Amy Mihalchik, Ph.D., DABT, RAC

SUPERVISING SCIENTIST

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Amy Mihalchik is a board-certified toxicologist with a Regulatory Affairs Certification (R.A.C.) from the Regulatory Affairs Professionals Society and expertise in risk assessment of pharmaceutical and medical device products. She integrates results from literature-based risk assessments with client-generated data, regulatory agency documents, and corporate technical reports to address complex issues of exposure and toxicity. To support workplace safety in the pharmaceutical manufacturing arena, Dr. Mihalchik derives occupational exposure limits (OELs) and acceptable daily intakes (ADIs) and develops permissible daily exposure limits (PDEs) and tolerable exposure values (TEs) for pharmaceutical compounds and devices, respectively. She has expertise in analyzing data from leachables and extractables testing of medical devices, including familiarity with ISO guidelines and ISO-10993 biocompatibility assessments of medical devices.

Dr. Mihalchik is trained in interpreting GLP and non-GLP study results for pharmaceutical and medical device products, has received training in study and laboratory audits of Contract Research Organization facilities, and routinely generates written communications (e.g., safety data sheets, drug labels) and internal documentation to address a variety of audiences (e.g., toxicologists, business development employees, EHS professionals, regulators, workers). With a strong background in drug impurity qualifications, she uses quantitative structure-activity relationship (QSAR) modeling to predict compound mutagenicity and is able to provide expert review of QSAR output. Her doctoral research at the National Institute for Occupational Safety and Health (NIOSH) focused on addressing potential toxicities associated with multi-walled carbon nanotubes using *in vitro* methods to support "safety by design" efforts.

Dr. Mihalchik is familiar with the body of regulatory documents issued by the FDA, ICH, ISO, and other entities, and she maintains current knowledge in toxicology and regulatory science through extensive commitment to Continuing Education courses, webinars/seminars, and active participation in professional societies. She has published multiple peer-reviewed book chapters and scientific articles and has presented at scientific conferences since 2014.

EDUCATION AND DEGREES EARNED

2016 Doctor of Philosophy (Ph.D.)
Pharmaceutical and Pharmacological Sciences (field: nanotoxicology)
West Virginia University, Morgantown, WV

2011 Bachelor of Arts (B.A.)
General Biology (minor: English)
Washington & Jefferson College, Washington, PA

AWARDS AND GRANTS

AAAS/Science Program for Excellence in Science

Society of Toxicology Student Travel Award, March 2015

Integrated Graduate Education and Research Training (IGERT) Fellow, 2014–2016

WV NANOSafe Graduate Fellow, 2013–2014

SELECTED PROFESSIONAL EXPERIENCE

Toxicology Consultant

- Contributed to risk assessments across sectors
- Prepared gap analyses in support of GRAS and GRASE dossiers.
    - Conducted targeted literature searches addressing key endpoints of toxicological relevance (e.g., reproductive and developmental toxicity, carcinogenesis, genotoxicity) in databases, including PubMed and Embase.
- Developed proficiency in gathering relevant toxicological data from databases—including ToxPlanet, EPA CompTox Dashboard, PubChem, and FDALabel—to support projects across sectors (e.g., consumer products, foods, pharmaceuticals).
- Utilized a variety of freely available (e.g., VEGA, EPA T.E.S.T., ToxTree) and commercial (Q)SAR platforms to address complex client queries regarding mutagenicity, genotoxicity, carcinogenicity, and target-organ effects.
- Assessed cosmetic ingredients using literature review and (Q)SAR techniques.
- Supported a litigation project by reviewing and summarizing available literature regarding the case.
- Reviewed and interpreted nonclinical study data intended to support pharmaceutical products and medical devices.
- Supported ISO 10993-compliant evaluations of medical devices, including:
    - Gap analysis of available biocompatibility data
    - Review of device components, extractables, and leachables, including derivation of TE values per ISO 10993-17

