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Committee on Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

Virtual Workshop 2 | Thursday, May 12, 2022 | 11:00am-3:30pm EDT

Public Handout

Project Website

National Academies Committee on Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

Workshop 2
Thursday, May 12, 2022
11 AM- 3:30 PM EST

MEETING OVERVIEW

Animal testing is often used to evaluate the potential risks, uses, and environmental impacts of chemicals. New Approach Methods (NAMs) are technologies and approaches (including computational modeling, in vitro assays, and testing using alternative animal species) that can inform hazard and risk assessment decisions without the use of animal testing.

This one-day virtual workshop will address the committee's charge and inform the consensus report by addressing elements of a scientific confidence framework for NAMs pertinent to risk assessment. A case study approach will be used to illustrate the strengths and weaknesses of traditional and non-traditional approaches and methods. Experts from academia, industry, the government, and other organizations will explore and discuss key cross-cutting themes including: public health goals and risk assessment issues; variability and concordance; in vivo and in vitro adversity; and data for benchmarking new approach methods.

All presentations were pre-recorded and will be made available via the event webpage for viewing before the workshop. Presentations will be briefly summarized during the live discussions.

Welcome and Introductions

11 AM **Welcome**

Introduction to the committee and the charge questions
Kate Guyton, National Academies Project Director
Weihsueh Chiu, Committee Chair

Session I: Mixtures

11:20 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderators: Kim Boekelheide and Weihsueh Chiu

Panelists:

- Carl-Gustaf Bornehag, Karlstad University
- Beate Escher, Helmholtz Centre for Environmental Research
- Chris Gennings, Icahn School of Medicine at Mount Sinai
- Cynthia Rider, National Institute of Environmental Health Sciences
- Tom Webster, Boston University School of Public Health

Break (10 min)

Session II: Developmental Neurotoxicity

12:40 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderators: Robyn Tanguay and Heather Patisaul

Panelists:

- Elaine Faustman, University of Washington
- Helena Hogberg, National Institute of Environmental Health Sciences
- Tim Shafer, Environmental Protection Agency
- Jason Stein, University of North Carolina, Chapel Hill
- Shirlee Tan, Senior Toxicologist for Public Health, Seattle and King County

Break (10 min)

Session III: Estrogenicity

2:00 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderator: Nicole Kleinstreuer and Marie Fortin

Panelists:

- Richard Judson, Environmental Protection Agency
- Paul Mermelstein, University of Minnesota
- Ruthann Rudel, Silent Spring Institute
- Laura Vandenberg, UMass Amherst
- Fred Wright, North Carolina State University

Public Comment Period

3:10 **Advance registration required and comment time is limited to 2 minutes.**

3:30 **ADJOURN**

Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

Animal testing is often used to evaluate the potential risks, uses, and environmental impacts of chemicals. New Approach Methodologies (NAMs) are technologies and approaches that can potentially provide the same hazard and risk assessment information without the use of animal testing. To further establish scientific confidence in these approaches, this study will review the variability and relevance of existing mammalian toxicity tests, specifically when it comes to human health risk assessment. The goal of this study is to set data-driven and science-based expectations for NAMs based on the variability and relevance of the traditional toxicity testing models.

Committee Membership

Weihsueh A. Chiu, PhD (Chair)
Texas A&M University

Kim Boekelheide, PhD
Brown University

Patience Browne, PhD
Organisation for Economic Co-operation and Development

Holly Davies, PhD
Washington State Department of Health

Corie A. Ellison, PhD
The Procter & Gamble Company

Marie C. Fortin, PhD
Toxicology, Rutgers University

Nicole C. Kleinstreuer, PhD
National Institute of Environmental Health Sciences

Nancy E. Lane, MD
University of California, Davis

Heather B. Patisaul, PhD
North Carolina State University

Elijah J. Petersen, PhD
National Institute of Standards and Technology

Kristi Pullen Fedinick, PhD
Natural Resources Defense Council

Martyn T. Smith, PhD
University of California, Berkeley

Robyn L. Tanguay, PhD
Oregon State University

Christopher Vulpe, MD
University of Florida, Gainesville

Tracey J Woodruff, PhD
University of California, San Francisco

Joseph C. Wu, PhD
Stanford University

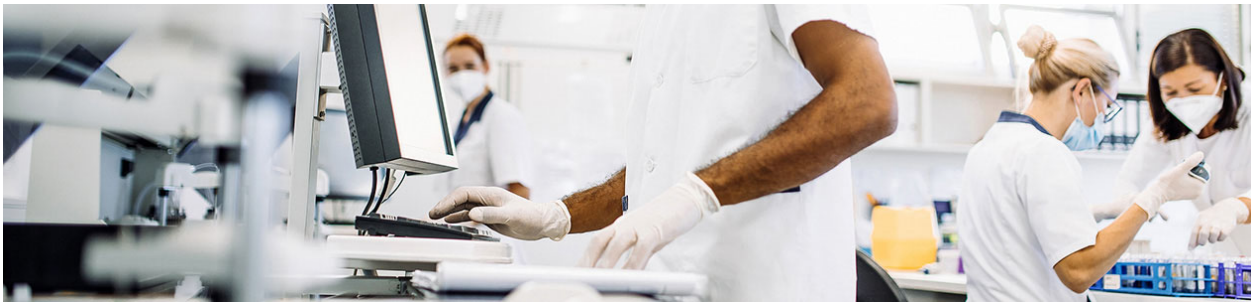
NASEM *Staff*

Kathryn Guyton, PhD
Project Director

Clifford Duke, PhD
BEST Board Director

Corinne Lutz, PhD
Program Officer

Tamara Dawson
Program Coordinator



Biographical sketch of the Committee on Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

