Nitrosamines as Impurities in Drugs; Health Risk Assessment and Mitigation Workshop
Panelists
March 29 – 30, 2021

Dr. Gerhard Eisenbrand - Gerhard Eisenbrand graduated 1967 in Pharmacy and Food Chemistry at the University of Freiburg/ Breisgau, Germany; Post graduate at Division of Experimental Therapy, University of Freiburg (1968); PhD Thesis at Max-Planck-Institute for Immune Biology, Freiburg (1971); Habilitation in Food Chemistry & Environmental Toxicology, University of Stuttgart, Germany (1977); Senior Scientist, Institute of Toxicology and Experimental Chemotherapy, German Cancer Research Centre, Heidelberg, Germany (1972-1982); Full Professor, Head of the Division of Food Chemistry and Toxicology, Department of Chemistry University of Kaiserslautern, Germany (1982-2009); Senior Research Professor (2009- 2013); Now Retired;

Main Research interests: Molecular Toxicology and Genotoxicity; Experimental Chemotherapy and anticancer drug development.; Mechanisms of Action; Food Chemistry; Functional effects of Food Constituents; Biomarkers of Exposure and Molecular Action.

Dr. Soterios Kyrtopoulos Ph.D - Soterios Kyrtopoulos is Emeritus research professor at the National Hellenic Research Foundation in Athens, Greece. He received a BSc degree and a PhD in Chemistry from King's College London. He entered the nitrosamine field in 1974, when he began to work as a post-doctoral researcher at Imperial College, London with Prof. Brian Challis on the mechanism of nitrosation by gaseous nitrogen oxides. This research demonstrated for the first time the rapid formation of nitrosamines from the reaction of gaseous nitrogen dioxide and trioxide with secondary amines in aqueous solution under physiological conditions. Subsequently he moved on to research on the biology of nitrosamines, working until roughly 2010 on their genotoxic and mutagenic properties of nitrosamines. His research in this context focused especially on DNA methylation by NDMA and other chemicals, the dosimetry of formation and the repair of methylated DNA adducts in various species, as well as the epidemiology of methylated DNA adducts in human populations.

Dr. Joseph Guttenplan

Education:
B.S., Brooklyn College, Ph.D., M.S., Brandeis University
Postgraduate Training and Fellowship Appointments:
Max Planck Institut fuer Spektroskopie, Goettingen, Germany, University of California, Berkeley, CA, Advisor, Dr. Melvin Calvin
Faculty appointments and positions:
Res. Assistant Professor Biochem., Mount Sinai School of Medicine, New York, NY (past position)
Assistant, Associate, full Professor of Biochemistry, N.Y. Univ. Dental College, New York, NY
Consultant, Mount Sinai School of Medicine, Dept. of Medicine, New York, NY (past position)
Assoc. Prof. Environmental Medicine (p.t.) New York Univ. School of Medicine
Coordinator, Biochemistry & Microbiology Unit New York Univ. College of Dentistry (past position)
Director, Office of Research New York Univ. College of Dentistry (past position)
Director of NYU College of Dentistry Summer Research Program
Director of the MS Oral Biology Program
Awards and Honors:
National Defense Education Act Title IV Fellowship, Planck Institute Stipendium,
NIH Postdoc.Fellow
NIH Special Fellow
Areas of expertise
Mechanisms of mutagenesis and carcinogenesis by N-nitrosamines, polycyclic aromatic hydrocarbons, estrogen metabolites; chemoprevention of carcinogenesis and mutagenesis; genotoxicity of tobacco smoke and e-cigarettes; mechanisms of oral cancer; genotoxicity of estrogen metabolites in vitro and in vivo; in vivo mutagenesis induced by exogenous and endogenous carcinogens in *lac* rodents organs; measurement of DNA damage and oxidative stress, spontaneous mutagenesis, measurement of metabolism of carcinogens.
Professional activities