Regulatory Toxicology Consultant

Performed risk assessments pertaining to pharmaceutical agents and medical devices:

- Provided literature-based risk assessments based on client data, regulatory agency documents and technical reports, and scientific literature
- Derived occupational exposure limits (OELs) and acceptable daily intakes (ADIs) to support workplace safety and appropriate cleaning carry-over limits in pharmaceuticals manufacturing
- Applied standard risk assessment methods to develop permissible daily exposure limits for pharmaceutical compounds and tolerable exposure values for medical devices
- Analyzed data derived from leaching and extraction testing of medical devices in compliance with ISO guidelines
- Performed ISO-10993 biocompatibility assessments of medical devices
- Determined F-values used to support child-proof packaging of pharmaceuticals.

Used Derek Nexus (knowledge-based), Leadscope Model Applier (statistics-based), and ToxTree software to predict mutagenicity and other endpoints associated with compounds in the absence of adequate data.

Provided expert review of QSAR output.

Identified appropriate surrogate compounds for assessment using read-across methods.

Guest Researcher/Worksite Student

Worked as a guest researcher for NIOSH:

- Studied effects of pristine multi-walled carbon nanotubes (MWCNT) and nitrogen-doped MWCNT (ND-MWCNT) at occupationally relevant doses on human lung small-airway epithelial cells
    - Conducted pioneering research on the impact of MWCNT physicochemical properties on the pulmonary system in a public health molecular toxicology lab
    - Provided an interface for translational interdisciplinary research between government and academic biomedical scientists and material scientists to address technical issues surrounding MWCNT safety
    - Determined that MWCNT and ND-MWCNT affect reactive oxygen species production, cell cycle progression, and cell signaling processes in lung cells.
- Studied effects of pristine MWCNT and ND-MWCNT on normal lung fibroblasts:
    - Investigated mechanisms of MWCNT-induced pulmonary fibrosis in an *in vitro* system using lung epithelial and fibroblast cells
    - Determined that MWCNT and ND-MWCNT induce production of mRNA for several genes that are key to pulmonary fibrosis.
- Gained experience in using and developing *in vitro* co-culture systems:
    - Used lung epithelial-endothelial co-culture to address toxicity of pristine MWCNT
    - Developed lung epithelial-fibroblast co-culture system to study mechanism of MWCNT and ND-MWCNT-induced pulmonary fibrosis.
- Also used various other techniques, including Western blotting, immunoprecipitation, confocal microscopy, ELISA, flow cytometry, cell cycle analysis, cell proliferation analysis, RNA extraction, and qRT-PCR.

Doctoral Research

Completed research rotations in three laboratories at West Virginia University:

- Assisted on a project to assess the toxicity and potential therapeutic uses of nanoparticles in the Department of Orthopedics
- Became proficient in cell culture and basic molecular biology techniques through a breast cancer–focused research project
- Assisted on a project to identify specific molecular recognition elements (MREs) to detect malignant prostate cancer cells using systematic evolution of ligands by exponential enrichment (SELEX).

PROFESSIONAL AFFILIATIONS

American Association for the Advancement of Science — Member

American College of Toxicology — Associate Member

Society of Toxicology — Member, Associate Member

Association of Inhalation Toxicologists — Member

North Carolina Society of Toxicology Chapter — Member

Rho Chi Academic Honor Society in Pharmacy — Member

MANUSCRIPTS

Mihalchik AL, Choksi NY, Roe AL, Wisser M, Whitaker K, Seibert D, Deore M, Pavlick L, Wikoff DS. 2024. Safety evaluation of 8 drug degradants present in over-the-counter cough and cold medications. Regul Toxicol Pharmacol 149:105621; doi: 10.1016/j.yrtph.2024.105621.

Tice RR, Bassan A, Amberg A, Anger LT, Beal MA, Bellion P… Mihalchik-Burhans AL, et al. 2021. *In silico* approaches in carcinogenicity hazard assessment: Current status and future needs. Comp Toxicol 20:100191 (Special issue: The in silico toxicology protocols initiative).