Weihsueh A. Chiu (*Chair*) is a professor in the Department of Veterinary Integrative Biosciences at Texas A&M University. He also has a Research Fellow appointment at the Institute for Science, Technology, and Public Policy at the Bush School of Government and Public Service. Before joining the university in 2015, he worked at the U.S. Environmental Protection Agency (EPA) for more than 14 years, most recently as branch chief in the Office or Research and Development. His research in human health risk assessment includes toxicokinetics, physiologically-based pharmacokinetic modeling, dose-response assessment, characterizing uncertainty and variability, systematic review, and meta-analysis, with particular interest in Bayesian and probabilistic methods. He is author/co-author of over 100 peer-reviewed journal publications, many governmental and international agency reports, and several book chapters. Dr. Chiu has participated or chaired expert review panels for multiple government agencies (including membership on EPA's Science Advisory Board with a dual appointment on the Chemical Assessment Advisory Committee), international committees, and work groups. He has served on six National Academies of Sciences, Engineering and Medicine committees, including the Committee on Predictive-Toxicology Approaches for Military Assessments of Acute Exposures, the Standing Committee on Use of Emerging Science for Environmental Health Decisions, and the Committee to Review the IRIS Handbook. Dr. Chiu received an AB in Physics from Harvard University, a MA and PhD in Physics from Princeton University, and a Certificate in Science, Technology, and Environmental Policy from the Princeton School of Public and International Affairs.

Kim Boekelheide is Professor (Research) and Professor (Emeritus) in the Department of Pathology and Laboratory Medicine at the Brown University School of Medicine. He received his B.A. from Harvard University, and M.D. and Ph.D. from Duke University. Current research projects include the development of novel in vitro approaches to safety assessment and the discovery of sperm molecular biomarkers that reflect testicular injury. He was Director (2005-2016) of the Brown University Superfund Research Program and Director (2014-2017) of the

Brown University Center to Advance Predictive Biology. His research has been continuously funded by the National Institute of Environmental Health Sciences since 1985 and he has received several awards including a Burroughs Wellcome Toxicology Scholar Award (1994-1999), and the Lifetime Achievement Award (2015) from the Reproductive and Developmental Toxicology Specialty Section of the Society of Toxicology. He served as member (2005-2007) of the NAS committee that produced the report "Toxicity Testing in the 21st Century: A Vision and a Strategy." Since 2012, he has been a member, Chair, and Co-Chair of the NAS committee Emerging Science for Environmental Health Decision Making.

Patience Browne currently leads the Hazard Assessment and Pesticide Programmes of the Environment, Health, and Safety Division of the Organisation for Economic Cooperation and Development (OECD) in Paris, France. She began at OECD in 2016 as a Research and Policy Analyst in the Test Guidelines Programme, where she contributed to the review, application, and validation of alternative methods in an international regulatory context. Dr. Browne coordinated the development of the OECD Guideline on Defined Approaches for Skin Sensitisation that replaces the need for mouse data in a regulatory context. In her current role, she oversees the work of the OECD IATA Case Studies Project, which provides research and regulatory scientists an opportunity to share experiences on the use of new approach methods for regulatory decision-making. Prior to joining the OECD, Dr. Browne was a Senior Scientist in the United States Environmental Protection Agency, Office of Science Coordination and Policy and helped to foster the use of high-throughput in vitro screening data for identifying endocrine active compounds.

Dr. Browne completed a Doctoral degree in Molecular Cellular and Integrated Physiology at University of California, Davis in 2004 and a Masters in Marine Biology and California State University in 1995. She held postdoctoral research positions in Molecular Endocrinology in the Department of Population Health and Reproduction at UC Davis and in Neuroendocrinology in the Department of Obstetrics and Gynecology at University of Washington. Throughout her career, Dr. Browne has continued to be interested in identifying non-invasive and alternatives to animal research methods.

Holly Davies is a Senior Toxicologist at the Washington State Department of Health with expertise in human health and ecological risk assessment, alternatives assessment, in vitro assay development, and chemical policy. Her work has focused on evaluating uses of toxic chemicals, including chemicals of emerging concern and persistent, bioaccumulative, and toxic chemicals (PBTs), and identifying actions needed to protect human health and the environment. Dr. Davies is a member of the Association for the Advancement of Alternatives Assessment and actively participates in the Children's Environmental Health Working Group within the Washington Chapter of the Collaborative on Health and the Environment. She has been a member of EPA's Chemical Safety Advisory Committee (CSAC) and Science Advisory Committee on Chemicals (SACC) and served on EPA's Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel on New Approach Methodologies. Her postdoctoral research is on mammalian reproduction and development, transcription factors, and genomics.