- Member numerous NIH study sections.
- Member, NIEHS and EPA Superfund study section
- Member editorial boards, “Mutation Research”, “Nutrition and Cancer” International Journal of Environmental. Res. and Public Health.
- Invited speaker at numerous national and international meetings, symposia and NIH focus groups.
- Summer Faculty Research Fellow, Air Force Office of Scientific Research, Dayton, OH
- Chaired scientific sessions at: Am. Assoc. for Cancer Res, Environmental Mutagen Society, Annual meetings, and a number of international meetings
- Visiting Scientist, NIH Rocky Mountain Laboratory
- Grant reviewer for the Medical Research Council of Canada (ad hoc).
- Numerous Invited talks

Memberships in Professional and Scientific Societies:
Soc. of Toxicol., AAAS, Am. Assoc. Cancer Res., Env. Mutagen Society, Am. Society of Molecular Biology and Biological Chemists (currently inactive), AADR/IADR, American Institute of Chemists (currently inactive), American Chemical Society (currently inactive)
Research Grants
Numerous NIH grants (NCI, NIEHS, NIDCR), DOD, Komen Foundation, Am Inst. For Cancer Res.,

Smokeless Tobacco Research council, Colgate, Air Force Office of Scientific Res., numerous internal NYU grants.

Other support:

Bioreliance/Sigma-Aldrich, Production and testing of phage packaging extract.

Publications

85 Peer-Reviewed Scientific Articles

Chapter in book, "Genotoxicology of N-Nitroso Compounds" (T. Rao, ed.): *Effects of pH and Structure on the Mutagenic Activity of N-Nitroso Compounds*

Over 100 published abstracts

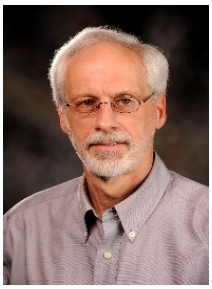
Book: *Biochemistry*, Sulzberger & Graham, New York, NY, 1994 (Coauthor with Dr. M. Oratz)

Dr. Mark Cronin - Mark Cronin is Professor of Predictive Toxicology at the School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool, UK. He has over 30 years expertise in the application of *in silico* approaches to predict the toxicity and fate of chemicals; in addition to development of strategies to develop alternatives to whole animal testing for toxicity. Current research includes the application of chemical grouping and read-across to assess human health and environmental endpoints, particular the linking of the Adverse Outcome Pathways (AOPs) to category formation. This research effort has resulted in four books and over 300 publications in all areas of the use of (Q)SARs, expert systems and read-across to predict toxicity. He has worked in numerous projects in this area including more than ten EU Framework Projects as well as assisting in the uptake of *in silico* methods for regulatory purposes.

Dr. Errol Zeiger - Dr. Errol Zeiger is an independent consultant in genetic toxicology and chemical carcinogenesis. He performed genetic toxicology research in the Genetic Toxicity Branch at the FDA prior to joining the National Institute of Environmental Health Sciences (NIEHS, NIH) National Toxicology Program, from which he retired in Dec 2000. He received his BS in Biology from City College of New York in 1960, MS (1969) and PhD. (1973) in Microbiology from George Washington University, Washington DC, and a JD (1991) from North Carolina Central University, Durham NC. At the NIEHS he was responsible for designing, implementing, and managing the NTP's genetic toxicity testing program, in addition to running his research lab where he studied in vitro metabolic activation of promutagens, and the validation of in vitro test genetic toxicity test systems.

Dr. Zeiger authored or co-authored more than 230 peer-reviewed, and other, publications, and co-edited the Handbook of Carcinogenic Potency and Genotoxicity Databases, and Jet Fuel Toxicology. He is an active member of the Environmental Mutagenesis and Genomics Society, serving as elected Councilor and Chair of a number of committees, the Society of Toxicology, and is a Fellow of the Academy of Toxicological Sciences. He was the Editor-in-Chief of Environmental and Molecular Mutagenesis, and is currently on the Editorial Boards of EMM and Genes and Environment, was a former member of the Mutation Research Editorial Board, and is a reviewer for approximately 10 journals. He has won a number of awards, including the EMS Recognition Award, the EM(G)S Service Award, DHHS Superior Performance

Award, NIH Merit Award, and the GEMS Lifetime Achievement Award. His current activities are primarily involved with the evaluation of genetic toxicity test methods and test data and their relationship to potential carcinogenicity and heritable genetic mutation. His consulting clients have included chemical and pharmaceutical companies, US and other Government and multinational organizations, consulting organizations and testing laboratories, and law firms. He has served as a consultant to the OECD in Paris for toxicology test guidelines and guidance documents, and supervising in vivo validation studies for endocrine disrupting chemicals.



