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Office of Research and Development
National Center Environmental Assessment

Symposium on New Scientific Research Related to the Health Effects of TCE

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Speaker Biographies

James Bruckner

James V. Bruckner has a B.S. in pharmacy and a M.S. in toxicology from the University of Texas, as well as a Ph.D. in toxicology from the University of Michigan. He has held faculty positions at the University of Kansas, the University of Texas Medical School at Houston, and the University of Georgia (UGA). He is currently Professor of Pharmacology and Toxicology at the UGA College of Pharmacy. He was director of UGA's interdisciplinary graduate program in toxicology for 15 years. He is actively engaged in graduate education and in federally-funded research projects.

Dr. Bruckner's research focus is on the toxicology and toxicokinetics of solvents, drug-solvent interactions at occupational exposure levels, and toxicokinetic bases for susceptibility of children to insecticides and other chemicals. The relevance of experimental designs to "real life" chemical exposures is of particular interest, as is evaluation of potential risks posed by environmentally-encountered levels of TCE and related solvents. Dr. Bruckner has published more than 200 journal articles, book chapters and abstracts, a number of which focus on TCE. He has served on a variety of expert panels and committees for the U.S. EPA, NIH, NASA, ATSDR, FDA and the National Academy of Sciences.

Richard Bull

Richard J. Bull has a B.S. in pharmacy from the University of Washington and a Ph.D. in Pharmacology from the University of California. He has worked on the toxicology of drinking water contaminants since 1971. He worked at the U.S. EPA Health Effects Research Laboratory in Cincinnati and its predecessor organizations from 1964 to 1984, where his last position was as Director of the Toxicology and Microbiology Division. In 1984 he accepted a position as Professor of Pharmacology and Toxicology at Washington State University and left this position in 1994 to work in the Pacific Northwest National Laboratory until 2000, when he returned to Washington State University. He retired from Washington State University in 2003. At EPA, his early research focused on neurodevelopmental effects of lead, specific studies of drinking water disinfectants and their by-products, and the toxicity and carcinogenicity of a number of drinking water contaminants, including acrylamide. Work on disinfection by-products continued at Washington State University and PNNL, but were extended to the study of mechanisms involved in the carcinogenicity of TCE and other solvents. With his return to Washington State University he also worked on a project with the Department of Energy's Low-Dose Radiation Research Program. He has authored or co-authored 114 peer-reviewed publications, numerous reviews and several book chapters and two books related to the toxicology of disinfection by-products. Approximately 40 of these publications involve studies of TCE or its metabolites.

Dick now works exclusively through MoBull Consulting. His work focuses on providing advice to water utilities and a number of water industry research organizations. This work includes the design of research projects, the design of monitoring programs (with emphasis on biomonitoring), and simple evaluations of the hazards associated with particular water contaminants. Currently, he has a project that is attempting to identify disinfection by-products that would be more plausible causes of the cancers associated with the chlorination of drinking water in epidemiological studies than the trihalomethanes or haloacetic acids that are commonly used for surrogates. A more recent activity has been to help industry develop comments on the scientific base of certain regulations of EPA and other Agencies. Dick has served on a number of advisory boards, including the U.S. Environmental Protection Agency's Scientific Advisory Board, as a member and/or chair of several NRC committees, as an advisor to national and international agencies related to contaminants drinking water, and on several IARC working groups. He is a member of the current NRC committee (2003-2004) charged with reviewing EPA's pending actions on perchlorate.