Corie A. Ellison received a Ph.D. degree in Pharmacology and Toxicology from the School of Medicine and Biomedical Sciences at The State University of New York at Buffalo. After graduation, he joined The Procter & Gamble Company as a Toxicologist in the Global Product

Stewardship organization. Currently, Dr. Ellison is a Group Scientist in the Central Product Safety division where he leads several research projects as well as the human safety program for multiple technologies in P&G's global cosmetic businesses. He has expertise in pharmacokinetics, i.e., Absorption, Distribution, Metabolism and Excretion (ADME), and uses this knowledge to develop innovative approaches using physiologically-based pharmacokinetic (PBPK) models to predict systemic exposure and refine/advance the quantitative risk assessment for consumer products. Additionally, Dr. Ellison has authored multiple publications showing the utility of new approach methods in an animal free human safety assessment.

Marie C. Fortin is Associate Director of Toxicology at Jazz Pharmaceuticals. In this role, she designs nonclinical safety drug development programs to meet regulatory expectations and support adequate safety evaluation while optimizing consideration of the 3Rs. She develops in vitro and in vivo study protocols and oversees safety pharmacology and investigative and regulatory toxicology (non-GLP and GLP) studies. In addition, she contributes critical input on other aspects of drug development such as pharmacology and pharmacokinetics, evaluation of the risk-benefit ratio, and determination of first-in-human dose. As toxicology lead on multiple cross-functional teams, she authors the relevant sections or regulatory submissions and represents the toxicology function in regulatory interactions. In addition, Dr. Fortin is Adjunct Professor in the Department of Pharmacology and Toxicology at the Ernest Mario School of Pharmacy at Rutgers University where she mentors graduate students, teaches in the Joint Program in Toxicology, and co-directs the graduate risk assessment course. In her previous industry and consulting roles, she authored or oversaw the development of multiple human health risk assessments for pesticides, metals, pharmaceuticals, cosmetic ingredients, and chemicals for all routes of exposure (oral, inhalation, dermal, parenteral) and managed an in vitro safety testing laboratory focused on organotypic models. Dr. Fortin is a Board-certified and European-registered toxicologist who is particularly interested in the integration of new approaches to support the safety evaluation of pharmaceuticals and their translational application to the risk assessment of chemicals. She has received both her M.Sc. in Neurosciences (2004) and Ph.D. in Public Health - Toxicology (2009) from the Université de Montréal and completed a Postdoctoral Fellowship at the University of Medicine and Dentistry of New Jersey (now part of Rutgers University) (2011).

Nicole C. Kleinstreuer focuses her research on mathematical and computational modeling of biological systems and their susceptibility to perturbations that result in adverse health outcomes. Dr. Kleinstreuer received B.S. degree in mathematics and biomedical engineering from the University of North Carolina at Chapel Hill (UNC-CH), a Ph.D. in bioengineering from the University of Canterbury, and completed her postdoctoral training at the U.S. EPA National Center for Computational Toxicology. Prior to joining the National Institute of Environmental Health Sciences (NIEHS), Dr. Kleinstreuer worked for Integrated Laboratory Systems, Inc., as director of the ILS computational toxicology group. She serves as the acting Director of the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), leading domestic and international efforts to develop novel testing and analysis strategies that provide more rapid, mechanistic, and human-relevant predictions of potential environmental chemical hazards. Dr. Kleinstreuer has a secondary appointment in the NIEHS Division of Intramural Research Biostatistics and Computational Biology Branch, and adjunct faculty positions in the Yale School of Public Health and the Eshelman School of Pharmacy at UNC-CH. She is the recipient of numerous prestigious awards including the 2008 B.H. Neumann Prize from the

Australian Mathematical Society, the 2012 Impact Award from the U.S. EPA's Office of Research and Development, the 2016 F. Clarke Fraser New Investigator Award from the Teratology Society and 2016 Young Researcher Americas Lush Prize, and the 2019 Society of Toxicology Achievement Award.

Nancy E. Lane *(NAM)* is an Endowed Professor of Medicine, Rheumatology, and Aging Research, Director for the Center for Musculoskeletal Health, Director of the K12 NIH Building Interdisciplinary Research Careers in Women's Health (BIRCWH), and Principal Investigator of the NIH funded Program on Sex Differences in Musculoskeletal Diseases Across the Lifespan at the University of California at Davis School of Medicine where she has served for the past 12 years. Dr. Lane is an internationally recognized scientist in the fields of both osteoporosis and osteoarthritis. As a translational scientist, she has significant experience in pre-clinical toxicity models for studies of human disease. She has supervised pre-clinical toxicology studies, including for FDA INDs, and has extensive experience in both validation and interpretation of the results. Her translational research team has been instrumental in defining the role of glucocorticoids in bone fragility including their effects on cell stress and vulnerable cell populations including osteocytes. As a faculty member at the University of California at San Francisco, she pioneered a seminal clinical trial to demonstrate that daily injections of the hormone PTH could reverse glucocorticoid induced osteoporosis, and performed research on the rate of recovery of immobilization induced bone loss. After transitioning to U.C. Davis, she a developed a novel compound to direct stem cells to the bone to grow new bone and treat osteoporosis. In addition she has uncovered novel genetic variations that predispose individuals to osteoarthritis and has studied novel treatments for osteoarthritis. Her research accomplishments have been recognized by the UC Davis School of Medicine Dean's Team Science Award (2012), the American College of Rheumatology for the Oscar Gluck Memorial Lecture for outstanding work in Osteoporosis (2011), the Remodeling in Bone "RIB Award" by the International Society of Bone and Mineral Research (2012), her election as a Master of the American College of Physicians (2012) and David Trentham Lectureship and Women in Medicine Lectureship at Harvard Medical School (2013).. She is also the recipient of the Bone and Joint Decade Outstanding Achievement Award for developing a mentoring program in grant writing (2009). Dr. Lane was President of the Board of the United States Bone and Joint Decade (2006-2008), co-led the International Bone and Joint Decade Conference in Washington DC (2010), was elected and served on the council of the American Society of Bone and Mineral Research (2010-2013), and the Orthopedic Research Society (2003-2005). Dr. Lane is on the editorial boards of Nature Reviews Rheumatology, Rheumatology (Associate Editor), Seminars in Arthritis and Rheumatism (Associate Editor), Co-editor Arthritis and Rheumatism (2005-2010), Journal of Rheumatology. Dr. Lane was elected to the National Academy of Medicine in 2013.