Dr. John R. Bucher - John R. Bucher, Ph.D., Senior Scientist and former Associate Director, National Toxicology Program (NTP) and Scientific Director, Division of the NTP, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC.

Ph.D. Pharmacology, University of Iowa; M.S. Biochemistry, University of North Carolina at Chapel Hill; B.A. Biology, Knox College; NIH Postdoctoral Fellow, Michigan State University; Diplomate' American Board of Toxicology, Fellow Collegium Ramazzini

Interests and responsibilities include research into the toxic and carcinogenic potential of chemicals, mixtures and physical agents, and improving assays for these purposes; providing direction for the literature analysis activities and preparation of the NTP Report on Carcinogens and Monographs from the Office of Health Assessment and Translation; initiatives examining the genetic and epigenetic bases for variations in response to environmental agents; and implementation of high throughput screening tools for toxicological testing termed "Toxicology in the 21st Century".

Dr. Jerry M. Rice - Jerry M. Rice, Ph.D.**,** received his doctorate in biochemistry from Harvard University in 1966. His research interests include comparative tumor pathology; perinatal and transplacental chemical carcinogenesis; tumor promotion; the molecular biology of transforming and tumor suppressing genes in tumors; and the carcinogenic hazards presented by infections and infectious agents. He joined the U. S. National Cancer Institute as a commissioned officer in the U.S. Public Health Service in 1966, becoming chief of the Laboratory of Comparative Carcinogenesis in 1981, and Associate Director for the Frederick Cancer Research and Development Center and Acting Director of the Division of Cancer Etiology in 1994. In 1996 he retired from the Public Health Service and joined the International Agency for Research on Cancer in Lyon, France, where he served as Chief of the Unit of Carcinogen Identification and Evaluation and Director of the IARC Monographs Programme on Evaluation of Carcinogenic Risks to Humans. He retired from the World Health Organization in 2002, but continued (through 2013) to be actively involved with the WHO in various capacities. He is currently Distinguished Professor of Oncology in the Lombardi Comprehensive Cancer Center at Georgetown University Medical Center, Washington, where he lectures in graduate courses. He has served on the

American Cancer Society's Committee on Cancer and the Environment, and consults internationally on issues related to carcinogenic hazard identification and carcinogenic risk assessment. He has also frequently served on review panels for U.S. Government agencies, including the National Center for Toxicological Research, the Environmental Protection Agency, the National Toxicology Program, the Food and Drug Administration's Center for Devices and Radiological Health, and the Department of Agriculture's intramural research program on mycotoxins. He has published more than 180 research papers and more than 70 book chapters, reviews, and editorials, and has co-edited nine books and scientific meeting proceedings. His awards include the Meritorious Service Medal of the U.S. Public Health Service and the Toxicology Forum's George Scott Award in Toxicology.

Dr. Stephen S. Hecht - Stephen S. Hecht, Ph.D. is Wallin Professor of Cancer Prevention at the University of Minnesota and an American Cancer Society Research Professor. He is an internationally recognized expert on carcinogens in tobacco products and their mechanisms. He is the co-discoverer of tobacco-specific nitrosamines, causative agents for tobacco-induced cancer. His current research focuses on the relationship of human carcinogen and toxicant metabolites and DNA adducts to cancer risk.

He has a B.S.in chemistry (Duke University) and a Ph.D. in organic chemistry (MIT). Prior to moving to the University of Minnesota in 1996, he conducted research at the American Health Foundation cancer prevention research institute in Valhalla, NY, where he was Director of Research from 1987-1996.

