

US EPA ARCHIVE DOCUMENT

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Reevaluation of Human Health Effects of Atrazine: Review of Non-cancer Effects, Drinking Water Monitoring Frequency, and Cancer Epidemiology

Dr. Susan F. Akana is currently an Instructor in the Department of Biological Sciences at the City College of San Francisco and she previously served as an Associate Research Scientist in the Physiology Department at the University of California at San Francisco where she designed and conducted neuroendocrine and behavioral studies in stress and obesity in rodent models. Dr. Akana has a Ph.D. in Physiology-Anatomy from the University of California at Berkeley and conducted her thesis work on neuroendocrine strategies for adaptation to high altitude. She was then awarded a National Institutes of Health (NIH)-National Research Service Award postdoctoral fellowship at UCSF and focused on corticosterone regulation of ACTH secretion. Dr. Akana advanced in the department, first as an assistant, and then as an associate researcher over the next 20 years and her areas of expertise honed in on normal and pathological patterns in circadian hormones, feeding behavior and energy balance in response to stress and often resulting in obesity. These advances were supported by her two NIH research grants (National Institute of Mental Health and National Institute of Diabetes, Digestive Disease and Kidney Disease). In turn, she has served on ad hoc NIH study sections for IFCN-1 (NMB), a 4-year term on a scientific review panel with the IFCN-2 (NNB), and reviewed an average of one NSF grant/year for the last 12 years. She served a 5-year term on the editorial board for the Journal of Neuroendocrinology, a 4-year term as a biology reviewer for Faculty of 1000, and regularly reviews manuscripts for Endocrinology, American Journal of Physiology, Neuroendocrinology, and other similar journals.

Dr. Frank J. Bove is Senior Epidemiologist with the Agency for Toxic Substances and Disease Registry (ATSDR), Public Health Service, Division of Health Studies, Epidemiology and Surveillance Branch. He directs technical aspects of the Hazardous Waste Workers Surveillance Project, supervises and reviews protocols and analysis plans for other epidemiologists in the branch, designs and conducts epidemiologic studies, provides technical backup on epidemiologic methods to the Branch Chief, represents the Agency, Division and Branch on technical issues and prepares reports, journal articles, and conference presentations. Dr. Bove has a Sc.D. in Epidemiology and an M.S. in Environmental Health Sciences from Harvard University School of Public Health. His undergraduate work was completed at the University of Pennsylvania in Philadelphia. Dr. Bove has been involved in considerable research and has many publications in the areas of epidemiology and occupational health as related to birth outcomes and reproductive health. He has previously served on panels for EPA, Health Canada, the National Academy of Sciences, American Water Works Association, and CDC.

Dr. Richard H. Coupe is a Supervisory Hydrologist with the U.S. Geological Survey (USGS) Mississippi Water Science Center in Jackson, Mississippi. He has been with the USGS for over 30 years and has worked on water-quality issues in Virginia and Illinois before moving to Mississippi in 1993. He has an undergraduate degree in Mathematics from George Mason University, a master's and a doctorate from the Plant and Soil Sciences (Weed Science) Department at Mississippi State University. His early career focused on water-quality database design and development, but in the mid-1980s he moved to Illinois where he served as the Illinois Water Science Center's Water Quality Specialist. He has spent the last 25 years studying the effects of production agriculture on the water quality of the Nation's ground and surface waters. He is currently the Chief of the Mississippi Embayment (MISE) National Water Quality Assessment (NAWQA) Program's study unit and also oversees the sample collection and design of the National Stream Quality Accounting Network (NASQAN) which operates on the major rivers throughout the United States. He has conducted numerous studies on the fate and transport of pesticides and nutrients across a range of basin scales from 12m x 4m test plots, to the entire Mississippi River Basin as well as the occurrence of pesticides in streams, rivers, reservoirs, groundwater, and in drinking water facilities in the United States. He has served on numerous committees and panels concerned with water quality in the Gulf of Mexico and on the development of water quality criteria for the State of Mississippi.

Dr. Kenneth Barry Delclos is a Research Pharmacologist in the Division of Biochemical Toxicology at the Food and Drug Administration's National Center for Toxicological Research. He has been employed at the FDA's National Center for Toxicological Research since 1985 where he has conducted research in diverse areas. Earlier efforts focused largely on chemical carcinogenesis, but more recently his focus has been on toxicities associated with endocrine active agents. He has and continues to serve as Principal Investigator on a series of studies conducted under an Interagency Agreement between the FDA and the National Toxicology Program to evaluate aspects of the hypothesis that exposure to low levels of hormonally active agents, particularly during development, adversely affects human health, including reproductive function and carcinogenesis. He has served on interagency committees evaluating carcinogens and endocrine active agents, including several EPA advisory panels relating to endocrine active chemicals.