Heather B. Patisaul is the Associate Dean for Research in the College of Sciences and a professor in the Department of Biological Sciences at North Carolina State University. She explores the mechanisms by which endocrine disrupting compounds (EDCs) alter neuroendocrine pathways in the brain related to sex specific physiology and behavior. She is specifically interested in phytoestrogens, flame retardants, and BPA (Bisphenol A). Dr. Patisaul is a NIEHS ONES Award recipient (2007) and has participated on several national and international expert panels and workshops related to health effects associated with soy, BPA, and other endocrine disruptors. She chaired the 2016 Gordon Research Conference on Environmental Endocrine Disruptors, and has

co-edited several special issues on endocrine disruptors, brain and behavior. In addition, Dr. Patisaul served on four previous National Academies committees: the Committee reviewing EPA's ORD Staff Handbook for Developing IRIS Assessments (or IRIS Handbook), the Workshop Planning Committee on Understanding the Paradigm Change at the Interface of Emerging Sources of Environmental Health Data and Decision Making, Committee on Incorporating 21st Century Science in Risk-Based Evaluations, and Committee to Review EPA's Draft Paper, State of the Science on Nonmonotonic Dose Response (NMDR). She received a PhD in Population Biology, Ecology & Evolution from Emory University with a research focus on comparative neuroendocrinology.

Elijah Joel Petersen completed his PhD at the University of Michigan in Environmental Engineering in 2007. Then, he completed postdocs at the University of Joensuu (Finland) on a Fulbright scholarship and then the University of Michigan before joining NIST as a National Research Council postdoctoral fellow. He became a staff scientist at NIST in 2010 and works in the Cell Systems Science group in the Biosystems and Biomaterials division. His research currently focuses on the development of robust, reproducible in vitro test methods. He is an associate editor for Nanotoxicology and Nanoimpact and on the editorial board of Environmental Pollution, Nanomaterials, and Environmental Toxicology and Chemistry. He recently was honored with the 2020 Chemical Research in Toxicology Young Investigator Award and the Presidential Early Career Award for Scientists and Engineers (PECASE) in 2019. He is the chair of the ICCVAM nanomaterials workgroup and a co-chair of the validation workgroup.

Kristi Pullen Fedinick is the Chief Science Officer of the Natural Resources Defense Council. She also holds a part-time faculty appointment in the Department of Environmental and Occupational Health of the Milken Institute School of Public Health at The George Washington University.

Dr. Pullen Fedinick's work focuses on the use of scientific tools and methods to inform and shape policies and narratives centered on chemical exposures in disproportionately burdened communities. She utilizes geospatial and statistical tools to assess the geographic distribution of chemicals in the environment, with a particular emphasis on drinking water and cumulative exposures. Her work also includes the evaluation of the use of high-throughput technologies, predictive toxicology, and computational approaches in chemical evaluations.

Dr. Pullen Fedinick has served on several committees of the National Academies, including the Committee on the Application of Systematic Review in TSCA Risk Evaluations, the Committee on Incorporating 21st Century Science in Risk-Based Evaluations, and the Standing Committee for Emerging Science for Environmental Health Decisions. She has also participated in multiple government, academic, and professional society panels and committees, including a recent appointment to the EPA Science Advisory Board.

Dr. Pullen Fedinick holds a Bachelor's degree in Biochemistry and Molecular Biology from the University of Maryland Baltimore County and a Ph.D. in Molecular and Cell Biology with a focus on Biochemistry, Biophysics, and Structural Biology from the University of California, Berkeley. She was a Robert Wood Johnson Foundation Health and Society Scholar at the Harvard T. H. Chan School of Public Health.

Martyn T. Smith is Professor of Toxicology and Kaiser Professor of Cancer Epidemiology in the Division of Environmental Health Sciences in the School of Public Health at the University of California Berkeley. He received his Ph.D. in Biochemistry from St. Bartholomew's Hospital in London and did Post-Doctoral training in toxicology at the Karolinska Institute in Stockholm. Dr. Smith is a laboratory scientist with expertise in molecular epidemiology, toxicology and genomics, and his research is aimed at finding the causes of chronic diseases, including cancer and diabetes. He currently teaches Toxicology and Health Risk Assessment and mentors graduate students and postdoctoral scholars in the Molecular Toxicology, Epidemiology and Environmental Health Science programs. Dr. Smith is a Fellow of the American Association for the Advancement of Science. He received the 2010 Children's Environmental Health Network Award, became an Elected Fellow of the Collegium Ramazzini in 2012, and received the Alexander Hollaender Award from the Environmental Mutagenesis and Genomics Society in 2014. Since its inception in 1987, Smith has directed the Superfund Research Program (SRP) Center at the University of California, Berkeley (UC Berkeley). This program combines basic research, engineering, population studies, training, and community engagement to understand cumulative impacts from multiple environmental stressors. Smith is best known for his work on benzene toxicity, the exposome concept and the key characteristics framework, which helps risk assessors better identify, organize, and summarize the potential health risks of different chemicals.