He received the AACR Award for Excellence in Cancer Prevention Research in 2006, and the Founders Award from the Division of Chemical Toxicology, American Chemical Society in 2009. He was elected an American Chemical Society Fellow in 2009, a Fellow of the American Association for the Advancement of Science in 2014, and was Editor-in-Chief of Chemical Research in Toxicology 2013-17. He has received a Merit Award and an Outstanding Investigator Grant from the National Cancer Institute.

He has published over 850 papers in the scientific literature.

Dr. Richard H. Adamson - Richard H. Adamson earned a B.A. in chemistry from Drake University, a M.A. in international affairs from the George Washington University, an M.S. and a Ph.D. in pharmacology from the University of Iowa, the latter at age 23. His career includes government research and management, academic research and industry management and consulting.

His government career includes serving as a commissioned officer in the Public Health Service and in the Civil Service as a Senior Investigator, Section Chief, Laboratory Chief, Division Director and Scientific Director at the National Cancer Institute, National Institutes of Health. He was also a Senior Policy Analyst at the White House Office of Science and Technology Policy 1979-1980.

His academic career included serving as a Fellow in the College of Medicine at the University of Iowa, a Lecturer in physiology, The George Washington University Medical School and a Visiting Scientist at St. Mary's Hospital Medical School, London, England.

In 1994, Dr. Adamson retired from government service after 14 years as Director, Division of Cancer Etiology, NCI, NIH, while also having other simultaneous positions in the civil service to become Vice President for Science and Technical Affairs at the American Beverage Association (ABA). In 2004 he became President of TPN Association, LLC. (consulting in Toxicology, Pharmacology and Nutrition) to date.

Richard H. Adamson has served on numerous committees and editorial boards, is a member of several professional societies, has published more than 250 papers and has been awarded several honors from the U.S. Government and from scientific organizations in the United States and abroad.

Dr. Michael DiNovi - Dr. Michael DiNovi received his undergraduate degree from MIT in 1977. His doctoral work in Organic Chemistry was completed under the supervision of Dr. Koji Nakanishi at Columbia University in New York in 1982. After a post-doctoral fellowship, studying the biosynthesis of beta-lactam antibiotics at the Johns Hopkins University in Baltimore, Dr. DiNovi became an assistant member at the Monell Chemical Senses Center in Philadelphia, studying the structural characteristics that affect the perception of taste for carbohydrates, including modified mono- and disaccharides. Dr. DiNovi joined the US Food and Drug Administration's Center for Food Safety and Applied Nutrition in July 1988 as a chemistry technical reviewer. He became a senior editor, and was named the Center's expert on the dietary exposure assessment of naturally occurring compounds in 1995. He was made a supervisory chemist in 2001 and was subsequently named the Center's international expert on dietary exposure assessment in late 2007. Dr. DiNovi has completed numerous important dietary exposure assessment projects, most notably the assessments for acrylamide, furan, and perchlorate contaminants in foods, published on the Food and Drug Administration website. Dr. DiNovi has served on a number of international expert workgroups, and has participated at meetings of the Joint FAO/WHO Expert Committee on Food Additives since 1999. He was a member of the EFSA expert panel on Contaminants in the Food Supply from 2012-2018. Dr. DiNovi is married with a 29 year old son, and resides in Baltimore Maryland.

Dr. Aisar Atrakchi - Dr. Atrakchi is a Supervisor of pharmacology and toxicology in the Division of Psychiatry in the Office of Neuroscience in the Center of Drug Evaluation and Research. She joined the FDA in 1992 as a Senior Pharmacologist Toxicologist reviewer in the Division of Neuropharmacology (currently Psychiatry), in 2008 she became a Team Leader in the same Division and in 2012 became a Supervisor. As a Chair, Co-Chair and/or a member of a number of CDER and International committees, Dr. Atrakchi has contributed to the development and writing of regulatory guidances and has presented at National and International conferences and published on these topics. Among these are the Safety Testing of Drug metabolites: Guidance for Industry, ICH S2(R1) on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, and the ICH M7 on Assessment and Control of DNA Reactive Mutagenic Impurities in Pharmaceuticals to limit Carcinogenic Risk. Since 2018 she has been on the Agency's Task Force related to nitrosamine drug contamination. Dr. Atrakchi earned a Ph.D. in pharmacology and toxicology from the University of California – Davis and a Master's from the University of Montana – Missoula, MT. She did a Postdoctoral Fellowship at the George Washington University Medical School, Division of Experimental Medicine, Department of Medicine, Washington, D.C. and was a Fogarty International Fellow at the NIH, NINDS, lab of Biophysics. Prior to joining the FDA, she was a Senior Toxicologist and Project Manager at the Dynamic Corporation in Rockville, MD.

