Division on Earth & Life Studies
Board on Environmental Studies and Toxicology

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 Workshop1 | Thursday, December 9, 2021 | 10:00am-3:00pm 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 1
Thursday, December 9, 2021
10 AM- 3 PM EST

MEETING OVERVIEW

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.

This one-day virtual workshop will address critical questions: How are traditional toxicity studies used in informing chemical safety decisions? What do we know about the variability and concordance of traditional mammalian toxicity studies? What are the needs and expectations of different stakeholders? Experts from academia, industry, the government, and other organizations will explore and discuss these issues and current scientific knowledge with regard to traditional toxicity studies.

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

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

Session I: How are traditional mammalian toxicity studies used in informing chemical safety decisions?

10:25 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderators: Weihsueh Chiu and Tracey Woodruff

Risk assessment introduction, contexts, and challenges
Thomas Burke, Johns Hopkins University

Hazard identification of endocrine agents
Sharon Munn, Joint Research Centre

Hazard identification and dose-response of carcinogens
Vincent Cogliano, California Environmental Protection Agency

Insights from recent NASEM committees: Predicting acute toxicity and a class approach to organohalogens
David Dorman, North Carolina State University

Session II: What do we know about the variability of traditional mammalian toxicity studies with different levels of complexity?

11:25 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderators: Nicole Kleinstreuer and Holly Davies

Variability within the same traditional mammalian toxicity studies
David Allen, Integrated Laboratory Systems, LLC

Variability among traditional mammalian toxicity studies of the same and different design
Katie Paul Friedman, US Environmental Protection Agency

Variability within and across species in traditional mammalian toxicity studies
Suzanne Fenton, National Toxicology Program

Systematic reviews and meta-analyses
Malcolm MacLeod, University of Edinburgh

Break

Session III: What do we know about the concordance of traditional mammalian toxicity studies with humans?

12:40 **Summary of Pre-recorded Presentations, Panel Discussion, and Committee Q&A**
Moderators: Nancy Lane and Patience Browne

Concordance of traditional mammalian toxicity studies with human clinical outcomes
Thomas Hartung, Johns Hopkins University

Concordance between animal and human toxicology
Joshua Robinson, University of California, San Francisco

Application of systematic review methods in low-dose endocrine toxicity
David Dorman, North Carolina State University

Session IV: Panel Reflections

1:40 **Panel Reflections and Q&A from Committee**
Moderators: Kristi Pullen Fedinick & Corie Ellison

- **David Dorman,** North Carolina State University
- **Helen Goeden,** Minnesota Department of Health

- **Rashmi Joglekar,** Earth Justice
- **Sharon Munn,** Joint Research Centre
- **Reza Rasoulpour,** Corteva

Public Comment Period

2:40 **Advance registration required and comment time is limited to 2 minutes.**

3:00 **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

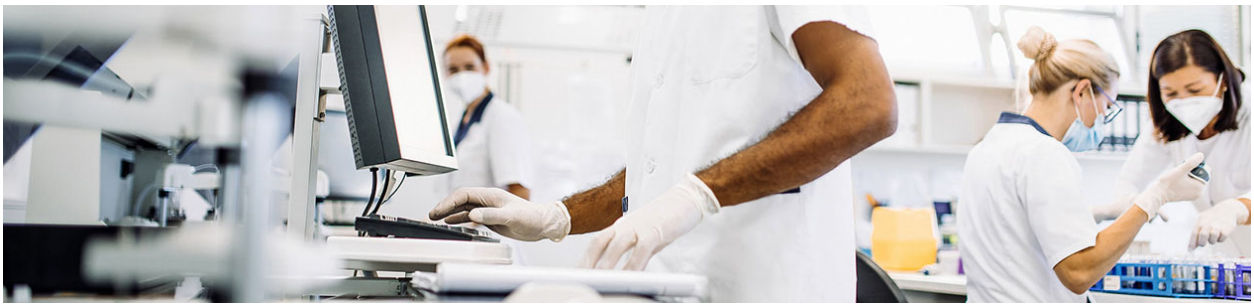
NASEM *Staff*

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 1
Thursday, December 9, 2021

Panelists Bios

Session I: How are traditional mammalian toxicity studies used in informing chemical safety decisions?