Robyn L. Tanguay is currently a University Distinguished Professor at Oregon State University in the Department of Environmental and Molecular Toxicology. She started her Academic career at the University of Colorado in the School of Pharmacy in 1999. She is a Molecular Toxicologist that primarily uses the zebrafish model to answer toxicological, developmental, and behavioral questions relevant to human health. She received her BA in Biology from California State University-San Bernardino in 1988, her PhD in Biochemistry from the University of California-Riverside in 1995, and postdoctoral training in Developmental Toxicology from the University of Wisconsin-Madison 1995-1999. Over the past several years, she has pioneered the use of zebrafish as a systems toxicology model. She has authored approximately 300 manuscripts and book chapters across disciplines, many focused on advancing zebrafish for environmental health sciences research. She also serves on numerous academic, federal and commercial advisory boards and as an editor for several scientific journals. She previously served on the National Academy of Sciences Committee on Incorporating 21st Century Science into Risk-Based Evaluations (2015-2016).

Christopher Vulpe is a Professor at the University of Florida, Gainesville in the Center for Environmental and Human Toxicology. Dr. Vulpe received his M.D. (1996), PhD (1994) in Genetics from the University of California, San Francisco. Dr. Vulpe's group uses functional, genomic, and genetic approaches to provide insight into mechanisms of toxicity in diverse model systems including human models such as human cell culture, organoids, and rodents, as well as ecologically relevant organisms such as Daphnia magna. Most recently, his laboratory is utilizing genome wide and targeted CRISPR screens to understand the mechanisms of toxicity of environmental chemicals. Dr. Vulpe is an author or co-author on >150 papers in peer reviewed journals and books. He recently participated in the NAS Emerging Genome Editing Tools to Advance Environmental Health Research Workshop.

Tracey J. Woodruff is the Alison S. Carlson Endowed Professor in the Department of Obstetrics, Gynecology, and Reproductive Sciences at University of California, San Francisco and the Director of the Program on Reproductive Health and the Environment. She is a recognized expert on environmental chemical exposures and impacts on health and health equity, with a focus on pregnancy, infancy and childhood. She has expertise in environmental exposures and epidemiology, hazard and risk assessment, and in silico/in vitro approaches to evaluating environmental chemical influences on health. She previously a senior scientist and policy advisor for the U.S. EPA's Office of Policy.

Joseph C. Wu *(NAM)* is Director of Stanford Cardiovascular Institute and Simon H. Stertzer, MD, Professor of Medicine and Radiology at Stanford University. Dr. Wu received his MD from Yale University and PhD (Molecular & Medical Pharmacology) at UCLA. He is board certified in cardiology. His lab works on cardiovascular genomics and induced pluripotent stem cells (iPSCs). The main goals are to (i) understand basic disease mechanisms, (ii) accelerate drug discovery and screening, (iii) develop "clinical trial in a dish" concept, and (iv) implement precision medicine for patients. Dr. Wu has published >400 manuscripts with H-index of 108 on Google scholar. He is listed as top 1% of highly cited researchers by Web of Science (2018, 2019, 2020). He serves on the FDA Cellular, Tissue, and Gene Therapies Advisory Committee. Dr. Wu is an elected member of American Institute for Medical and Biological Engineering (AIMBE), American Association for the Advancement of Science (AAAS), American Association of Physicians (AAP), and National Academy of Medicine (NAM).

National Academies Committee on Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

Workshop 2
Thursday, May 12, 2022

Panelists Bios

Session I: Mixtures

Carl-Gustaf Bornehag, Karlstad University

Carl-Gustaf Bornehag is Professor and head of Public Health Sciences at department of health at Karlstad University, Sweden. He is adjunct professor at Icahn School of Medicine at Mount Sinai, New York, USA. His research focus is on early life exposure for environmental factors such as endocrine disrupting chemicals and the importance for children´s health and development. He is principal investigator of two major epidemiological studies in Sweden, the Dampness in Buildings and Health (DBH) study (following more than 10,000 children from childhood up in adulthood) and the SELMAstudy (following more than 2,000 mother-child pairs from early pregnancy, over birth and up in school age). Bornehag is co-PI for EDC-MixRisk, a project recently awarded by Horizon 2020 with a 6.2 million Euro grant, a study integrating epidemiological studies with experimental cell- and animal models in order to learn about how mixtures of endocrine disrupters impact on children´s health development in three domains (sexual development, neurodevelopment and metabolism), which biological mechanisms that may be in action, and finally by the use of such data improve risk assessment of endocrine disrupting chemicals. Bornehag is further involved in three major Horizon 2020 project (ENDpoiNTs, ATHENA, and INQUIRE), two US NIH projects (PRIME, A-PED) and he is PI for RACH-Mix, a project focusing on risk assessment of chemicals funded by FORMAS.

