



MDCPSS FALL NEWSLETTER

Volume 10 / Issue 1

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PRESIDENT'S MESSAGE

Dear Medical Device and Combination Products (MDCPSS) Colleagues,

Thank you for your membership in the Medical Device and Combination Product Specialty Section (MDCPSS). We hope you enjoy the Fall newsletter. We are celebrating our 10th year as a Specialty Section, and we have come a long way. I am honored to be your MDCPSS President, but I couldn't do this without the strong support of the excellent executive committee. This year our Executive Committee includes Taylor Builee (Past President), Whitney Christian (Vice President), Jan Oberdoerster (Vice President-Elect), Shelby Skoog (Secretary/Treasurer), Melissa Badding (Councilor), James Kleinedler (Councilor), Kazi Tasneem, (Graduate Student Representative) and Dakshesh Patel (Postdoctoral Representative).

As President of the MDCPSS, I have three primary goals:

- To increase the visibility of our Specialty Section both inside and outside of SOT
- To provide you with meaningful webinars, useful ToXchange and website postings, and worthwhile SOT meeting activities
- To continue to grow our membership by reaching out to students, international members, and members of other Specialty Sections with mutual interest

Our programs committee, led by Whitney and including Taylor, Shelby and Jim, has been busy. So far this year, we have hosted two webinars, one jointly with the Ocular Toxicology Specialty Section. May 22, 2019, Alan Hood, Berk Oktem, and Jennifer Goode, Center for Devices and Radiological Health, US Food and Drug Administration presented a webinar titled "CDRH Scientific Perspective on Analytical Testing and Toxicological Risk Assessment for Medical Devices". This webinar provided useful information on current regulatory considerations for submissions to FDA/CDRH that contain analytical chemistry data and toxicological risk assessment information.

A second webinar jointly hosted with OTSS titled "Biological Risk Assessments for Ocular Medical Devices" was presented August 28, 2019, by Simona Bancos, Center for Devices and Radiological Health, US Food and Drug Administration. This webinar provided an overview on recent changes to ISO 10993-1: 2018, 2016 FDA Biocompatibility Guidance, and Vertical Guidance for ophthalmic devices, and chemical characterization of

ophthalmic devices. Both webinars were well attended, and slides and recordings of the webinar are available on the MDCPSS website <https://www.toxicology.org/groups/ss/MDCPSS/pastevents.asp>. More exciting webinars are in the planning process, as we look forward to bringing you more interesting and useful content.

Shelby and Taylor have been working hard to keep you informed of MDCPSS sponsored events, and programs of interest through eBlasts and ToXchange. Please check out our website and ToXchange bulletin board, as we continue to update these sites, and will include information about the upcoming SOT Annual Meeting in Anaheim, CA March 15-19, 2020.

Our membership continues to grow, and thanks to Jan for leading the membership committee. We now have a record membership of 193 members, up from 53 members since 2010, the inaugural year of the Specialty Section. We continue to encourage student and postdoctoral membership through waiving of student MDCPSS fees, travel awards, mentoring programs, and outreach through our student and postdoctoral executive committee members Kazi and Dakshesh.

A big thank you to Whitney for continuing to take the lead and continuously improving our mentoring events at SOT. Medical device toxicology is a growing field with many job opportunities and these outreach activities should be of great interest to potential student and postdoctoral members. Our newsletter provides industry updates and articles of interest to the specialty section, MDCPSS updates and sponsored events, and important upcoming dates. Thank you to Melissa for putting together this newsletter.

Please don't hesitate to contact me or any other Executive Committee members with ideas for programs, outreach, webinars, or suggestions for continuing to serve you better. I am excited about our 10-year anniversary, and I am looking forward to planning the upcoming events for the 59th Annual Meeting in Anaheim.

Sincerely,

Sherry Parker
MDCPSS President
sherry.parker@wuxiapptec.com



MDCPSS Webinars

MDCPSS and OTSS co-hosted a webinar titled “Biological Risk Assessments for Ocular Medical Devices”, held August 28, 2019.