Sisler JD, Li R, McKinney W, Mercer RR, Ji Z, Xia T, Wang X, Shaffer J, Orandle M, Mihalchik AL, Battelli L. 2016. Differential pulmonary effects of CoO and La_2O_3 metal oxide nanoparticle responses during aerosolized inhalation in mice. Particle Fibre Toxicol 13(1):42.

Sisler JD, Pirela SV, Shaffer J, Mihalchik AL, Chisholm WP, Andrew ME, Schwegler-Berry D, Castranova V, Demokritou P, Qian Y. 2016. Toxicological assessment of CoO and La_2O3 metal oxide nanoparticles in human small airway epithelial cells. Toxicol Sci 13(1):42.

Mihalchik AL, Ding W, Porter D, McLoughlin C, Schwegler-Berry D, Sisler JD, Stefaniak A, Snyder-Talkington BN, Cruz-Silva R, Terrones M, Tsuruoka S, Endo M, Castranova V, Qian Y. 2015. Effects of nitrogen-doped multi-walled carbon nanotubes compared to pristine multi-walled carbon nanotubes on human small airway epithelial cells. Toxicology 333:25–36.

BOOK CHAPTERS

Mihalchik-Burhans AL, Rogers EN. 2019. Considerations for leachables and extractables testing. In: Gad S (ed), Integrated Safety and Risk Assessment for Medical Devices and Combination Products, pp. 239–263. Springer.

Mihalchik-Burhans AL, Sullivan DW. 2019. Bridging issues of route. In: Gad S (ed), Integrated Safety and Risk Assessment for Medical Devices and Combination Products, pp. 273–297. Springer.

Mihalchik AL, Rogers EN. 2018. Classes of compounds with GI tract toxicity. Chapter 13 in: Gad SC (ed), Toxicology of the Gastrointestinal Tract. CRC Press.

ABSTRACTS AND PRESENTATIONS

Petrick J, **Mihalchik A**, Tiwary A, Kreidl L, Swartz C, Bhattarai N. Nonclinical safety evaluation of 1-monoacetin and 2-monoacetin as potential impurities in pharmaceutical excipients. Abstract 3107, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Lea IA, Feifarek D, **Mihalchik A**, Heintz M, Haws L, Nyambego H, Goyak K, Borghoff SJ. Evaluation of the endocrine disrupting potential of di-isodecyl phthalate. Abstract 3930, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Borghoff SJ, Feifarek D, **Mihalchik A**, Heintz M, Haws L, Nyambego H, Goyak K, Lea IA. Evaluation of the endocrine disrupting potential of di-isononyl phthalate. Abstract 3931, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Brown L, McMillan DA, Urban JD, **Mihalchik AL**. A tiered approach for assessing the safety of polymeric ingredients in cosmetics and personal care products. Poster presented at Society of Toxicology Annual Meeting, Nashville, TN, March 2023.

Mihalchik AL, Choksi NY, Wood ML. Toward best practices for read-across in evaluation of drug impurities, extractable, and leachable compounds. Poster presented at Society of Toxicology Annual Meeting, Nashville, TN, March 2023.

Mihalchik AL, Choksi NY, Lea I, Wood ML. Modern strategies to evaluate drug impurities. Session presented at Society of Toxicology Annual Meeting, Nashville, TN, March 2023.

Mihalchik A, Wood M. Considerations for standardization and derivation of pediatric and neonatal tolerable exposure limits for extractable and leachable compounds from medical devices. Poster presented at Society of Toxicology Annual Meeting, San Diego, CA, March 2022.

Rogers EN, **Mihalchik AL**, Gad SC. Comparison and analysis of discrepancies among commonly used Cramer decision tree methods in Toxtree software. Annual Meeting, Society of Toxicology, Abstract no. 1517, 2020.