Beate Escher, Helmholtz Centre for Environmental Research

Beate Escher is internationally recognized for her work on chemical pollution in the environment. She pioneered the field of water quality assessment by addressing complex mixtures of chemical pollutants using in vitro bioassays. Beate Escher obtained her PhD 1995 and her Habilitation in 2002 at the Swiss Federal Institute of Technology ETH, Zürich, Switzerland and is head of the Department of Cell Toxicology at the Helmholtz Centre for Environmental Research in Leipzig, Germany, and professor at the Eberhard Karls University Tübingen, Germany. She is also lecturer at ETHZ, Switzerland, holds an honorary professorship at the University of Queensland and an adjunct professorship at Griffith University, Australia. She was Associate Editor with Environmental Science and Technology from 2012 to 2020 and is member of the Board of Reviewing Editors at Science. In 2020, she was among the “Highly Cited Researcher”. From 2011 to 2014 she held an Australian Research Council Future Fellowship. In 2013 she won the Australian

Water Association AWA National Research Innovation Award for her work on cell-based bioassays in water quality assessment.

Beate Escher has been working on developing scientifically sound assessment tools and methodologies for risk assessment of mixtures of chemicals in the environment and in people. Escher's expertise includes mode-of-action based effect assessment, and methods for hazard screening of organic micropollutants including pharmaceuticals, pesticides and persistent organic pollutants, environmental transformation products, and mixtures. She is working on unbiased extraction methods to capture the entire exposome with chemical analytical and effect-based tools. She works on improving dosing and interpretation of high-throughput in vitro bioassays and runs the robotic bioassay platform CITEPro at UFZ (www.ufz.de/citepro).

Chris Gennings, Icahn School of Medicine at Mount Sinai

Dr. Chris Gennings is professor and Director of the Biostatistics Division within the Department of Environmental Medicine and Public Health at the Icahn School of Medicine at Mount Sinai in New York. She serves as the Director for the Statistical Services and Analysis Resource of the Human Health Exposure Assessment Resource (HHEAR) Data Center and the Director of the Biostatistics and Bioinformatics Core of the of the Mount Sinai P30 Center, Transdisciplinary Center on Early Environmental Exposures. Her research interests focus on design and analysis methodologies for studies of complex mixtures, with recent focus on the development and extensions of Weighted Quantile Sum (WQS) regression, methods for risk assessment of environmental mixtures, development of a nutrition index called My Nutrition Index with a web-based nutrition app, and using g computation methods with indices such as the My Nutrition Index and a WQS index of environmental exposures to address the counterfactual question of "what if" exposures were reduced and dietary nutrition was improved.

Cynthia Rider, National Institute of Environmental Health Sciences

Cynthia Rider, Ph.D., is a toxicologist in the Systems Toxicology Branch of the National Institute of Environmental Health Sciences (NIEHS). As a study scientist, she designs and evaluates results from toxicological studies of chemicals selected for investigation by the National Toxicology Program. She is particularly interested in developing and refining methods for evaluating the toxicity of mixtures to inform risk assessment. Currently, she is the project leader for polycyclic aromatic compounds, which are being used as a case study to evaluate the joint action of chemicals with component-based approaches (e.g., dose addition models). She is also leading an effort to inform the safety evaluation of complex mixtures. Toward this goal, she is using botanical dietary supplements, such as Ginkgo biloba extract, to develop methods for determining sufficient similarity of complex mixtures. She currently serves as co-chair of the Botanical Safety Consortium, a public-private partnership aimed at developing a framework for using new approach methodologies to evaluate botanical dietary supplement safety. Dr. Rider received her B.S. from Tulane University, New Orleans, LA in Environmental Studies and Biology and her Ph.D. from North Carolina State University, Raleigh, NC in Environmental Toxicology. She completed post doctoral training in the Reproductive Toxicology Branch of the National Health and Environmental Effects Research Laboratory, U. S. Environmental Protection Agency and the Nicholas School of the Environment at Duke University. She joined the NIEHS in 2010.

Tom Webster, Boston University School of Public Health

Tom Webster has several main research areas: 1) exposure routes and health hazards of chemicals used in consumer products, especially flame retardants, plasticizers and emerging compounds, as

well as perfluoralkyl compounds (PFCs) that are also found in water; 2) health impacts of exposure to mixtures of chemicals, with applications in toxicology and epidemiology; 3) endocrine disruption; 4) methodological aspects of environmental epidemiology, particularly causal inference, ecologic bias, the use of combinations of individual and group level data, and disease mapping and clusters. Like the rest of my department, I am very interested in the community context of environmental health.

Dr. Webster served on the National Research Council's Subcommittee on Fluoride in Drinking Water and the Institute of Medicine's Committee on Making Best Use of the Agent Orange Exposure Reconstruction Model.

The work of Dr. Webster and his colleagues and students has been featured in Environmental Health Perspectives ("PFCs and Cholesterol: A Sticky Connection," "Unwelcome Guest: PBDEs in Indoor Dust"), Bostonia Magazine ("Trouble at Home," "You Are What You Eat, Including Your Sofa"), Discovery News ("Handwashing Cuts Flame Retardant Exposure") and the National Public Radio show "Living on Earth," among other places.