Thomas A. Burke, **PhD, MPH**, Johns Hopkins University Bloomberg School of Public Health

Thomas A. Burke, is the Jacob I and Irene B. Fabrikant Professor and Chair in Health Risk and Society at Johns Hopkins University Bloomberg School of Public Health, Department of Health Policy and Management. He holds joint appointments in the Department of Environmental Health Sciences and the School of Medicine Department of Oncology. He is also Director of the Johns Hopkins Risk Sciences and Public Policy Institute. Dr. Burke was nominated by President Barack Obama to serve as EPA Assistant Administrator for the Office of Research and Development. From January 2015 until January 2017 Dr. Burke was the EPA Science Advisor and Deputy Assistant Administrator for Research and Development. His research interests include environmental epidemiology and surveillance, evaluation of population exposures to environmental pollutants, assessment and communication of environmental risks, and application of epidemiology and health risk assessment to public policy. Before joining the University faculty, Dr. Burke was Deputy Commissioner of Health for the State of New Jersey and Director of Science and Research for the New Jersey Department of Environmental Protection. In New Jersey, he directed initiatives that influenced the development of national programs, such as Superfund, the Safe Drinking Water Act, and the Toxics Release Inventory. Dr. Burke served as a member of the National Academy of Sciences Board on Environmental Studies and Toxicology. He was Chair of the National Academy of Sciences Committee on Improving Risk Analysis that produced the report Science and Decisions, and chaired the NAS Committee on Human Biomonitoring for Environmental Toxicants. He is a Fellow of the Society for Risk Analysis and a lifetime National Associate of the National Academies. Dr. Burke received his BS from St. Peter's College, his MPH from the University of Texas and his PhD in epidemiology from the University of Pennsylvania.

Sharon Munn, Joint Research Centre

Sharon Munn studied Applied Biology at Cardiff University in the UK. Her professional experience is in the field of human toxicology and risk assessment. She is currently working for the European Commission's Joint Research Centre (JRC), which provides science-based advice to the European Commission in support of policy and regulatory decision-making. She has spent the last 12 years within the Chemicals Safety and Alternative methods unit working on new approaches to risk assessment with the aim of placing less reliance on in vivo animal testing. Her particular focus has

been on the identification of endocrine disrupting chemicals, as well as on the utility of the Adverse Outcome Pathway framework for the better application of mechanistic knowledge in chemical hazard assessment. She supported the development of the recently published EFSA/ECHA guidance on implementation of the criteria for the identification of endocrine disruptors in the context of the EU biocide and plant protection products regulations and is currently chairing the OECD's Endocrine Disrupter Testing and Assessment Advisory Group.

She was seconded for two years (2007-2009) to the European Chemicals Agency (ECHA) in Helsinki to set up the new Agency and serve as the first Chair of the Committee for Risk Assessment. Prior to this she spent 12 years in the JRC's European Chemicals Bureau (ECB) supporting the implementation of the Existing Substances Regulation and the development of the REACH regulation.

Vincent J. Cogliano, PhD, California Environmental Protection Agency

Dr Cogliano is the deputy director for scientific programs at the California Office of Environmental Health Hazard Assessment. The office protects and enhances the health of Californians and the state's environment through scientific evaluations that inform, support, and guide regulatory and other actions.

Previously at the U.S. Environmental Protection Agency, Dr Cogliano directed its Integrated Risk Information System program and served as deputy to the agency's scientific integrity official.

Dr Cogliano also was head of the IARC Monographs program at the International Agency for Research on Cancer (part of the World Health Organization) in Lyon, France. The IARC Monographs are a series of scientific reviews that identify environmental factors that may increase the risk of human cancer.

