

MDCPSS SUMMER NEWSLETTER

President's Message



It is an honor to serve you as MDCPSS President. As you will see in this edition of the MDCPSS newsletter, there is a lot of interest in toxicological science for medical devices within the MDCPSS community. I am excited to highlight this newsletter, as well as,

communicate some of the goals for MDCPSS community during 2015-2016.

The March 2015 SOT Annual Meeting held in sunny San Diego, California was a great success. A first was two MDCPSS sponsored Continuing Education (CE) courses (Sunday, March 22, 2015), which were well attended with 150+ learners in each course. MDCPSS community turned out for this year's reception and business meeting in record attendance (90+), evidence to the growing interest in medical devices within SOT. Read more about MDCPSS activities at the 2015 SOT annual meeting on page 5.

I welcome each of our newly-elected MDCPSS Executive Committee (EC) members, Barb Henry (Vice President-Elect), Sherry Parker (Councilor), Shawn Deng (Councilor), and Sandra Chang (Postdoctoral Representative). Sandra Chang is our newest member who is mentored by 2012-2013 MDSS Past President Rich Hutchinson. 2015-2016 will mark the first year since MDCPSS began in 2010 that the EC membership will not have an open position. The diversity of individuals willing

to participate in MDCPSS leadership will ensure years of future successes.

One of the changes you will notice in this newsletter is the increased number of sections, indicating more to report for the community. The increased content is a result of MDCPSS members contributing information and spreading the word. Be sure to check out the update on the upcoming revision to USP <661> by Sandi Schaible (page 2). Don't miss the announcement of the next webinar in the Events section (page 4). If you weren't able to attend the Annual meeting in San Diego last March, you cannot miss Lori Moilenen and Ron Brown's 2015 Medical Device Poster Session (page 6) on the high quality MDCPSS posters that were presented.

The MDCPSS EC is working hard for a great 2015-2016 year. Our goal is to foster dissemination of important toxicology issues throughout the MDCPSS community facing current medical device toxicologists. MDCPSS will leverage SOT HQ webinar technology throughout 2015 and 2016, so expect some announcements very soon. I cannot forget that an extremely important goal is the generation and communication of emerging toxicological science into future updates of medical device regulations and standards. Increasing membership is always a high priority for the EC and new contacts were made at this year's annual meeting that we hope to capitalize to continue increasing our membership numbers.

I look forward to serving the MDCPSS community throughout 2015-2016!

Alan Hood,

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Medical Device News

TTC194, Technical Committee for ISO 10993 will meet in Lund, Sweden, June 8-12, 2015.

Delegates from around the world discuss new test methods, new assessment approaches, and future updates to the medical device biocompatibility standard.

New Technical Report: ISO/TR 10993-33

ISO/TR 10993-33 (Biological Evaluation of Medical Devices-Part 33: Guidance on tests to evaluate genotoxicity-Supplement to ISO 10993-3) was released in March 2015. It is referenced in the latest version of ISO 10993-3:2014, and provides more background details on the methods, and considerations for test selection and conduct of in vitro and in vivo genotoxicity testing. It is available for purchase from the following ISO link.

http://www.iso.org/iso/catalogue_detail.htm?csnumber=65052

Combination Product News

Updates to USP 661

Contributed by: Sandi Schaible, WuXi Apptec

The USP general chapter <661> is currently undergoing revision and while the chapter has served its purpose, the need for revision is important for safety and quality of the plastic components of medical materials. The current chapter lacks specific test methods for commonly used plastics other than polyethylene, polypropylene and polyethylene Terephthalate. The current test methods and specifications are not necessarily quantitative and do not provide complete information on the safety and quality of the materials. The test methods are not modernized and harmonized with other test methods related to the general chapter, for instance Heavy Metals testing described in <231> is being replaced by instrumental methods described in <232> Elemental Impurities-Limits and <233> Elemental Impurities-Procedures. Finally the <661> chapter could include plastics for use beyond packaging to include other concerns such as manufacturing suites, administration systems and medical devices.

Once revised, the chapter will be titled: Plastic Packing Systems and Their Materials of Construction <661> and will provide the testing rationale for plastic materials of construction and packaging systems used for the pharmaceutical industry.