Session II: Developmental Neurotoxicity

Elaine Faustman, University of Washington

Elaine M. Faustman is Professor and Director of the Institute of Risk Analysis and Risk Communication, School of Public Health at the University of Washington, Seattle. She is a member of the Washington Academy of Sciences. She has recently completed her service as co-chair of the steering committee of the International Science Council World Data Systems. Dr. Faustman's research expertise is on identifying molecular mechanisms of developmental, reproductive, and neuro toxicants; characterizing in vitro techniques for toxicology assessment; and developing biological based dose-response models. Recent research efforts include her leadership as PI for the EPA Predictive Toxicology Center and her work with the National Institute of Child Health and Human Development's Health Measurement Network Environmental Domain Working Group and Lifecourse Health Sciences Working Group. She is an elected fellow of the American Association for the Advancement of Science and the Society for Risk Analysis. She has served as a member of the USEPA Science Advisory Board, NIEHS National Advisory Environmental Health Sciences Council, and National Toxicology Program's Board of Scientific Counselors. In addition, she has served as the Secretary General for the International Union for Toxicology. Dr. Faustman has more than 200 peer reviewed research publications and reports. She earned a B.A. in Chemistry and Zoology from Hope College, and PhD in Biochemical Toxicology from Michigan State University. Her service on National Academies committees includes chair of the Committee for Developmental Toxicology.

Helena Hogberg, National Institute of Environmental Health Sciences

Helena Hogberg PhD recently joined the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) within the Division of the NTP, National Institute of Environmental Health Sciences (NIEHS) where she is conducting research drawing on her broad expertise in applying in vitro methods to assessing developmental neurotoxicity (DNT) potential of chemicals.

Previously she was the Deputy Director of the Center for Alternatives to Animal Testing (CAAT) within the Johns Hopkins University Bloomberg School for Public Health. She received her Ph.D. her in toxicology from Stockholm University but performed her research at the European Centre for the Validation of Alternative Methods (ECVAM) in Ispra, Italy.

She has been advising a number of governmental entities and serves on the expert group for DNT including OECD, U.S. EPA, and the European Commission-funded Horizon 2020 grant ENDpoiNT

Tim Shafer, Environmental Protection Agency

Dr Tim Shafer is a Research Toxicologist and Principal Investigator in the Biomolecular and Computational Toxicology Division in the Center for Computational Toxicology and Exposure in the Office of Research and Development at the U.S. Environmental Protection Agency. Tim earned his PhD from the Department of Pharmacology and Toxicology at Michigan State University.

Dr. Shafer's research career has focused on examining mechanisms of neurotoxicant effects mediated through disruption of ion channels and cellular neurophysiology. This has included examination of the actions of heavy metals, PCBs, herbicides and pesticides on neuronal function using a variety of approaches including patch-clamp recordings, oocyte recordings and imaging experiments using ion- or voltage-sensitive dyes.

For the past decade, Tim's work is directed towards development of new alternative methods for assessment of neurotoxicity and developmental neurotoxicity hazards of chemicals. He has published over 100 peer-reviewed journal articles, book chapters and reports; has received 8 Scientific and Technological Achievements Awards and Bronze and Gold medals for outstanding service to the Agency.

Dr Shafer has also served as/on:

Acting Assistant Laboratory Director for Human Health Research
Acting Director of the Integrated Systems Toxicology Division.
ALTOX3/NAL study section at NIH
Society of Toxicology Program Committee.
Secretary/Treasurer of the Society of Toxicology's Neurotoxicology Specialty Section
President of the International Neurotoxicology Association.
Associate Editor for the journal NeuroToxicology
Editorial Board of Toxicology and Applied Pharmacology.

Jason Stein, University of North Carolina, Chapel Hill

Jason Stein is an Associate Professor in the Department of Genetics and the UNC Neuroscience Center at the University of North Carolina at Chapel Hill. His lab explores how genetic variation influences brain structure, function, and risk for neuropsychiatric illness. He co-founded and co-led the first international consortium to discover the specific genetic variants affecting gross brain structure in the living human brain measured via MRI: the Enhancing Neuroimaging Genetics through Meta-analysis (ENIGMA) consortium. His lab also models the effect of genetic variation in human neural progenitor cells and iPSC-derived cortical organoids. Finally, his lab has also developed tools to analyze 3D cellular resolution brain images derived from tissue clearing and light sheet microscopy. Jason received a BA from Northwestern University in the Integrated Science Program and then pursued post-baccalaureate work at the intramural program of the

National Institute of Mental Health. He received his PhD in Neuroscience and completed his postdoc at the University of California, Los Angeles.

Shirlee Tan, Senior Toxicologist for Public Health, Seattle and King County

Shirlee Tan is the Senior Toxicologist for the Seattle & King County Public Health Department where she serves as a technical advisor for the department on issues related to chemical exposures, impacts and policies. She works directly with communities and individuals to address ways to reduce chemical exposures and effects. Dr. Tan serves on numerous advisory groups for WA State, focused on chemical policy and regulation around chemical use, toxics cleanup, and environmental justice. She is a member of EPA's Children's Health Protection Advisory Committee (CHPAC). Dr. Tan previously worked for the Organization for Economic Cooperation and Development (OECD) and the US EPA on the development of regulatory assays for endocrine disrupting chemicals, with a particular focus on thyroid and in vitro assays. She also worked for the Smithsonian Institution's National Zoological Park on pesticide misuse in Southeast Asia. She also consults for the Endocrine Society on science policy issues related to endocrine disrupting chemicals. Dr. Tan holds a PhD in cell and molecular biology from the University of San Diego, CA and conducted her postdoctoral research studying dopaminergic receptors and neurodegenerative pathways.