Dr Cogliano received his PhD from Cornell University. Professional interests include qualitative and quantitative health risk assessment and its application to the protection of public health.

David Dorman, PhD, DVM, North Carolina State University

David C. Dorman is a professor of toxicology in the Department of Molecular Biomedical Sciences at North Carolina State University. His research interests include neurotoxicology, nasal toxicology, pharmacokinetics, and cognition and olfaction in animals. He is an elected fellow of the Academy of Toxicological Sciences, a fellow of the American Association for the Advancement of Sciences, and a diplomate of the American Board of Veterinary Toxicology and the American Board of Toxicology. Dr. Dorman is a National Associate of the Academies and has chaired or served on multiple National Academies committees including current service as chair of the Emerging Science on Indoor Chemistry committee and previous service as chair for the Committee to Develop a Scoping Plan to Assess the Hazards of Organohalogen Flame Retardants, the Committee on Endocrine-Related Low Dose Toxicity, and the Committee on Predictive-Toxicology Approaches for Military Assessments of Acute Exposures. He completed a combined PhD and veterinary toxicology residency program at the University of Illinois at Urbana-Champaign and holds a DVM from Colorado State University.

Session II: What do we know about the variability of traditional mammalian toxicity studies with different levels of complexity?

David Allen, PhD, Integrated Laboratory Systems, LLC

David Allen, is the President of Integrated Laboratory Systems, LLC (ILS) with over 20 years of experience in regulatory toxicology, test method evaluation, and in vitro biology. Dr. Allen is the PI and of the current NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) support contract, providing scientific oversight of all projects and senior leadership for all ILS staff working on the current contract. As the President at ILS, Dr. Allen also provides scientific leadership, management, and direction to the Predictive Toxicology and Information Sciences Program at ILS, overseeing a variety of government and commercial projects associated with the application of in vitro and in silico approaches to identifying potential hazards. Dr. Allen participates in local, national, and international meetings relevant to new approach methodologies. He has been a member of international Validation Management Teams for in vitro alternative test methods, during which he provided input on validation study design, data analyses, and test method recommendations. He also has participated on international expert consultations for new and revised Organisation for Economic Co-operation and Development (OECD) Health Effects Test Guidelines for alternative test methods.

Katie Paul Friedman, PhD, US Environmental Protection Agency

Dr. Katie Paul Friedman joined the Center for Computational Toxicology and Exposure in the Office of Research and Development at the US EPA in August 2016, where she is currently focused on application of new approach methodologies to chemical safety assessment, with additional interests in variability and uncertainty in alternative and traditional toxicity information; endocrine bioactivity and developmental neurotoxicity prediction; and in vitro kinetics. One of her roles in the Center is to run the ToxCast program. Previously, Dr. Paul Friedman worked as a regulatory toxicologist at Bayer CropScience with specialties in neuro-, developmental and endocrine toxicity, and predictive toxicology. She has been actively involved in multi-stakeholder projects to develop adverse outcome pathways, alternative testing approaches, and the regulatory acceptance of new approach methodologies. Her laboratory background includes development of high-throughput screening assays, the combined use of myriad in vitro and in vivo approaches, including receptor-reporter and biochemical assays, primary hepatocyte cultures, and targeted animal testing paradigms, to investigate the human relevance of thyroid and metabolic adverse outcome pathways using probe chemicals. Dr. Paul Friedman received a Ph.D. in Toxicology from the University of North Carolina at Chapel Hill.

Sue Fenton, PhD, National Toxicology Program

Dr. Suzanne “Sue” Fenton is a senior scientist specializing in Reproductive Endocrinology in the Division of the National Toxicology Program at NIEHS. Her laboratory has expertise in discovery of chemicals or environmental factors contributing to mammary gland developmental defects or cancer, pregnancy-related disease, and persistent adverse health effects in developmentally exposed offspring. She has received several NIH and EPA-based awards for her research on perfluorinated chemicals and endocrine disruptors.