Mihalchik A (contributor). In vitro and alternative models for regulatory submission. Podcast presentation available from American College of Toxicology, December 2018.

Mihalchik-Burhans A. And you want this by when? Making the successful transition from the bench to consulting. Oral presentation at the American College of Toxicology 39th Annual Meeting, West Palm Beach, FL, November 2018.

Mihalchik A (contributor). ACT annual meeting in West Palm Beach: Highlights and preview. Podcast presentation available from American College of Toxicology, October 2018.

Mihalchik AL, Rogers EN, Gad-McDonald SE, Sullivan DW Jr, Gad SC. Development of dermal permissible daily exposure (PDE) levels for elemental impurities by utilizing data from alternative routes. Poster presented at the Society of Toxicology 57th Annual Meeting, San Antonio, TX, March 2018.

Mihalchik AL. Effects of nitrogen-doped and pristine multi-walled carbon nanotubes in human bronchial epithelial cells and lung fibroblasts. Presented at Society of Toxicology 55th Annual Meeting, New Orleans, LA, March 2016.

Mihalchik AL. Addressing toxicity: In vitro caveats to the understanding of nanoparticle research and human health. Oral talk presented at the REN@WVU-NEEP Symposium, Morgantown, WV, October 2015.

Mihalchik AL. Nanoparticles: it's the little things in life that count. Oral talk presented at Davis & Elkins College in Elkins, WV, April 2015.

Mihalchik AL, Ding W, McLoughlin CE, et al. Effects of pristine and nitrogen-doped multiwalled carbon nanotubes (ND-MWCNT) on reactive oxygen species (ROS) and cell cycle progression. Presented at Society of Toxicology 54th Annual Meeting, San Diego, CA, March 2015.

Mihalchik AL, Ding W, Porter D, McLoughlin C, Schwegler-Berry D, Sisler JD, Stefaniak A, Snyder-Talkington BN, Cruz-Silva R, Terrones M, Tsuruoka S, Endo M, Castranova V, Qian Y. Effects of pristine and nitrogen-doped multiwalled carbon nanotubes (ND-MWCNT) on reactive oxygen species (ROS) and cell cycle progression. Poster session presented at the Society of Toxicology 54th Annual Meeting, San Diego, CA, March 2015.

Mihalchik AL, Ding W, Porter D, McLoughlin C, Schwegler-Berry D, Sisler JD, Stefaniak A, Snyder-Talkington BN, Cruz-Silva R, Terrones M, Tsuruoka S, Endo M, Castranova V, Qian Y. Effects of nitrogen-doped multi-walled carbon nanotubes compared to pristine multi-walled carbon nanotubes on human small airway epithelial cells. Poster session presented at the West Virginia University E.J. Van Liere Memorial Convocation & HSC Research Day, Morgantown, WV, February 2015.

Mihalchik AL, McLoughlin C, Schwegler-Berry D, Farcas M, Shvedova A, Porter D, Tsuruoka S, Endo M, Castranova V, Qian Y. Nitrogen-doped multi-walled carbon nanotube-induced effects in human small airway epithelial cells. Poster session presented at the West Virginia University Bench to Bedside: Translational Pharmacy Meeting, Morgantown, WV, June 2014.

Mihalchik AL, Porter D, Castranova V, Tsuruoka S, Endo M, Qian Y. Effects of MWCNT and nitrogen-doped MWCNT in lung epithelial cells. Presented at Society of Toxicology 53rd Annual Meeting, Phoenix, AZ, March 2014.

Mihalchik AL, McLoughlin C, Schwegler-Berry D, Farcas M, Shvedova A, Porter D, Tsuruoka S, Endo M, Castranova V, Qian Y. Nitrogen-doped multi-walled carbon nanotube-induced effects in human small airway epithelial cells. Poster session presented at the NIOSH Intramural Science Meeting, Morgantown, WV, July 2014.