Dr. Penelope A. Fenner-Crisp is currently a private consultant. She is the former Executive Director of the Risk Science Institute of the International Life Sciences Institute (ILSI), a global, non-profit, scientific organization dedicated to seeking scientific solutions to important public health issues related to food and nutrition, food safety, water quality, chemical safety and environmental health and assessment of human health and environmental risk. She received a B.S. in Zoology from the University of Wisconsin-Milwaukee, an M.A. and Ph.D. in Pharmacology from the University of Texas Medical Branch-Galveston and spent two years at Georgetown University Schools of Medicine and Dentistry as a post-doctoral fellow. Dr. Fenner-Crisp's areas of expertise include human health and environmental risk assessment, toxicology, science policy and its integration into regulatory decision-making and familiarity with environmental regulatory programs and practices, all of which are a continuation of her activities and responsibilities during her 22 years at EPA where she served as a staff toxicologist in the Office of Drinking Water followed by senior management positions in the Office of Pollution Prevention and Toxics and the Office of Pesticide Programs. Her service on EPA advisory committees includes current membership on the Drinking Water Committee of the Science Advisory Board, and past membership on OPPT's National Pollution Prevention and Toxics Advisory Committee and as an ad hoc member of the FIFRA Scientific Advisory Panel (February 2007). She is a member of the board of GreenBlue, a Charlottesville, VA-based not-for-profit organization whose mission is to inspire a transformation in the design of human industry to achieve sustainability. She has served on the board of the American Board of Toxicology. She is a Charter member of the Society for Risk Analysis (SRA), having received its first Risk Practitioner's Award in 1996, the Capital Area Chapter of SRA, and a long-time member of the Society of Toxicology and its National Capital Area Chapter.

Mr. Robert J. Gilliom directs the Pesticide National Synthesis Project of the National Water Quality Assessment Program, U.S. Geological Survey, a position he has held since 1990. In this role, he has had responsibility for the design, execution, and data analysis of studies of pesticides in streams and ground water nationwide. Mr. Gilliom has been a hydrologist with the U.S. Geological Survey since 1978. Prior to directing the Pesticide Project, he served as project chief for USGS San Joaquin Valley Studies from 1984-1989 and was with the Systems Analysis Group, a USGS data-analysis research team, during 1981-1984. Mr. Gilliom received his MS in hydrology from the University of Washington, College of Engineering in 1978, and a BS in Environmental Systems Analysis from Huxley College of Environmental Studies in 1976. Research and publications have focused on water-quality assessment, ranging from statistical methods for data analysis, to regional and national assessments of nutrients, trace elements, and pesticides. Specific research interests and publications have included statistical analysis of data with non-detections, national-scale analysis of pesticide occurrence in hydrologic systems, and the significance of pesticide mixtures to stream ecosystems. Mr. Gilliom has served on numerous advisory committees and groups, including the ILSI committee on "Assessment of Methods to Estimate Pesticide Concentrations in Drinking Water Sources", an EPA committee on "Ecological Impacts from Plant-Incorporated Protectants (PIPs)", and numerous USGS and interagency workgroups involved with the design of water-quality monitoring.

Dr. Ellen B. Gold is Chair of the Department of Public Health Sciences and Chief of the Division of Epidemiology in that Department in the University of California Davis School of Medicine and former Chair of the Graduate Group in Epidemiology. After receiving her PhD, she became a faculty member at The Johns Hopkins University until she moved to the UC Davis faculty in 1988. She has been Principal

Investigator on a number of NIH-funded, peer-reviewed grants and has had continuous NIH research grant funding for over 20 years. These research grants have largely focused over the past 30 years on lifestyle and environmental factors that affect women's reproductive health and cancer risk and include her work for the past 15 years studying the natural history of the menopausal transition, including hormonal and symptomatic changes, in a longitudinal study of a large, multi-racial/ethnic national cohort. She has also authored or co-authored over 150 peer-reviewed publications. She has mentored numerous graduate students and junior faculty and has received a number of outstanding faculty and mentoring awards, is co-Director of the UC Davis Building Interdisciplinary Research Careers in Women's Health program and is a Fellow in the American Association for the Advancement of Science.