Webinar speaker was Simona Bancos, PhD, Center for Devices and Radiological Health, US Food and Drug Administration

Abstract: This webinar will focus on reviewing the changes to the International Standard Organization (ISO) Fifth edition 10993-1:2018 and whether these changes have an impact on ophthalmic device biocompatibility assessments and on 2016 FDA Biocompatibility Guidance. The discussion will include an overview of relevant vertical standards and FDA guidance documents for ophthalmic devices including ISO 11979-5 Ophthalmic implants – Intraocular lenses- Part 5: Biocompatibility and Premarket notification (510(k)) FDA guidance document for daily wear contact lenses. The applicability of chemical characterization to the biological evaluation of ophthalmic medical devices will also be discussed.

This webinar is available on the MDCPSS website:

<http://www.toxicology.org/groups/ss/MDCPSS/pastevents.asp>

MDCPSS hosted a webinar titled “CDRH Scientific Perspective on Analytical Testing and Toxicological Risk Assessment for Medical Devices”, held May 22, 2019.

Webinar speakers were Alan Hood, Berk Oktem, and Jennifer Goode, Center for Devices and Radiological Health, US Food and Drug Administration

Abstract: Analytical testing as part of chemical characterization is used to determine the extractable or leachable substances (E/L) including additives, degradants and impurities, present in patient contacting components of medical devices. Analytical testing generally involves one or more extractions followed by use of multiple analytical methods with sufficient sensitivity to identify and quantify E/L substances that could raise a toxicological concern. In this presentation, we will provide an overview of current regulatory review considerations for submissions to FDA/CDRH that contain analytical chemistry data and toxicological risk assessment information. Specific topics covered will include methodological approaches and reporting, including but not limited to, extraction design, analytical instrument/tool selection, sample manipulation, system suitability, calibration, identification/quantification, and data reporting. The selection and application of the analytical evaluation threshold (AET) will be discussed. There will also be discussion on when to conduct a toxicological risk assessment, the current state of reporting, and some considerations for assessing hazard, exposure, dose-response and risk characterization.

This webinar is available on the MDCPSS website:

<http://www.toxicology.org/groups/ss/MDCPSS/pastevents.asp>

2020 SOT Annual Meeting

SOT 2020 **59th Annual Meeting & ToxExpo**
Anaheim, California • March 15–19



The SOT 59th Annual Meeting and ToxExpo will be held in Anaheim, California March 15 – 19, 2020. Meeting [registration](#), [housing](#), and [abstract submission](#) sites are currently open.

Important deadlines:

- Early-Bird Registration:** January 10, 2020
- Standard Registration:** February 7, 2020
- Abstract Submission:** 11:59 pm (EDT) on October 18, 2019

SOT is looking for volunteers to Chair Poster and Platform Sessions for the 2020 meeting. If you are interested, visit the [ToXchange website](#) to volunteer.

Volunteer

If you are interested in volunteering to chair a session, please familiarize yourself with the procedures by visiting the 2020 SOT Annual Meeting website to review the [Poster Session Chair](#) and [Platform Session Chair](#) guidelines.

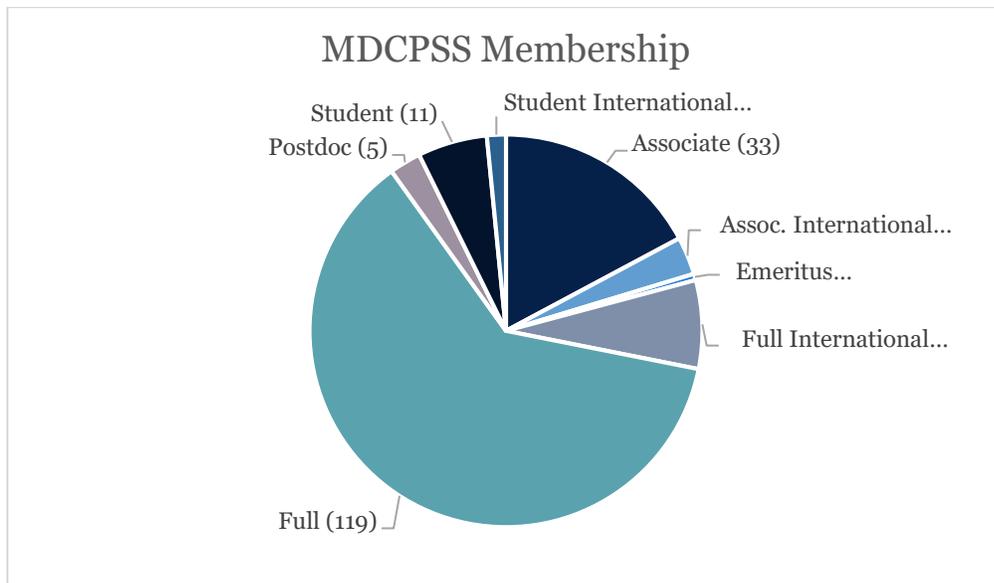
To volunteer to serve as an SOT Poster or Platform Session Chair, use this form to provide your information, including the topic(s) of interest. If selected, you will be sent an invitation in early December requesting your assistance.