A second new general test chapter entitled Plastic Materials of Construction <661.1> will help determine whether an individual material is deemed well characterized by establishing its:

- 1) Identity (via FTIR, DSC and/or other means to confirm identity)

OFFICERS

(2015-2016)

Click on names

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Alan Hood

Vice President

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Past President

Gregory L. Erexson

Vice President-Elect

Barbara Henry

Treasurer/Secretary

Jim Kleinedler

Councilors

Shawn Deng

Sherry Parker

Student Representative

Kevin Trout

Postdoctoral Rep

Sandra Chang

MDCPSS Website

MDCPSS EC

Newsletter Editors

Sherry Parker

Shawn Deng

Alan Hood

MDCPSS EC



Combination Product News (continued)

- 2) Biocompatibility (biological reactivity via USP<87> and/or USP<88>)
- 3) Physiochemical Properties (e.g., TOC, UV absorbance, acidity/alkalinity)
- 4) Extractable Metals (via ICP or other applicable technique)
- 5) Plastic Additives (via establishment of material composition/polymer additives)

Alternative test methods and conditions can be used but must be demonstrated to be suitable by means of appropriate and sufficient validation data. It's also important to note that materials not specifically addressed in the chapter may require further consideration for additional testing as appropriate.

A third general test chapter: Plastic Packaging System for Pharmaceutical Use <661.2> will provide test methods and standards for assembled plastic packaging systems. This chapter will focus on biological reactivity, physiochemical tests and extractables and leachables testing along with the relevant toxicological assessment. Extractable and Leachable testing will not be defined or specified in this chapter but rather will reference new USP chapters <1663> for extractables and <1664> for leachables. Both of these chapters will provide the framework (scientific principles and best practices) for the design justification and execution of an extractable or leachable assessment for pharmaceutical packaging and delivery systems.

Other test chapters entitled Plastic Systems Used for Manufacturing Pharmaceutical Products<661.3> and Plastic Medical Devices Used to Deliver or Administer Pharmaceutical Products <661.4> will be proposed in the future and will address the characterization of plastic materials used in the manufacturing process and medical devices.

General chapters associated with containers include USP <659> Packaging and Storage Requirements for which changes are underway and planned for publication in PF41(4) July 2015. Elastomeric Closures for injection <381>, Containers -Glass <660> will be up for modernization in the future.

While revisions to USP<661> and the establishment of new chapters referenced within USP <661> are ongoing and open for comments an implementation date for the revisions has not been set to date.

Additional information can be found at the following links.

<http://www.usp.org/meetings-courses/workshops/suitability-and-compatibility-packaging-and-delivery-systems->

http://www.usp.org/sites/default/files/events/stakeholder_forums/2013/meeting-5/04b-extractables-leachables-

Job Opportunities

Job Postings:

Sr. Toxicologist, Medtronic, Jacksonville, FL

[http://jobs.medtronic.com/jacksonville/quality-assurance/jobid7673525-sr-toxicologist-\(stqra\)-jobs](http://jobs.medtronic.com/jacksonville/quality-assurance/jobid7673525-sr-toxicologist-(stqra)-jobs)

Check out SOT Job Bank site for additional medical device related opportunities:

<http://www.toxicology.org/application/jobbank/jobSeeker/login.aspx>

Events

EPA/NCEA Public Workshops on Issues in Risk Assessment

Several workshops have been planned into 2016. Upcoming workshops include the following:
September 2-3, 2015 – Epigenetics and Cumulative Risk Assessment

This workshop will examine the role that data on epigenetic changes may play in assessing cumulative risks in human populations exposed to multiple stressors.

October 19-21, 2015 – Temporal Exposure Issues for Environmental Pollutants: Health Effects and Methodologies for Estimating Risk. This workshop will explore the state-of-the-science with respect to various exposure scenarios and associated human health effects (cancer and non-cancer) and focus on multiple environmental pollutants.

For more information visit the EPA website: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=3077>

MDCPSS Webinar Medical Device Color Additives: Legislative History and Regulatory Perspective by Brenda Seidman, M.S., Ph.D., RAC

June 24th, 2015 from 11:00AM-1:00PM Eastern Daylight Time MARK YOUR CALENDARS!