Dr. Richard Greenwood is a Research Scientist and Lecturer Emeritus in the School of Biological Sciences at the University of Portsmouth, and is the University Research Degrees Coordinator. In 2007/8 he held a visiting Professorship in L'École des Mines d'Alès, France. He served between 2000 and 2007 on the Board of Directors and as a Trustee of a not for profit company (Lhasa Ltd.) that produces software for the prediction of toxicity. He has been an active member of the Society of Chemical Industry (SCI) since 1978, and has served the Pest Management, and BioActive Sciences Committees in a number of roles including Chair, and Honorary Treasurer. As a member of SCI he has been involved in organising many national and international scientific meetings, including the Neurotox series of meetings. He has worked in a number of areas including mode of action of insecticides, and environmental monitoring. For 20 years he worked on the design, synthesis and toxicity of pyrethroid insecticides, and in particular on the pharmacokinetics of these compounds in insects. More recently he has worked on the toxicodynamics of the neonicotinoid insecticide imidacloprid. He has applied multivariate analytical techniques to this area, with the aim of evaluating the relationships between physicochemical properties and the toxicokinetic behaviour of insecticides. The candidate has over the last ten years applied similar modeling methods in the area of monitoring the chemical quality of environmental waters. This work has led to his coordinating, and being involved in the management of major EU projects, and he is now a contributor to an EU mandated advisory document on best practice in monitoring the chemical quality of surface waters. He is currently serving on the British Standards Institution (BSI) Environmental Monitoring Committee and is project leader for the development of an ISO standard on the application of passive sampling in surface waters. Richard Greenwood's work has been applied in nature and he has worked with pharmaceutical, and agrochemical companies. Work over 4 years (1999-2003) with Bayer led to the development of physiologically based pharmacokinetic models for the behaviour of a wide range of compounds in lepidopteran larvae, and these have been patented. Dr. Greenwood's publications include a range of papers on analytical models of pharmacokinetics and QSAR studies of toxicokinetics of pyrethroids. He has been a member of two previous FIFRA SAPs, one in August, 2007, and one in June, 2009; both panels dealt with aspects of the toxicity of pyrethroid insecticides.

Dr. Daniel A. Griffith is an Ashbel Smith Professor and a faculty member in the School of Economic, Political and Policy Sciences (previously, Social Sciences) at UT-Dallas, Associate Program Head of the Geography-Geospatial Sciences Program in the Geographic Information Sciences, editor of Geographical Analysis (2008-2011), and a member of the Steering Committee of the Commission of Modeling Geographical Systems, International Geographical Union (2008-2012). He teaches courses about spatial statistics, GIScience research design, mathematical statistics, and spatial organization and concepts. His primary areas of research are in spatial statistics, quantitative urban and economic geography, and applied statistics. In chronological order, he held faculty positions at Ryerson Polytechnical University, at SUNY/Buffalo, at Syracuse University, and at the University of Miami, before moving to UT-Dallas in 2005. He has been a visiting professor at Oregon State University (under the auspices of the USEPA EMAP Program), Erasmus University/Rotterdam, University of Rome I (La Sapienza), Cambridge University (under the auspices of the Leverhulme Trust), and University of Jyväskylä. He also has been an American Statistical Association Research Fellow to USDA-NASS, a visiting researcher at the Max Planck Institute for Demographic Research/Rostock (Germany), a Fulbright Research Fellow (to the University of Toronto), a Fulbright Senior Specialist (to the University of Alberta), a Guggenheim Fellow, an elected Fellow of the New York Academy of Sciences, an elected founding fellow of the Spatial Econometrics Association, and a past president of the North American Regional Science Council.

Dr. William Hayton is a Professor Emeritus of Pharmacy in the Division of Pharmaceutics at The Ohio State University where he also serves as the Associate Dean for Graduate Studies and Research. His formal training includes the BS in Pharmacy degree (1967, University of Washington, Seattle), and the PhD degree in Pharmaceutics (1971, State University of New York at Buffalo). Dr. Hayton's expertise is pharmacokinetics, particularly construction and validation of mathematical models that describe or explain the kinetics of complex biological systems. Dr. Hayton's expertise extends to interspecies scaling of pharmacokinetic model parameter values and xenobiotic metabolism. Dr. Hayton was a member of the Washington State University College of Pharmacy faculty for 19 years before coming to Ohio State in 1990 as Chair of the Division of Pharmaceutics. Dr. Hayton is author or co-author of more than 100 peer-reviewed scientific publications, many of which report on the pharmacokinetics of xenobiotics. He served on the EPA Science Advisory Board Perfluorooctanoic Acid Risk Assessment Review Panel (2005) and as a peer reviewer of EPA's document "Harmonization in Interspecies Extrapolation: Use of BW^{3/4} as Default Method in Derivation of the Oral RfD" (2006). He has held peer-reviewed grant support from the NIH, EPA, AFOSR, FDA, and USFWS.