[Volunteer](#)

Membership Update

The MDCPSS was formed in 2009 with 51 founding members. Since then we've grown steadily and now have 193 members.

Our members come from industry, government, consulting, and academia (see Figure below). The majority of our membership includes Full SOT Members, followed by Associate Members, Student Members, and Full International Members. Educational backgrounds range from BS degrees to those with MBAs, MPHs, PhDs, DVMs, and MDs.



Postdoc Member Highlight



I am Dakshesh Patel currently working as an ORISE Fellow in the stem-cell electro physiology laboratory in the Division of Biomedical Physics at US FDA. My research is focused on validating multiple lines of healthy and diseased human induced pluripotent stem-cell cardiomyocytes (iPSC-CMs) and neurons.

With the state-of-the-art biophysical and electrophysiological techniques, our group is exploring the potential application of stem cell cardiomyocytes in personalized medicine and drug toxicity screening. We validate standard protocols, assess electrophysiological properties of iPSCs, and investigate newer technologies for efficient screening of drugs for cardiovascular toxicities.

The ORISE program at FDA provides an exceptional opportunity to perform regulatory-based research as well as get acquainted with the regulatory mission of FDA. This intersection puts me in a unique position to make direct impacts towards improving public health – an issue I strive for.

Internally, the program also offers wonderful opportunities to get acquainted with all aspects of medical device, food and drug regulations. I myself have benefitted greatly from seminars on food and drug laws with a focus on medical devices, biocompatibility guidance (ISO 10993-1) and drug-development. Apart from regulatory trainings, FDA also focuses on inculcating soft-skills through non-technical sessions focused on topics like ‘technical writings’, ‘communication skills’, and ‘conflict resolution’ to name a few.

Prior to FDA, I graduated from SUNY Upstate Medical University, in Syracuse, NY with a PhD in Pharmacology under the mentorship of Dr Richard Veenstra in Fall 2016. My thesis project was focused on identifying molecular and electrophysiological mechanisms responsible for cardiac toxicity of histone deacetylase inhibitors (FDA approved for cutaneous and peripheral T-cell lymphoma) in the clinic. I utilized single and dual whole cell patch clamping to study the role of pan-HDAC inhibitors on individual ion channels.

Outside the laboratory, I like to stay tuned with the current affairs, engage in sporting activities, and consider myself as an amateur investor in stocks.

MDCPSS Member Achievements

The MDCPSS Executive Committee would like to congratulate our members on their professional accomplishments.

Awards, promotions, certifications:

Kazi Tasneem won the Best Research Paper Award, Chemical and Biomolecular Eng., Vanderbilt University; and 2nd Prize at the Graduate Collegiate Competition, WE Local Tampa, Society of Women Engineers

Elissa Wong started a new position as a Biologist at FDA in CDRH OPEQ

Melissa Badding was promoted to Managing Scientist at Exponent, Inc

Relevant publications:

Schuh JCL and Funk KA. (2019). Compilation of international standards and regulatory guidance documents for evaluation of biomaterials, medical devices, 3D printed and regenerative medicine products. *Toxicol. Pathol.*, 47; 344-357.

Badding MA, Barraji L, Williams AL, Scrafford C, and Reiss R. (2019) CLARITY-BPA Core Study: Analysis for Non-Monotonic Dose-Responses and Biological Relevance. *Food and Chemical Toxicology*, 131; September 2019, 110554.