Malcolm MacLeod, PhD, University of Edinburgh

Malcolm Macleod is Professor of Neurology and Translational Neurosciences and Academic Lead for Research Improvement and Research Integrity at the University of Edinburgh. With Howells he co-founded the CAMARADES collaboration in 2005, and he is Academic Coordinator of the European Quality in Preclinical Data IMI consortium. He was a lead author in the Lancet Series on Research Waste in 2014, and is a member of the UK Reproducibility Network steering committee. His current research interests relate to providing evidence for the effectiveness (or not) of strategies which might be adopted by funders, journals and institutions to improve the quality of their research.

Session III: What do we know about the concordance of traditional mammalian toxicity studies with humans?

Thomas Hartung, **MD, PhD**, Johns Hopkins University

Thomas Hartung, is the Doerenkamp-Zbinden-Chair for Evidence-based Toxicology in the Department of Environmental Health and Engineering at Johns Hopkins Bloomberg School of Public Health, Baltimore, with a joint appointment at the Whiting School of Engineering. He also holds a joint appointment for Molecular Microbiology and Immunology at the Bloomberg School. He is adjunct affiliate professor at Georgetown University, Washington D.C.. In addition, he holds a joint appointment as Professor for Pharmacology and Toxicology at University of Konstanz, Germany; he also is Director of Centers for Alternatives to Animal Testing (CAAT, http://caat.jhsph.edu) of both universities.

CAAT hosts the secretariat of the Evidence-based Toxicology Collaboration (http://www.ebtox.org), the Good Read-Across Practice Collaboration, the Good Cell Culture Practice Collaboration, the Green Toxicology Collaboration and the Industry Refinement Working Group. As PI, he headed the Human Toxome project funded as an NIH Transformative Research Grant. He is Chief Editor of Frontiers in Artificial Intelligence. He is the former Head of the European Commission's Center for the Validation of Alternative Methods (ECVAM), Ispra, Italy, and has authored more than 600 scientific publications (h-index 100).

Joshua Robinson, PhD, University of California, San Francisco

Dr. Robinson is an Assistant Professor in the Department of Obstetrics, Gynecology & Reproductive Sciences at the University of California, San Francisco (UCSF). His experience includes a MS and PhD in Toxicology from the University of Washington and over six years of postdoctoral training at the National Institute for Public Health and the Environment (RIVM) in the Netherlands and UCSF. At UCSF, he leads a research program focused in the areas of developmental toxicology and environmental health. His research group aims to determine the health risks of environmental chemical exposures during early human pregnancy and the underlying mechanisms linked to placental and neurodevelopmental disease. He is particularly interested in the application of toxicogenomic-based approaches and the advancement of "relevant" alternative model systems in the field of developmental toxicology. He has co-authored > 45 manuscripts in peer-reviewed journals and was granted the competitive NIH K99/R00 Pathway to Independence Award and the F. Clarke Fraser New Investigator Award for

his early research accomplishments. He is an active member of the Society of Toxicology and the Society for Birth Defects Research and Prevention

David Dorman, PhD, DVM, North Carolina State University

See Session I above

Session IV: Panel Reflections

David Dorman, PhD, DVM, North Carolina State University

See Session I above

Helen Goeden, **PhD**, Minnesota Department of Health (TBC)

Dr. Goeden has been a toxicologist and risk assessor for over 35 years in the area of environmental health. Her career focus has been on development and improvement of risk assessment methods and policies. For the past 20 years she has worked at the Minnesota Department of Health (MDH) where she led the effort to expand the methods used for deriving human health-based drinking water guidance to include multiple exposure durations and to explicitly consider sensitive or more highly exposed populations (e.g., infants and children). In 2009 she helped to create MDH's Drinking Water Contaminants of Emerging Concern Initiative. She currently co-leads MDH's projects specific to emerging environmental health threats such as the PFAS chemicals as well as alternative methods for providing risk context for chemicals with little or no toxicity data.