SOT 2015 Annual Meeting Recap

The SOT meeting began with a Sunday (March 22, 2015) morning and afternoon MDCPSS sponsored Continuing Education (CE) courses. The two CE courses were titled: "Toxicology and Regulatory Considerations for Combination Products" (AM07) and "Advances in Safety Assessment of Medical Devices" (PM 08). Both courses were well attended with 150+ attendees in each course. The designated poster session for Medical devices was also expanded compared to the 2014 meeting.

Tuesday (March 24th) the MDCPSS business meeting and reception was held, with approximately 90 people in attendance, the most in attendance to date. Dr. Greg Erexson called the meeting to order at 6 PM followed by meeting speakers: Greg Erexson (chair); Alan Hood (MDSS awards); Kelly Coleman (membership update); and Jim Kleinedler (budget update). The highlight of the MDCPSS Business Meeting was announcing and congratulating the 2015 award recipients, who included:

- Medical Device SS Best Overall Abstract Award for 2015: L.H. Moilanen and B.D. Bagley (3M Company). "Assessment of the Safety of Co-Exposure to Dental Device Extractables Using the Maximum Cumulative Ratio Approach".
- Medical Device SS Best Published Paper in 2015: W.V. Christian, L.D. Oliver, M. Kreider, D.J. Paustenbach, and B.L. Finley (Cardno ChemRisk). "Toxicology-Based Cancer Causation Analysis of CoCr-Containing Hip Implants: A Quantitative Assessment of Genotoxicity and Tumorigenicity Studies" J Appl Toxicol. (2014) 34:939-967.
- Medical Device SS Student Travel Award for 2015: Kevin L. Trout (University of Montana, Missoula, MT). "Macrophage Fusion into Multinucleated Giant Cells In Vitro".

In addition, the EC chose to present two additional awards. First, recognition for outstanding scientific work in toxicological science was awarded to Nichole Young (a high school student), mentored by Dr.

SOT 2015 Annual Meeting Recap (continued)

Ron Brown, for her work on Conversion Factors to Estimate Oral NOAEL Values from LD50 Values: Implications for Medical Device Toxicology. Second, a service award (engraved plaque) was presented to Jon Cammack for his years of excellent and dedicated service to our Specialty Section. The hard work Kelly Coleman has done was reflected in the increasing MDCPSS membership the past two years.

Membership Update

- The MDCPSS was formed in 2009 with 51 founding members. As of May 2015, membership has tripled its membership number and grown to 153.
- Our members come from industry, government, consulting and academia.
- Educational backgrounds range from BS degrees to those with MBAs, MPHs, PhDs, DVMs, and MDs.

Treasury Update

MDCPSS Financial Information 2015

General Fund

November 2014	\$16,359
December 2014	\$16,859
January 2015	\$17,359
February 2015	\$17,041

2015 MDCPSS Sponsors

Medtronic
MedImmune
AlterNetMD Consulting
NAMSA
WL Gore & Associates
Abbvie
American Preclinical Services
Kelly Coleman
Ron Brown

MDCPSS had a successful year in member registrations and net assets, with modest expenses. Thanks to a strong year of support from sponsors, MDCPSS net assets increased throughout the year. The MDCPSS Executive Committee thanks all this year's sponsors for helping to make MDCPSS 2014 activities possible. Please consider making a tax-deductible donation of any amount to support MDCPSS. MDCPSS accepts donations by check or credit card. Checks can be sent to SOTHQ, and other forms of payment may be completed by email or by phone directed to Raul A. Suarez (raul@toxicology.org) at SOT Headquarters (703) 438-3115 x1461. All donations should have the minimal information, donor's name, contact information, amount of donation and payment information directed to the Medical Device and Combination Product Specialty Section, Society of Toxicology, 1821 Michael Faraday Drive, Suite 300, Reston, VA 20190. When the donation is completed a receipt will be sent to the donor and SOT will notify the MDCPSS President and Treasurer.

