrill⁷, Joanna Matheson⁸, João Barroso⁹, Krystle Yozzo¹⁰, Warren Casey¹¹ & David Allen¹


¹Integrated Laboratory Systems, Inc., Research Triangle Park, NC, USA.
²Lebrun Labs LLC, Anaheim, CA, USA.
³MB Research Laboratories, Spinnerstown, PA, USA.
⁴Cyprotex US, LLC, Kalamazoo, MI, USA.
⁵Division of Pharmacology and Physiology Assessment, U.S. Consumer Product Safety Commission, Rockville, MD, USA.
⁶Office of Cosmetics and Colors, U.S. Food and Drug Administration, University Station, College Park, MD, USA.
⁷Dermatologic and Dental Drug Products, U.S. Food and Drug Administration, Silver Spring, MD, USA.
⁸Division of Toxicology and Risk Assessment, U.S. Consumer Product Safety Commission, Rockville, MD, USA.
⁹European Commission, Joint Research Centre (JRC), Ispra, VA, Italy.
¹⁰Office of Pesticide Programs, Health Effects Division, U.S. Environmental Protection Agency, Washington, DC, USA.
¹¹National Toxicology Program, National Institutes of Environmental Health Sciences, Research Triangle Park, NC, USA.
Winner

Jonathan Lin

Assessment of Corneal Alkali Injury in a Murine Model with Anterior Segment Optical Coherence Tomography

J. Lin*, J. Luissi**, E.R. Kraft¹, S.A. Giannos¹, M.E. Schmitz-Brown¹, M. Motamedi¹, P. Gupta¹

¹University of Texas Medical Branch at Galveston, Galveston, TX, USA
* Awardee
** Presenting Author

Ocular Toxicology Poster Session on March 18 (Thu) 11:15-1:00pm EST
OTSS Career Achievement Award, 2020

Winner

Brian Short, DVM, PhD, DACVP

Brian Short Consulting, LLC

- 22 years in ocular toxicology and pathology after 11 years in toxicology (systemic routes) field.
- Contributed to successful development of numerous ocular drugs as a Senior Director of Toxicology and then Pathology departments at Allergan (1998-2015). Consulted for over 80 ocular projects as a consultant (2015-present).
- 16 presentations on ocular drug safety evaluation for international societies (SOT, ACT, STP, ARVO and ARVO) and government agencies including FDA. Authored 11 publications and 1 book chapter related to ocular drug development.
- Currently serve as Councilor for Roundtable of Toxicology Consultants (RTC), a member of STP’s International Harmonization of Nomenclature and Diagnostic Criteria (INHAND) Special Senses for NonRodents, and currently working on a manuscript for standardization of ocular toxicologic pathology terminology for rabbits, dogs, minipigs and monkeys. Spearheaded the charge for STP’s Scientific and Regulatory Policy Committee (SPRC) to form the NonRodent Ocular Trimming and Sectioning (NOTS) Working Group in 2019.
Thank You OTSS Executive Committee!!

I’m addicted to placebos. I could quit, but it wouldn’t matter.

- Steven Wright
Thanks to Allergan Ocular Team

- **Toxicology**
  - Anne Wiese
  - Ed Chow
  - Melva Rios-Blanco
  - Steve Matsumoto
  - Diana Auyeung-Kim
  - Chang Vangyi
  - Lisa Kloft
  - Brenda Smith
  - Andrea Rodrigues

- **Pathology**
  - Meg Ferrell Ramos
  - Jackie Brassard
  - Iona Raymond
  - Vinsa Sun

- **Pharmacokinetics/Bioanalytical**
  - Diane Tang-Liu
  - Mayssa Attar
  - Jie Shen
  - Devin Welty
  - Gabriella Szekely

- **Pharmacology**
  - James Burke
  - Jerry Rodrigues

- **CMC**
  - Patrick Hughes
  - Bruce Firestone

- **Ophthalmology/Clinical**
  - Mike Robinson
  - Scott Whitcup
  - Janet Cheetham
Thanks to Other Ocular Drug Developers and Reviewers