Dr. Nelson D. Horseman is a Professor in the Department of Molecular and Cellular Physiology and the Department of Medicine at the University of Cincinnati. Dr. Horseman has a Ph.D. in Physiology from the Louisiana State University and an M.S. and a B.S. degree in Biology from Eastern Kentucky University. The Horseman Lab at the University of Cincinnati currently conducts research in the area of hormonal control of breast development, breast cancer risk and mammary biology. The lab's current research focuses on identifying genes that act during the earliest stages of mammary gland differentiation. Dr. Horseman has many publications related to endocrine hormones and their role in mammary gland development and physiology.

Dr. Travis Jerde is currently an Assistant Professor of Pharmacology and Toxicology in the Department of Pharmacology and Toxicology at the Indiana University School of Medicine. He completed his Ph.D. in Pharmaceutical Sciences and the University of Wisconsin School of Pharmacy and undergraduate work in Bacteriology at the College of Agriculture and Life Sciences at the University of Wisconsin in Madison. In 2005 - 2010 he was a Postdoctoral Fellow at the Paul P. Carbone Comprehensive Cancer Center at the University of Wisconsin School of Medicine and Public Health. His current research focuses on studying how inflammatory and developmental signaling interplay to promote cell survival and proliferation in the inflamed microenvironment of the prostate. Dr. Jerde has received a number of honors and awards related to his research and has a number of recent publications related to inflammation and hyperplasia of the prostate.

Dr. James L. McManaman is a Professor of Obstetrics and Gynecology and Chief of the Division of Reproductive Sciences at the University of Colorado, Anschutz Medical Campus. He joined the Neurology Faculty at Baylor College of Medicine where he worked on motoneuron survival factors. Dr. McManaman was recruited to Synergen Inc. in 1992 as head of their Neuroscience Group. Following the sale of Synergen to Amgen in 1993, Dr. McManaman returned to academics at the University of Colorado's medical campus where he remains. At the University of Colorado, Dr. McManaman developed active interest in mammary gland biology, lipid metabolism, preterm birth and perinatal biology, which are currently his primary research interests. Dr. McManaman is the Research Director of the NIH funded Women's Reproductive Health Research Program at the University of Colorado and he directs the University's Frontiers in Pregnancy Research Symposia, a nationally recognized symposia that focuses on biological, psychosocial and clinical research related to pregnancy and perinatal biology. Dr. McManaman is also the Co-Director of the Adipose Biology Program of the University of Colorado's Obesity Research Initiative. He has served on a number of advisory panels including being a regular member of the Integrated Clinical Endocrinology and Reproduction (ICER) Study Section at NIH from 2005-2009 and an Ad Hoc reviewer for a variety of other NIH Study Sections.

Dr. M.E. (Bette) Meek is currently the Associate Director of Chemical Risk Assessment with the McLaughlin Institute of the University of Ottawa on interchange from Health Canada, where she manages the Existing Substances Division in the Safe Environments Programme. Her responsibilities in this capacity relate to development and implementation of process and methodology for the assessment of the effects on human health of Existing Substances under the Canadian Environmental Protection Act,

including setting priorities for assessment from among all 23, 000 commercial chemicals used in Canada by September, 2006 (i.e., categorization). She has considerable experience in the development of methodology for and evaluation of health-related data on environmental contaminants, having also managed previously programmes within Health Canada on contaminants of drinking water and air. She acts as an advisor to several international organizations and has authored over 150 scientific publications in this area. Specific areas of experience include development of frameworks to increase transparency in the assessment of human relevance of animal modes of action, increasing incorporation of biological data in dose-response as a replacement for default, development of predictive exposure and hazard modeling and increasing efficiency in assessment through effective problem formulation and early and continuing peer engagement. Dr. Meek has an M.Sc. in Toxicology from the University of Surrey, U.K. and a Ph.D. in Risk Assessment from the University of Utrecht, the Netherlands.