2015 Medical Device Poster Session

Medical Device Poster Session at the 2015 Annual Meeting of the Society of Toxicology

Contributed by: Lori Moilanen and Ron Brown

2015 marked the fifth consecutive year that the SOT Annual Meeting has included a poster session devoted to medical devices. The well-attended 2015 medical device poster session included two thematic tracks: risk assessment and test methods. The session also included posters describing development and testing of new drug delivery systems. A total of 21 posters were presented by authors from industry, contract test laboratories, and government agencies. Many attendees commented on the high quality and broad scope of the information presented in the session.

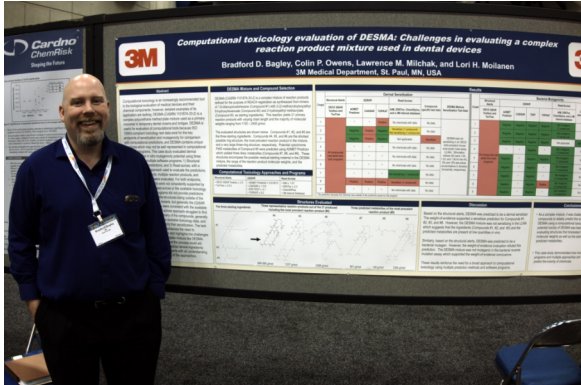
The majority of posters presented in 2015 concerned development and/or validation of new test methods for familiar biological evaluation endpoints, highlighting continued active interest in refinement of medical device test methodology and reduction of animal use. Four posters addressed approaches to testing of blood contacting devices, including evaluation of thrombogenicity potential and hemocompatibility. Four posters described development and ongoing validation of in vitro methods for evaluation of dermal sensitization and irritation potential. Two posters compared outcomes of cytotoxicity testing depending on the assay method or serum content of the extraction medium. Crosscutting topics among the posters included development of new positive control materials, development of in vitro approaches, and comparison of results obtained using various test models or methodologies. The presence of two posters describing testing of new drug delivery approaches underscored the recently expanded scope of the MDCPSS beyond devices.

The other major theme represented at the poster session was risk assessment. Three of the posters explored computational approaches to address risk assessment issues, notably, the use of LD50 values to predict NOAELs from long-term toxicity studies, the use of QSAR models and read across programs to predict the toxicity of a compound used in dental devices, and a comprehensive approach to assess the likelihood of toxicological interactions occurring among the constituents of complex chemical mixtures. In addition, there were a number of posters that used risk assessment approaches to evaluate the safety of specific device-related compounds or materials, like siloxanes, cobalt-chromium alloy, and a cadmium-containing color additive.

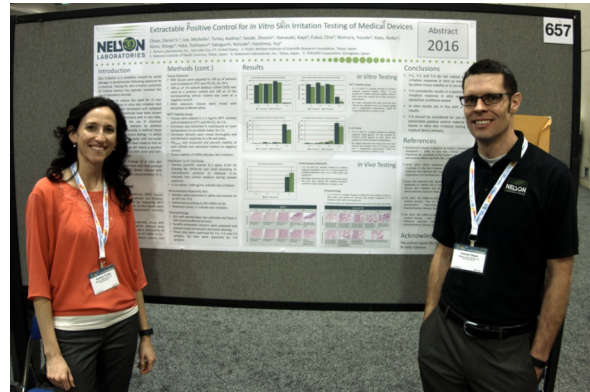
Medical device toxicology is undergoing an exciting transformation with an increased emphasis on the use of alternative test methods and risk assessment. These emerging themes were well represented in this year's poster session. To continue the success of the medical device poster session, MDCPSS members are encouraged to submit abstracts for next year's meeting as well.