Prior to coming to MDH she worked at the Minnesota Pollution Control Agency and was responsible for the development and implementation of multi-media, multi-duration human health risk assessment methodology for evaluating and prioritizing contaminated sites.

Dr. Goeden has served on several scientific review boards at the national level and is active in both the Society of Toxicology and the Society of Risk Analysis.

Dr. Goeden received her Bachelor's degree from the College of St. Scholastica in Duluth, MN and her Ph.D. from the Medical College of the University of Cincinnati, Ohio.

Rashmi Joglekar, PhD, Earth Justice

Rashmi Joglekar, Ph.D., is a Staff Scientist in the Toxic Exposure and Health Program at Earthjustice, a leading nonprofit environmental law organization. In this role, Dr. Joglekar synthesizes scientific material for use in legal advocacy aimed at strengthening agency action and risk assessment of toxic chemicals. Dr. Joglekar has drafted comments on agency proposals, coordinated expert testimonies for legal cases, and advocated issues regarding toxic chemicals through blog posts, public databases, reports, and op-eds. Her work also involves examining cumulative exposures in highly exposed and susceptible communities and building the strongest scientific case for federal agencies to protect these communities. Dr. Joglekar received her Ph.D. in Toxicology from Duke University with a research focus on neurodevelopmental toxicology, and her B.S. in Biotechnology from Indiana University.

Sharon Munn, Joint Research Centre

See Session I above

Reza Rasoulpour, PhD, Corteva Agriscience

Reza Rasoulpour is the Director of Global Regulatory and Stewardship (RAS) organization for Corteva Agriscience. His accountability is to provide strategic and operational leadership to the global RAS organization to design, evaluate, develop, and steward registrations and their supporting regulatory science to enable sustainable business growth. The RAS organization encompasses regulatory science, global and regional regulatory affairs, product stewardship, and operations functions around the world. Previously, Rasoulpour was the Leader of Global Crop Protection and North American Crop Protection and Seeds Regulatory organizations within Corteva and prior to that he served as Global Leader for the Predictive Safety Center, which he helped establish as a cross-disciplinary team of regulatory scientists who partner with R&D Discovery to design products with more favorable environmental and human health safety profiles. Dr. Rasoulpour joined the organization in 2007 with a background in reproductive toxicology and molecular biology.

Dr. Rasoulpour's primary research focus has been in leading *in silico, in vitro,* and *in vivo* approaches to discover and develop products with a more favorable human health and environmental profile. Areas of exploration have included toxicogenomic, epigenetic, toxicokinetic, and systems biology research programs to accelerate pipeline product development as well as investigative mode-of-action research to characterize molecular mechanisms and their impact to product safety assessment. Dr. Rasoulpour currently serves on the Presidential Progression (2018-2022) of the Reproductive and Developmental Toxicity Specialty Section for the Society of Toxicology (SOT), as an appointed member on the National Academy of Sciences (NAS) Emerging Science for Environmental Health Decisions standing committee (2016 to present) as well as the NAS Board of Environmental Studies and Toxicology (2017 to present), he serves on the Board of Director for the Toxicology Forum (2018-present), he is on the editorial board of the Environmental and Molecular Mutagenesis journal (2017 to present), was nominated to the SOT Membership Committee (2016 to present), and served as Jr/Sr Councilor of the Reproductive and Developmental Toxicology Specialty Section for SOT (2014-2015). He has organized numerous symposia and workshops at the Society of Toxicology meetings, has served as an invited speaker and panelist for scientific sessions at the National Academy of Sciences, ICCA-LRI workshops, ILSI-HESI, ECETOC, Crop Life America, Society for Toxicologic Pathology, and the Teratology Society. To date, he has authored/coauthored 41 peer-reviewed publications to the scientific literature, as well as authored a book chapter on the topic of male reproductive biology.

Dr. Rasoulpour earned a B.S. from the University of Connecticut, where he received the title of University Scholar, the university's highest academic honor. He then embarked on researching reproductive toxicology in the laboratory of Kim Boekelheide and was awarded his Ph.D. from Brown University.