Session III: Estrogenicity

Richard Judson, Environmental Protection Agency

Dr. Judson is with the EPA Center for Computational Toxicology and Exposure where he is developing computer models, databases and web-based dashboards to help predict toxicological effects of environmental chemicals. Current focus areas for his team are prediction of endocrine effects of chemicals, modeling the effects of PFAS compounds using in vitro methods and development of computational methods to use high-throughput transcriptomics data. He has published in areas including computational biology and chemistry, bioinformatics, genomics, human genetics, toxicology and applied mathematics. Dr. Judson has a BA in Chemistry and Chemical Physics from Rice University and an MA and PhD in Chemistry from Princeton University.

Paul Mermelstein, University of Minnesota

Paul G. Mermelstein is the Associate Head and Robert and Elaine Larson Professor of Neuroscience at the University of Minnesota. He received his Ph.D. with Jill B. Becker at the University of Michigan and trained as a postdoctoral fellow with D. James Surmeier followed by Richard W. Tsien. For over three decades, his research interests have included the study of novel actions of estrogen signaling within the central nervous system. Utilizing approaches from cell assays to behavior, his work has examined sex differences in estrogen action, coordination of multiple, and sometimes seemingly opposing processes of estradiol signaling within and across specific brain regions, and functional consequences of perturbing estrous cycle function. Recent activities include being Chairperson for the Neurobiology of Motivated Behaviors NIH study section, as well as being the Program Director for three separate NIH supported training programs focused on the mentoring undergraduates, graduate students, postdoctoral fellows, and early-stage faculty on careers in academic science.

Ruthann Rudel, Silent Spring Institute

Ruthann Rudel is the director of research at Silent Spring Institute, where she leads exposure and toxicology research programs focusing on hormonally active chemicals and biological mechanisms by which chemicals may influence breast cancer. Her recent study-- recognized by NIEHS as one of the most influential papers of 2021-- identified 296 potential breast carcinogens based on their ability to increase estradiol and progesterone synthesis in the H295R in vitro steroidogenesis assay. In 2007, she published the first comprehensive list of chemicals that induce mammary gland tumors in rodent assays. Her innovations in "breast cancer toxicology" include reviews of methodological issues in toxicity and risk assessment for endocrine disruptors and carcinogens; and analyses of chemicals that cause mammary tumors, alter mammary gland development, or activate biological pathways in breast cancer. In fact, in 1997 she published an article closely related to the topic of this meeting, entitled "Predicting Health Effects of Exposures to Compounds with Estrogenic Activity: Methodological Issues." She has published reviews of biomonitoring methods for breast cancer-related chemicals and evaluated the consistency of breast cancer epidemiological studies with mechanistic findings from experimental studies. Her research in exposure science was the first to measure large numbers of endocrine disruptors in U.S. homes, and established consumer products as a major source of exposure. She served on EPA's Scientific Advisory Committee on Chemicals, the National Academy of Sciences panel Unraveling Low Dose Toxicity, and the U.S. National Toxicology Program Board of Scientific Counselors. She is an adjunct Research Associate in the Brown University School of Medicine and a Visiting Scholar at Northeastern University. Rudel earned her B.A. in chemistry and neuroscience from Oberlin College, and an M.S. in environmental management and policy from Tufts. Silent Spring Institute is dedicated to scientific research on the environment and women's health with a goal of breast cancer prevention.

Laura Vandenberg, UMass Amherst

Dr. Laura Vandenberg is a Professor in the Department of Environmental Health Sciences in the University of Massachusetts Amherst, and Associate Dean of Undergraduate Academic Affairs in the School of Public Health and Health Sciences. Trained as a developmental biologist and endocrinologist, Dr. Vandenberg's laboratory research examines the effects of endocrine disrupting chemicals on function and disease of the mammary gland and other hormone-sensitive outcomes. Outside of the lab, her research critically evaluates issues that affect risk and hazard assessments for endocrine disrupting chemicals including low dose effects, non-monotonic dose responses, and methods used to evaluate hazard. Dr. Vandenberg is an author on more than 100 peer reviewed papers and seventeen book chapters.

Fred Wright, North Carolina State University

Fred Wright is Goodnight Innovation Distinguished Professor of Statistics and Biological Sciences and Director of the Bioinformatics Research Center at North Carolina State University. He is a statistical geneticist with wide-ranging research interests, including genomics, bioinformatics, toxicogenomics, and the statistical principles underlying high-dimensional data analysis. Dr. Wright has been principal investigator on numerous grants with activities ranging from development of new methods of gene mapping to expression-quantitative trait mapping for multiple tissues. He has been principal investigator and co-PI US Environmental Protection Agency–funded STAR Centers to apply genomics principles to long-standing problems in toxicology, and Director of a T32 training grant in Environmental Bioinformatics. He is an elected fellow of the American Statistical Association and of the Delta Omega Honor Society for Public

Health. Dr. Wright received his PhD in Statistics from the University of Chicago. He previously served on the National Academy of Sciences Committee on Incorporating 21st Century Science into Risk-Based Evaluations (2015-2016).