Saylor DM, Chandrasekar V, Simon DD, Turner P, Markley LC, Hood AM. (2019) Strategies for rapid risk assessment of color additives used in medical devices. *Toxicol Sci.* 2019 Aug 6. [Epub ahead of print]

Auner, A.W.*, Tasneem, K.M.*, Markov, D.A., McCawley, L.J., and Hutson, M.S., “Chemical-PDMS binding kinetics and implications for bioavailability in microfluidic devices,” *Lab on a Chip*, 2019, *equally contributed first authors

Please submit your achievements for the next newsletter to Melissa Badding (mbadding@exponent.com).

Treasury Update

The MDCPSS Executive Committee would like to thank our sponsors for helping to make MDCPSS 2019 activities possible. MDCPSS had a successful year in member registrations and net assets, with modest expenses.

2019 Net Assets

February 2019	\$20,023
March 2019	\$9,262
April 2019	\$9,262
May 2019	\$9,532
June 2019	\$12,704

2019 MDCPSS Sponsors

Malek Toxicology Delaware, LLC
WL Gore & Associates Inc.
WuXi AppTec, Inc.

To support MDCPSS activities, please consider making a tax deductible donation. If you would like to dedicate a contribution to supporting one or more activities, the EC will gladly facilitate your tax free donation and recognize your support at the annual event and in our communication. MDCPSS accepts donations by check or credit card. For additional information regarding donations to MDCPSS, please contact the MDCPSS Secretary/Treasurer, Shelby Skoog (Shelby.Skoog@fda.hhs.gov), or Mina Klier (mina@toxicology.org) at SOT Headquarters.

ISO 10993 Updates

By Sherry P Parker*

*WuXi AppTec Medical Device Testing, St. Paul, MN

The ISO 10993 series of harmonized standards to address the biological evaluation of medical devices are developed by the ISO Technical Committee 194 (TC 194). The 29th international meeting of the ISO TC 194 was held from December 3-7, 2018 in Berlin. Because the next international meeting is not scheduled until 2020, it was decided by the committee to hold interim TC 194 Working Group meetings during the week of October 14-17, 2019 in Arlington VA, at the AAMI Headquarters. Many of the standards are in the process of significant revision, and provided here is a brief summary of the most significant changes.

ISO 10993-10 Biological Evaluation of Medical Devices-Part 10: Tests for irritation and skin sensitization will be split into two separate standards. ISO 10993-10 will be Tests for Skin Sensitization; and ISO 10993-23 will be Tests for Irritation. ISO 10993-10 is now a new Committee Draft under development and will focus on sensitization only. ISO 10993-23 Tests for Irritation is a Draft International Standard (DIS). This new standard provides in vitro test methods for skin irritation testing that were developed using reconstructed human epidermis (RhE) models. The method was adapted for detection of irritant chemicals in medical device extracts, and was evaluated with a large round robin study, recently published by De Jong W.H. et al., 2018 <https://www.sciencedirect.com/science/article/pii/S0887233318300018?via%3Dihub>. The standard still provides in vivo test methods, and the human skin irritation test.

A new version of ISO 10993-12 Biological Evaluation of Medical Devices-Part 12: Sample preparation and reference materials is now DIS. Primarily there is a change of scope to cover extractions only for biological evaluation tests, harmonization of terms and definitions with ISO 10993-18, and additional guidance on exhaustive extractions.

There is a new Technical Specification was published in February 2019 (ISO/TS 21726: Biological evaluation of medical devices - Application of the threshold of toxicological concern (TTC) for assessing biocompatibility of medical device constituents. This document was recently recognized in its entirety by the US FDA (FR Recognition number 2-268), and provides information about the general applicability of a threshold of toxicological concern (TTC) value for a constituent present in/on a medical device or released from a medical device. This TS is relevant for the analytical evaluation threshold (AET) for setting limits for identification and quantification of medical device constituents (per ISO/FDIS 10993-18), and for setting thresholds for identified chemicals in the absence of toxicity data (per ISO/WD ISO 10993-17).

ISO 10993-7:2008 Ethylene oxide sterilization residuals has a Final Draft Amendment 1, soon to be published. The primary reason for this amendment was to update the requirements for devices used in special populations (e.g. premature neonates, neonates or children). The appropriate patient body mass shall be used for the derivation of the allowable limits, and the allowable limits shall be derived using the TI values derived in Annex G. The entire standard will soon be updated by the Working Group.