2015 MDCPSS Posters Revisited

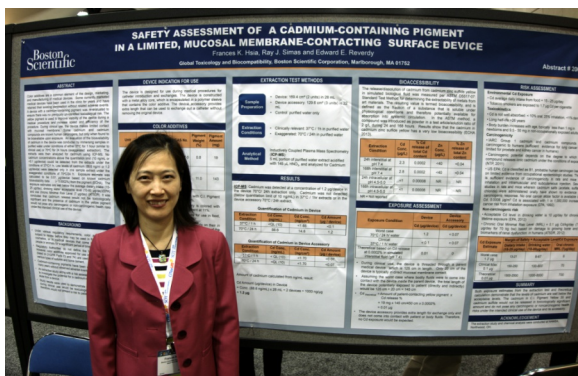
Photos provided by Kelly Coleman



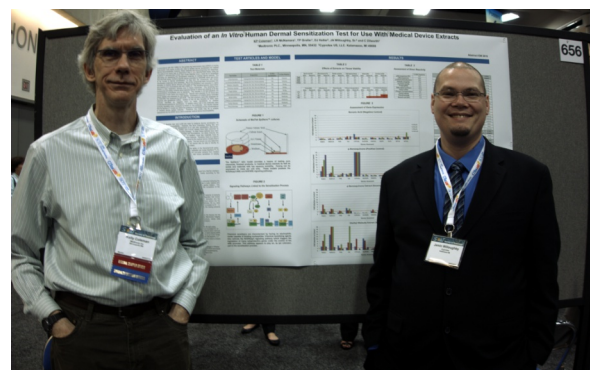
Bradford Bagley



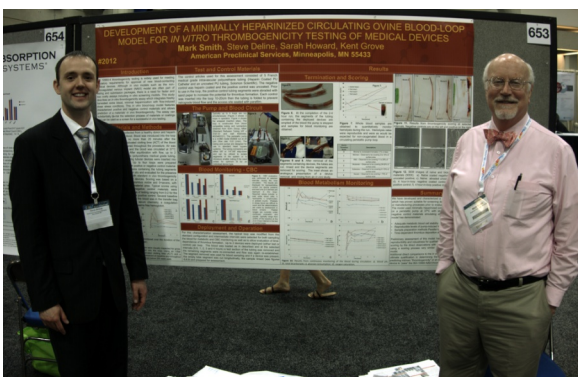
Audrey Turley and Daneiel Olsen



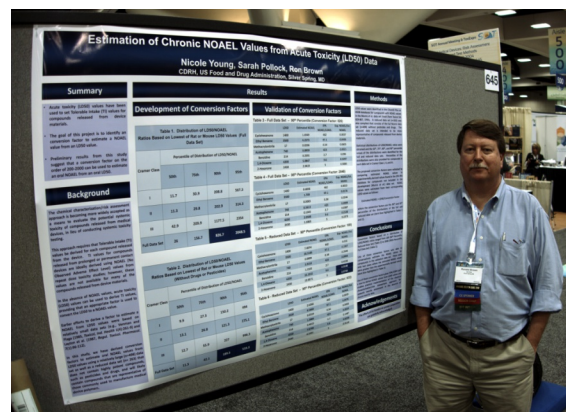
Frances Hsia



Kelly Coleman and Jamin Willoughby



Kent Grove and Mark Smith



Ron Brown

Remembering 2015 MDCPSS Reception

A few photos of awardees, presenters, and attendees from this year's annual meeting in San Diego

Photos provided by Kelly Coleman



MDSS Reception



MDSS Reception



Best Overall Abstract
L. H. Moilanen and B. D. Bagley, 3M



Best Published Paper
W. V. Christian, L. D. Oliver, D. J. Paustenbach, M. L. Kreider and B. L. Finley, Cardno ChemRisk



Student Travel Award
K. L. Trout, University of Montana

SOT 2016 Annual Meeting

It's been several months since the San Diego meeting, and now is the time to starting planning for the next SOT Annual meeting in New Orleans.



Some New Orleans photos are courtesy of New Orleans Convention & Visitors Bureau. Some photos by Pat Garin.

MDCPSS Mission

The objectives of the Medical Device and Combination Products Specialty Section of the SOT are to:

- Provide an international focus group for toxicologists working in the area of medical devices and combination products including a device component.
- Promote the development of new experimental methods for the evaluation of medical devices.
- Sponsor scientific and educational programs that emphasize current developments and issues in the toxicological evaluation of medical devices.
- Promote proactive communication and interactions among toxicologists in government regulatory agencies, regulated industry, and academia regarding current issues in medical device toxicology.
- Stimulate interest in medical device safety as a career path for new toxicologists.