Dr. Kevin T. O'Byrne is a Research Scientist within the Division of Reproduction and Endocrinology at King's College London, UK. Dr. O'Byrne has a Ph.D. in Neuroendocrinology from the University of Bristol and is a specialist in stress physiology. Kevin O'Byrne has over thirty years experience in integrative neuroendocrinology focusing on the impact of stress on the gonadotrophin-releasing hormone (GnRH) pulse generator, a hypothalamic oscillator that is critical for controlling the reproductive system. During this period he has not only identified several key neural mechanisms underlying stress-induced infertility in a wide range of species, but elucidated long-term programming effects of adverse early life events on stress responsiveness in adulthood. Additionally, the impact of gonadal steroids, xenoestrogens and phytoestrogens (plant derived) on the operational characteristics of the GnRH pulse generator have been studied. He also has a heavy teaching and administrative load within King's College London. He has been an advisor to the UK Home Office on animal experimental procedures and helped establish a Centre of Neuroendocrinology at the University of Wenzhou Medical School, China. Kevin O'Byrne serves on the executive committee of several scientific societies in the UK and editorial board member of several international journals.

Dr. Katherine Roby is a Research Associate Professor of Anatomy and Cell Biology and the Director of the Reproductive Endocrinology Laboratory within the Center for Advanced Reproductive Medicine at the University of Kansas Medical Center. Dr. Roby received her Ph.D. from the University of Kansas Medical Center in Reproductive Physiology studying the role of tumor necrosis factor in ovarian follicle development and ovulation. Following her Ph.D. studies she carried out two post-doctoral fellowships first in the laboratory of Dr. Michael J Soares focusing on placental trophoblast differentiation and the role of the fetus in placental development and then in the laboratory of Dr. Joan S Hunt focusing on the immunology of the uterus and placenta. During her post-doctoral fellowships Dr. Roby received a Wesley Foundation Fellowship for Cancer Research and a National Institutes of Health (NIH)-National Research Service Award. Dr. Roby's current research is focused in two areas. The first area of focus is in understanding the role of intraovarian factors in follicle development and ovulation including tumor necrosis factor, Src tyrosine kinase, and serum amyloid A. The second area of focus is the biology of ovarian cancer including identifying new drug targets, developing new drug treatments and defining ovarian cancer specific genetic signatures that will allow for the development of clinical screening methods. She has served on multiple scientific review panels for NIH and The Department of Defense. Dr. Roby is the Director of the Reproductive Endocrinology Laboratory a high complexity CLIA certified laboratory carrying out clinical endocrinology and andrology testing.

Dr. Barry G. Timms is a Professor in the Division of Basic Biomedical Sciences, Sanford School of Medicine, at the University of South Dakota. He has a Ph.D. from University of Wales College of Medicine in the U.K. and a M. Phil. in Biological Sciences from the Aston University also in the U.K. Dr. Timms studies prostate growth and development, and in particular, the complex ductal architecture of the gland during fetal development using sophisticated 3-dimensional computerized serial section reconstruction. His current research focuses on two main areas: a) the cellular mechanisms controlling proliferation and differentiation of the prostate, and b) the effect of environmental endocrine disruptors on ductal growth patterns. Dr. Timms has published extensively in the area of prostate growth and development and has current support from several organizations to continue research in this area.

Dr. Heather A. Young is an Associate Professor of Epidemiology and Biostatistics at The George Washington University School of Public Health and Health Services. She has ten years of experience in epidemiologic and biostatistical consulting and has taught numerous courses in graduate epidemiology and biostatistics to public health and health professions students. She completed her MPH and PhD in epidemiology at The George Washington University. She currently teaches courses in Advanced Data Analysis for Public Health, Design of Health Studies, and Pesticides and Cancer. Her areas of research interest include cancer particularly reproductive cancers, environmental and occupational exposure assessment, reproductive outcomes related to environmental and occupation exposures, pesticide exposure assessment, and health of military and veteran populations. Dr. Young is involved in research examining cancer patterns in Gulf War veterans, reproductive outcomes in Army Chemical Corps Veterans exposed to dioxin during Vietnam, cancer disparities in the District of Columbia, and breast cancer patient navigation in the District of Columbia. In addition, she has served as a technical advisor for data issues for DC's HIV AIDS Administration and as a statistical consultant on several veterans' health studies for the Institute of Medicine's Medical Follow-Up Agency. She has also published papers examining ovarian cancer risk in the Central Valley of California as related to triazine exposure and has extensive knowledge of California's Pesticide Usage Database.