ISO 10993-17 Biological Evaluation of Medical Devices-Part 17: Allowable Limits of Leachable Substances is now a new Working Draft that has been distributed to the Working Group for balloting. The proposed title is "Toxicological Risk Assessment of Medical Device Constituents," and the revised standard will expand from current guidance on establishing allowable limits of leachable substances, to conducting a toxicological risk assessment of medical device constituents. Topics to be addressed will include hazard identification, exposure assessment, dose-response assessment, and risk characterization. There will be emphasis on the use of expert judgement to determine whether the toxicological risks of exposure to extractable or leachable chemicals in medical devices are acceptable, what additional steps may be taken to mitigate risk, and when to recommend risk control.

ISO 10993-18 Biological Evaluation of Medical Devices-Part 18: Chemical Characterization of Medical Device Materials within a Risk Management Process was issued as a Final Draft International Standard (FDIS), and is expected to be published as an International Standard by the end of 2019 (latest early 2020). This FDIS has greater harmonization with ISO 10993-1, ISO 10993-12 (definitions), and ISO 10993-17. There will be greater emphasis on the Analytical Evaluation Threshold (AET) Concept, and more guidance on gathering and generating chemical information. This includes guidance on the planning and conduct of extractables and leachables studies to support toxicological risk assessments of medical devices.

At the US level, ISO 10993 standards are reviewed by the AAMI/Biological Evaluation Committee for comments and approval. Participating in the standards development can be a very rewarding. Recently we reported that AAMI is reaching out to academic institutions in the US who conduct research related to biological response to medical devices to see if they would be willing to participate in our standards development work. For representatives of the "user" category, AAMI membership is not required. If you have names/contact information (email preferred) you can share for individuals or departments conducting research on the development of medical device materials or test systems to evaluate the response to medical devices/materials, please email this information to Colleen Elliott, celliott@aami.org.

Cobalt Hazard Up-Classification

Medical Device Companies Come Together to Address the Potential Regulatory Consequences of Cobalt Up-Classification in Europe

By Whitney V. Christian[‡] and Edward E. Reverdy[‡]

[‡]Medtronic PLC, Jacksonville, FL

[‡]Johnson & Johnson, Somerville, NJ

In 2018, cobalt metal (CASRN 7440-48-4) was included in the draft 14th Adaptation to Technical and Scientific Progress (ATP) amending the Classification, Labelling and Packaging of Substances and Mixtures Regulation, referred to as the CLP1. Within the 14th ATP, up-classification of cobalt metal to a CMR 1B substance (carcinogen 1B, reprotoxin 1B, mutagen 2) is proposed. Although the REACH Committee (consisting of Member State Competent Authorities) has not yet voted on the proposal, up-classification will bring cobalt in scope of the European Union (EU) Medical Devices Regulation² Annex I, Section 10.4, if accepted. In turn, invasive medical devices constructed from cobalt chromium and stainless-steel alloys, such as orthopedic implants, vascular products, and surgical instruments, will require hazardous substances labelling and risk justification due to the presence of cobalt above 0.1% w/w.

Pending the potential up-classification decision of cobalt by the EU Commission, fourteen medical device companies working through MedTech Europe and in collaboration with Cardno ChemRisk are compiling scientific, medical, and epidemiology data related to the hazard and risk of cobalt-containing alloys to show that these materials do not present a safety concern for patients. In anticipation of the potential reactions from healthcare professionals, patients, media, and the public that may follow from the up-classification of cobalt as a carcinogen/reprotoxin, the collaboration has three main objectives:

- Provide toxicology and epidemiology data on the hazard and risk of carcinogenicity and reproductive toxicity for cobalt-containing alloys to surgeons and patients.
- Inform Notified Bodies and Health Authorities on the data regarding carcinogenicity hazard and risk, and thereby guide policy and regulatory decision making.
- Create a base of evidence for an Industry-wide justification for the use of cobalt when it is present in devices above 0.1% w/w.

The final due date for the decision is expected by December 2019. The Medical Device Industry and MedTech Europe are following this issue and the decision process very closely. This is a good example of how medical device companies are able to come together to ensure that the relevant data are assessed and used to appropriately inform patients and healthcare professionals about the safety of their products.

References

1. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.
2. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

MDCPSS Mission

The mission of the Medical Device and Combination Product Specialty Section is 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.

Don't forget to visit the MDCPSS Website for regular updates:

<https://www.toxicology.org/groups/ss/MDCPSS/index.asp>