James Burch

Dr. Burch is an Assistant Professor in Department of Environmental Health and Radiological Health Sciences at Colorado State University with a Ph.D. in Environmental Health and a M.S. degree in the Pharmaceutical Sciences. His research focuses on environmental and occupational epidemiology. Dr. Burch is active in areas of research involving hazardous wastes, air pollution, breast cancer, and non-ionizing radiation. Dr. Burch studied symptom and disease prevalence among residents in the vicinity of the Rocky Mountain Arsenal hazardous waste site in Colorado and more recently conducted statistical analyses of the neurobehavioral effects associated with exposure to contaminated ground water through the local municipal water supply in that area. His current research includes the development of biomonitoring approaches to identify pathological responses and markers of genetic susceptibility to air pollutants. He is currently Co-PI of a research grant that will evaluate concentrations of hormones and growth factors, as well as the proliferative properties of breast cyst fluids among women with gross cystic breast disease. He is also co-investigator and field supervisor of a NIEHS-funded study that will evaluate the effects of radio frequency non-ionizing radiation on several biological markers in a residentially exposed population in the Denver metropolitan area. Dr. Burch has more than 7 years of experience as a professional consultant and has performed numerous human health risk assessments for hazardous waste sites, incinerators, landfills, and other types of environmental contamination. He has also served as a scientific advisor in several capacities including membership on the Citizen's Advisory Board for the Rocky Flats Nuclear Weapons Production Facility, a Superfund hazardous waste site in Jefferson County, Colorado.

John Cherrie

John Cherrie has a B.Sc. in physics from the University of Edinburgh and a Ph.D. in occupational hygiene from the University of Aberdeen. He has worked on human exposure research for more than 25 years at the Institute of Occupational Medicine in Scotland, where he is currently Director of Special Projects.

His main research interests are in exposure assessment for occupational cancer epidemiological studies, plus dermal and ingestion exposure assessment. Current research projects include exposure assessments for a cohort study of tetrafluoroethylene exposed workers. He has collaborated closely with the International Agency of Research on Cancer (IARC) in a number of projects, most recently in an epidemiological study of titanium dioxide manufacturing workers. John Cherrie is a member of the Scientific Advisory Board for a case-control study of kidney cancer and TCE exposure in the Arve Valley, France. He is also the scientific chair of the conference X2004: Exposure Assessment in a Changing Environment (www.iras.uu.nl/X2004).

Jeffrey W. Fisher

Dr. Fisher has a B.S. degree in biology from the University of Nebraska at Kearney, a M.S. degree in biology from Wright State University, and a Ph.D. in Zoology/Toxicology from Miami University. He has work as a research toxicologist for 18 years specializing in the development and application of physiologically-based pharmacokinetic (PBPK) models for risk assessment. He worked for 25 years in a toxicology laboratory at Wright-Patterson AFB and for the last four years at the University of Georgia.

Dr. Fisher is currently a Professor and Department Head in the Department of Environmental Health Science. He teaches a graduate class in PBPK modeling and trains graduate students in the application of PBPK models in toxicology and environmental health. Dr. Fisher has published over 50 papers on pharmacokinetics and PBPK modeling, including several PBPK models for TCE and its metabolites in laboratory animals and humans. He has also published PBPK models for different life stages for TCE and perchlorate and as well as PBPK models for other solvents. He has served on several panels and advisory boards for DoD, ATSDR, U.S. EPA and non-profit organizations. He was a U.S. delegate for NATO and a visiting scientist at CIIT and NIOSH.

Frederick Peter Guengerich

Professor Guengerich holds a B.S. in Agricultural Science from the University of Illinois (1970) and a Ph.D. in Biochemistry from Vanderbilt University (1973). He was a Research Fellow at the University of Michigan Medical School (Biological Chemistry) from 1973-1975, when he joined the Department of Biochemistry at Vanderbilt University School of Medicine as an Assistant Professor. He was promoted to Associate Professor in 1980 and to Professor in 1983. Since 1987 he has been the Director of the NIEHS-supported Center in Molecular Toxicology at Vanderbilt.

Professor Guengerich has been studying aspects of the metabolism of halogenated hydrocarbons since 1977, including TCE, vinyl chloride, and vinylidene chloride, particularly with regard to cytochrome P450 and glutathione transferase enzymes. Other research has been directed towards understanding the reactions of the products with proteins and nucleic acids. Professor Guengerich has served on a variety of advisory groups in NIH, journals, research organizations, and the chemical and pharmaceutical industries. He has been Associate Editor of Toxicology and Applied Pharmacology (1980-1984), Molecular Pharmacology (1982-1985), and Chemical Research in Toxicology (1989-present). Prof. Guengerich has received a number of awards, including the SOT Achievement (1982) and Burroughs-Wellcome Toxicology Scholar (1983) Awards, the J. J. Abel (1984) and the B. B. Brodie (1992) Awards from ASPET, the CIIT Founders' Award (1999), the Scott Award from Toxicology Forum (1994), and the ISSX North American Section Scientific Achievement Award (2003).