- **Toxicology**
  - Mark Vezina
  - Brian Christian
  - Evan Thackaberry
  - Vladimir Bantseev
  - Doug Kornbrust
  - JoAnn Schuh
  - Hassam Younis
  - Chuck O’Neil

- **Pathology**
  - Ken Schafer
  - Cindy Farman
  - Typhaine Lejune
  - Steve Sorden
  - Dick Dubielzig
  - Leandro Teixeira
  - Margarita Gruebbel
  - Stephanie Shrader

- **Ophthalmology**
  - Bob Munger
  - Chris Murphy
  - Paul Miller
  - Seth Eaton
  - Joshua Bartoe
  - Ryan Boyd
  - Martin Bussières
  - Brian Gilger

- **Pharmacokinetics/Pharmacology**
  - Craig Struble
  - Gary Novack

- **FDA**
  - Lori Kotch
  - Maria Rivera
  - Andrew McDougal
  - Aaron Ruhland
  - Aling Dong
  - Zhou Chen
Safety Evaluation of Ocular Drug Delivery Formulations: Techniques and Practical Considerations

BRIAN G. SHORT

From Allergan, Inc., Irvine, California, USA.

Symposia Review

Toxicology Evaluation of Drugs Administered via Uncommon Routes: Intranasal, Intraocular, Intrathecal/Intraspinal, and Intra-Articular

Armaghan Emami¹, Jeff Tepper², Brian Short³, Tony L. Yaksh⁴, Alison M. Bendele⁵, Thulasi Ramani⁶, Alvaro F. Cisternas⁷, Jay H. Chang¹, and R. Daniel Mellon¹
Selected Aspects of Ocular Toxicity Studies With a Focus on High-Quality Pathology Reports: A Pathology/Toxicology Consultant’s Perspective

Brian Short
So You Want To Be a Rock N’ Roll Star Ocular Toxicologist and/or Pathologist?

Ocular Toxicity Studies and High-Quality Reports: Brian’s Top Ten
1. Insight to ocular toxicity studies, ocular and systemic safety margins, and other aspects of nonclinical ocular drug development rely heavily on FDA reviews of approved ocular drug products, but also keep your eye on literature.
2. Keep an open mind for ocular toxicity species

- IVT/subretinal > topical ocular

- Intracameral > topical ocular/eyelid margin > IVT/subretinal

- NZW/DB: Topical ocular/eyelid margin > IVT/subretinal > intracameral

- IVT/subretinal (safety parameters in rodent efficacy models with gene/cell therapies) > topical ocular (cenegermin)

- Periocular/eyelid > IVT/subretinal
3. Unilateral dosing offers many advantages to bilateral dosing

- Understand test article-, vehicle- and/or injection-related vs artifactual changes
- Maximizing systemic exposure for an ocular NME can be addressed with a systemic study and/or an IV group
- Ocular reformulations [505(b)(2)] usually have established nonclinical and clinical systemic safety at similar or higher doses/systemic exposure
4. Ocular and systemic parameters should be ‘fit for purpose’
   - Nonpivotal vs pivotal studies
   - Depends on class (small molecule, biotherapeutic, oligonucleotide, gene therapy) and route of administration
   - Systemic ADAs analysis is adequate to understand adaptive immune reaction for correlation with ocular inflammation in individual animals; ocular ADA analysis not needed
5. Negligible systemic exposure means
   - LLOQ is well below indices of potential functional activity ($IC_{50}$ and/or $EC_{50}$)
   - No systemic effects in ocular toxicity studies or clinical studies
6. Engage a study pathologist and peer review pathologist before ‘end of the parade’ to:

- Provide input to protocol
- Review INHAND terminology, previous pathology reports and relevant literature
- Review ophthalmology data
- Provide input to guide ocular trimming and histology before and after necropsy
7. Regulatory expectations for ocular histopathology include:

- Assess a full range of ocular tissues
- Examine adequate number of sections/eye ($\geq 3$), with a full assessment of the macula/fovea or visual streak
- Consider ophthalmic findings regarding microscopic sectioning
- Justify sectioning and assessment approach in pathology report
8. Pathology report should:

- State what is test article-, vehicle- and/or injection-related vs artifactual
- Address adversity (but not NOAEL)
- Correlate key microscopic findings with key ophthalmic findings and/or histology trimming observations
- Reflect clear communication with ophthalmologist and perspective of pathology peer reviewer
9. Ophthalmology report should:

- Contain narrative that characterizes ophthalmic examination findings including range of severity
- State what is test article-, vehicle- and/or injection-related
- Address adversity (but not NOAEL) to make it easier for study director to do this in toxicology report
### Brian’s Top Ten

10. Use animal vitreal volumes based on frozen eye values for intravitreal ocular safety margins and consider new human data

<table>
<thead>
<tr>
<th>Species</th>
<th>Intravitreal Injection Volume (µL)</th>
<th>Vitreous Volume (mL)</th>
<th>Human 4.0 mL /Animal X mL Ratio for HED Calculation</th>
<th>Human 4.6 mL /Animal X mL Ratio for HED Calculation</th>
</tr>
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<tbody>
<tr>
<td>Rabbit</td>
<td>50</td>
<td>1.4(^1)</td>
<td>2.9X</td>
<td>3.3X</td>
</tr>
<tr>
<td>Monkey</td>
<td>50</td>
<td>2.0(^1)</td>
<td>2.0X</td>
<td>2.3X</td>
</tr>
<tr>
<td>Dog</td>
<td>50</td>
<td>2.2(^1)</td>
<td>1.8X</td>
<td>2.1X</td>
</tr>
<tr>
<td>Minipig</td>
<td>50</td>
<td>2.3(^1)</td>
<td>1.7X</td>
<td>2.0X</td>
</tr>
<tr>
<td>Human</td>
<td>50</td>
<td>4.0(^2)/4.6(^3,4)</td>
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NEW OTSS $I^2$ (Innovation and Impact) Award: Description

Presented by Ted Ira @ Biomere

- Recognizes Innovations and/or scientific advances that Impact the field of ocular toxicology based on papers published (or in press) in the calendar year (January 1 through December 31) prior to the annual Society of Toxicology meeting.

- Applicants for the award must be an author of the peer-reviewed paper and a member of the OTSS at the time they apply.

- The applicants shall submit a copy of the publication and a description or other documentation describing how the subject work is Innovative in ocular toxicology or Impacts the scientific advancement of ocular toxicology.

- A committee appointed by the OTSS executive committee reviews the applications and determines the award winner. A single award will be conferred each year. The winner will receive a plaque and a $1000 cash award to recognize their accomplishment.
NEW OTSS
I² (Innovation and Impact) Award, 2020

Winner
Neera Tewari-Singh, MS, PhD
Michigan State University

A Supersaturated Oxygen Emulsion for the Topical Treatment of Ocular Trauma
Mil. Med. 2020 Mar 2;185(3-4):e466-e472.
Passing the Mallet
Incoming Executive Committee Officers (2021-2022)

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<td>Johnson &amp; Johnson</td>
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Contact [Ocular.sot@gmail.com](mailto:Ocular.sot@gmail.com) if you know someone interested in these positions!
We are Grateful for Your Service!

Social Networking
5:10-5:35pm EST

- Participants will randomly be assigned to a breakout room (up to 5-6 people/room)
- Each room has at least one OTSS board member as a facilitator
- Social Networking Topics
  - Introduction
  - Ocular-tox trivia/ice breaker
  - Share your thoughts on
    - What would you like OTSS to do/improve in near future?
    - Suggestions on recruiting new OTSS members
    - Any other topics
Closing
Thank You for Your Attendance!

- Suggestions?
  - How are we doing? Contact OTSS (Ocular.SOT@gmail.com) for any suggestions, ideas, or needs at any time!

Enjoy the Annual 2021 SOT Meeting!