Dr. Sruthi King - Sruthi King earned her Ph.D. in pharmacology from Georgetown University and completed postdoctoral training at Stanford University in the Department of Dermatology. Sruthi joined FDA in 2008 as a Pharmacologist in the Division of Gastroenterology and Inborn Error Products within the Office of New Drugs and later moved to the Office of Generic Drugs as team leader in 2015. Sruthi now serves as an Associate Director of Pharmacology and Toxicology in Division of Clinical Review within the Office of Generic Drugs (OGD) at the Food and Drug Administration (FDA). Sruthi has been a member of the CDER nitrosamine task force for the past 2.5 years and also serves on several working groups with international regulators to harmonize approaches related to nitrosamine safety assessments.

Dr. David Keire - David Keire received a Ph.D. in Analytical Chemistry at the University of California, Riverside in 1990. Currently he is the Acting Office Director of the Office of Testing and Research (OTR) which is part of the CDER Office of Pharmaceutical Quality. Dr. Keire joined the FDA in 2008 and attained a Senior Biomedical Research Scientist (SBRS) designation in 2018. At FDA, David's analytical chemistry skills have been put to use at the FDA on studies of complex drugs (e.g., heparin, protamine sulfate, glatiramer acetate, transdermal systems, inhalers, modified release dosage forms and protein therapeutics). He maintains a research program in the identification and evaluation of state-of-the-art analytical technologies for complex drug analysis to provide scientific input on drug quality questions to FDA assessor staff. He has over 100 peer reviewed research articles describing his work. For the past two and a half years he has been involved in developing and implementing tests for nitrosamine impurities in pharmaceuticals.

Dr. Deborah Johnson - Deborah Johnson has a Ph.D. in Organic Chemistry from Brigham Young University. She worked as a pre-formulation chemist for Wyeth Pharmaceuticals for 4 years and then joined the US FDA in Aug 2010 as an CMC assessor for Abbreviated New Drug Applications (ANDAs). In 2012 she joined the newly formed Drug Masterfile Review team. After the Office of Pharmaceutical reorganization this group became known as the Division of Lifecycle API (DLAPI) and is now located in the Office of New Drug Products. In 2014 Deborah became a branch chief and is still serving in that position.

Dr. Timothy McGovern - Dr. McGovern is an Associate Director for Pharmacology/Toxicology in FDA CDER's Office of New Drugs where he interacts with nonclinical review teams in the review of IND, NDA, and BLA submissions, advises Office Directors on nonclinical issues, and is involved in development of policy and guidances related to nonclinical and regulatory issues. Tim is a member of CDER's Nitrosamines in Drugs Task Force and a member of the ICH M7 [Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential of Carcinogenic Risk] Expert Working Group. He has published in the areas of inhalation toxicology, carcinogenicity testing, evaluation of genotoxic impurities, and evaluation of leachables and extractables.

Dr. Robert T. Dorsam - Robert T. Dorsam earned his Ph.D. in Pharmacology from Temple University School of Medicine and conducted post-doctoral research in the laboratory of Silvio Gutkind, Ph.D. at the National Institutes of Health. His research was focused on the contribution of G-protein signaling in cancer and thrombosis.

Bob then joined FDA where he was a Pharmacology/Toxicology reviewer in FDA's Office of New Drugs in the areas of oncology and nonprescription products. Bob later joined the Office

of Generic Drugs (OGD) as a team leader and then became Associate Director of Pharmacology/Toxicology in OGD's Division of Clinical Review. He has been a member of CDER's Nitrosamines Task Force since its inception and is involved in the safety assessments for nitrosamines in generic drug products.