Johnni Hansen

Johnni Hansen has a M.S. from the Royal Pharmaceutical University of Copenhagen, and a Ph.D. in occupational epidemiology from the Technical University of Copenhagen. He has previously worked at the National Institute of Occupational Health as epidemiologist. He has 15 years of research experience, particularly in occupational cancer, and has about 50 publications in the international scientific literature, and over 60 reports in Danish. He is co-author of four papers concerning TCE exposure and cancer risk, and is still working on studies related to this issue.

Johnni Hansen is currently employed as head of the Occupational Unit at the Institute of Epidemiology under the auspices of the Danish Cancer Society. He is also teaching medical students in epidemiology at the University of Copenhagen, and pharmaceutical students in occupational health. He is reviewer for over 10 international scientific journals, and has given over 100 invited presentations at international and Danish scientific meetings. During the last five years, he has received 18 grants from international and Danish funds. He is a senior adviser for the National Danish Labour Inspection Service and for the Danish Environmental Protection Agency concerning chemicals and cancer risk.

Paula Johnson

Paula Johnson has a D.V.M. in Veterinary Medicine from Colorado State University and a M.S. in Animal Science from the University of Arizona. She has worked as a private practitioner and currently serves in the U.S. Army Reserve as a Veterinarian. She has 15 years of research experience at the University of Arizona.

Paula is currently an Investigator on the TCE exposure project at the University of Arizona. In the past, this project has examined the gross effects of TCE exposure to the fetal rat heart and is currently examining specific cardiac developmental gene alterations due to TCE exposure. Most recent publications can be found in *International Toxicological Sciences*, *Environmental Health Perspectives*, and *Birth Defects Research*.

James Lacey

James V. Lacey, Jr., earned a B.S. (1993) in Psychology as a Natural Science from the University of Michigan and a M.P.H. (1995) and Ph.D. (1998), both in epidemiology, from the University of Michigan School of Public Health. His dissertation work on systemic sclerosis (scleroderma) and undifferentiated connective tissue disease evaluated the potential risk associated with reproductive exposures such as menopausal hormone therapy, implanted medical devices such as silicone breast implants, and occupational exposures such as solvent use.

He joined the National Cancer Institute's Division of Cancer Epidemiology and Genetics as a postdoctoral fellow in 1998 and became a tenure-track investigator in 2001. A member of the Hormonal and Reproductive Epidemiology Branch, he investigates hormonal carcinogenesis in the ovary, endometrium, breast, and cervix. His work continues to focus on risks associated with exogenous hormones, particularly menopausal hormone therapy, but also includes emphasis on natural history models and endogenous hormones.

Lawrence H. Lash

Dr. Lash has a B.A. in biology from Case Western Reserve University and a Ph.D. in biochemistry from Emory University. After completing a postdoctoral fellowship in pharmacology and toxicology at the University of Rochester with Professor M.W. Anders, Dr. Lash joined the faculty in the Department of Pharmacology at Wayne State University School of Medicine in Detroit, Michigan, where he has been since 1988. He received a National Research Service Award from the NIEHS (1986-1988) and a Research Career Development Award from the NIDDK (1993-1998). He has 23 years of research experience in various aspects of glutathione metabolism and transport and glutathione-dependent drug metabolism and nephrotoxicity. Much of that research has focused on various aspects of TCE metabolism and toxicity, including studies of sex- and species-dependent differences and biochemical and molecular mechanisms of action of key metabolites of TCE in various in vitro preparation of rat and human kidney.

Dr. Lash is currently a Professor in the Department of Pharmacology at Wayne State University School of Medicine. His current research interests focus on three projects. The first project involves study of mechanisms of sublethal injury, repair, and enhanced cell proliferation induced by the TCE metabolite S-(1,2-dichlorovinyl)-L-cysteine (DCVC) in primary cultures of human proximal tubular cells, and is funded by NIEHS. The second project involves the development and use of human proximal tubular cells to model transport and metabolism of various classes of therapeutic drugs under clinical investigation. Expression and catalytic activity of a battery of membrane transporters and Phase I and Phase II drug metabolism enzymes are being determined so that pharmacokinetic modeling of drug handling can be accurately undertaken. This project is funded by a contract from Pfizer, Inc. The third project involves study of the molecular regulation and role in determining susceptibility to chemically induced injury of mitochondrial glutathione transport in renal proximal tubules, and is funded by NIDDK. Dr. Lash has published more than 120 peer-reviewed papers, reviews, and book chapters, has edited four books on mitochondrial function, renal toxicology, and drug metabolism, and is an Associate Editor for two leading journals, *Toxicology* and *Applied Pharmacology* and the *Journal of Pharmacology and Experimental Therapeutics*. He is also on the editorial board of *Drug Metabolism and Disposition*, has served on NIH study sections, and has been a consultant to the National Research Council subcommittee on urinary toxicology and the U.S. Environmental Protection Agency for their human health risk assessments of TCE and perchloroethylene.

JoEllyn McMillan

Dr. McMillan received a B.A. in Biology and Chemistry from Southern Illinois University at Edwardsville. She received a Ph.D. in Toxicology from Texas A&M University under the guidance of Dr. Stephen Safe. Her research focused on the alteration of adult rat drug metabolizing enzyme activities following neonatal exposure to dioxin and PCB congeners. After obtaining her degree, she worked as a post-doctoral fellow at the National Center for Toxicological Research. She did a second post-doctoral fellowship at the Medical University of South Carolina, where she stayed on as a research assistant professor. She has worked in the area of drug and xenobiotic effects on liver function for the past 15 years.

Dr. McMillan is currently employed by at the Medical University of South Carolina as an assistant professor. She is working on elucidating the effects of environmental contaminants on the liver that may impart susceptibility to development of hepatocarcinogenesis. In particular she is interested in the use of hepatocyte cultures from humans and rodents as comparative model systems for the liver. In addition to her publications on the hepatotoxic effects of TCE metabolites, she has published on the effects of polyhalogenated aromatics on liver drug metabolizing enzymes and on the mechanisms of chemical-induced hepatotoxicity. She has presented her research at numerous national and international meetings.

Michael A. Pereira

Dr. Pereira has a B.S. in microbiology and a Ph. D. in pharmacology and toxicology from Ohio State University. He has 37 years of research experience in toxicology and pharmacology. After a Damon Runyon Cancer Research Fellowship at the National Institutes of Health, he has worked at the New York Blood Center; New York University Medical Center, Department of Environmental Medicine; the US EPA, Health Effects Research Laboratory; Environmental Health Research and Testing, Inc.; and the Medical College of Ohio. He is presently Professor, Division of Hematology and Oncology, Ohio State University.

Dr. Pereira's research has been in the area of cancer etiology and prevention. His laboratory has two main focuses. One focus is the mechanism of chemical carcinogenesis with emphasis on nongenotoxic mechanisms. The other focus is the identification and mechanism of cancer chemopreventive agents, again emphasizing epigenetic mechanism and the development of surrogate end-point biomarkers. With respect to TCE, his research has included the first demonstration that its metabolites dichloroacetic acid and trichloroacetic acid are mouse liver carcinogens. He then investigated the mechanism of TCE and its two metabolites, demonstrating that they are tumor promoters in mouse liver. His research strongly suggests that their carcinogenic mechanism involves the induction of DNA hypomethylation.

Beate Pesch

Beate Pesch is an expert in occupational and environmental epidemiology, in particular the exposure assessment and gene-environment interactions. She has been involved in various epidemiological and molecular-epidemiological studies in national and international co-operations. She has particular expertise in cancer research of the German Human Genome Project. In 1995 she won the Leo Brandt Award for her contribution to the 'Atlas of Cancer Mortality in Northrhine Westphalia'.

Neil Pumford

Neil Pumford has a B.S. in medical technology from the University of Arkansas for Medical Sciences and a Ph.D. in toxicology from the University of Arkansas for Medical Sciences. He has worked academia for thirteen years. He has over ten years of research experience with TCE. Initial work involved covalent binding of TCE to proteins. He has identified a major protein adduct as cytochrome P450 2E1.

Neil Pumford is currently employed by the University of Arkansas at Fayetteville as an Adjunct Professor. He is working on the investigation of the role of TCE in autoimmune disease. His group has shown that TCE can exacerbate the development of autoimmune hepatitis in autoimmune-prone mice. He is investigating the mechanisms involved in the acceleration of autoimmune disease in animals treated with TCE. He has published over 16 manuscripts on halogenated solvents with 11 of the manuscripts on TCE. Six of these manuscripts describe his work on the effects of TCE on T cells and the development of autoimmune disease in mice.

Yih-Horng Shiao

Dr. Yih-Horng Shiao is currently employed by the National Cancer Institute, National Institutes of Health as a Staff Scientist. He is working on the role of von Hippel-Lindau tumor suppressor in human and animal tumors. His laboratory has been developing many animal models to test the carcinogenicity of environmental factors and to identify molecular mechanisms contributing to tumorigenesis. He has also participated in other research areas, such as molecular pathology and molecular epidemiology. He has been routinely invited to peer review manuscripts for scientific journals and to write review articles and book chapters. He is a member of the American Association for Cancer Research and the American Chemical Society.

Jung-Der Wang

Jung-Der Wang has an M.D. in Medicine from the National Taiwan University College of Medicine, an M.I.H. in industrial hygiene, and an Sc. D. in occupational medicine from the Harvard School of Public Health. He is board certified by the American Board of Preventive Medicine (specializing in Occupational Medicine). He has worked as a professor and director in the Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University and he has 22 years of research and teaching experience in epidemiology, occupational and environmental medicine, and quality of life in the National Taiwan University. In addition, he has an active clinical practice, seeing patients with occupational and environmental diseases in the National Taiwan University Hospital.

Jung-Der Wang currently serves as the Dean of College of Public Health, National Taiwan University and as visiting staff in the Department of Internal Medicine, National Taiwan University Hospital. He is developing methods and conducting empirical research for health risk assessment on occupational and environmental health, quality of life, and cost-effectiveness. He has served on many committees to draft and develop occupational and environmental standards and laws for Taiwan. He was elected as a fellow of Rammazzini Collegium in 2001. He has also served on the editorial boards of the following journals: Occupational and Environmental Medicine, Biomarkers, Journal of Occupational Health, Journal of Epidemiology, and the International Journal of Occupational and Environmental Health. He has published an English textbook of epidemiology entitled "Basic Principles and Practical Applications in Epidemiological Research," (Singapore: World Scientific, 2002), and over 200 papers in peer reviewed academic journals, including six articles on vinyl chloride and the following recent articles for the health risks of chlorinated alkenes and alkanes:

Lee LJH, Chan CC, Chung CW, Ma YC, Wang GS, Wang JD. Health risk assessment on residents exposed to chlorinated hydrocarbons contaminated in groundwater of a hazardous waste site. *J Toxicol Environ Health* 2002; 65: 219-235.

Wang FI, Kuo ML, Shun CT, Ma YC, Wang JD, Ueng TH. Chronic toxicity of a mixture of chlorinated alkanes and alkenes in icr mice. *J Toxicol Environ Health* 2002; 65: 353-365.

Lee LJH, Chung CW, Ma YC, Wang GS, Chen PC, Hwang YH, Wang JD. Increased mortality odds ratio of male liver cancer in community contaminated by chlorinated hydrocarbons in groundwater. *Occup Environ Med* 2003;60:364-9.