

Predicting human dose-response relationships
from multiple biological models:
Issues with *Cryptosporidium parvum*

September 28, 2000

USDA Center at Riverside
Riverdale, Maryland

The purpose of this meeting is to facilitate discussion with the scientific community and the public on dose-response modeling of foodborne pathogens. We will discuss the use of human and nonhuman models of infection and disease to predict human dose-response relationships, focusing on the water- and foodborne parasite *C. parvum* as a model organism for other foodborne pathogens.

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multiple biological models:
Issues with *Cryptosporidium parvum***

Interagency Risk Assessment Consortium
Public Meeting
September 28, 2000

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PROGRAM

8:30 - 9:00 Registration

Morning Session I

9:00 - 9:20 Welcome and introduction
Wes Long, Ph.D., Food and Drug Administration, Center for Food Safety and Applied Nutrition, Washington, D.C., and Joint Institute for Food Safety and Applied Nutrition, Washington, D.C., and College Park, Md.

9:20 - 9:45 The Importance of Dose-Response Modeling to the Public
William K. Hallman, Department of Human Ecology, Rutgers University, New Brunswick, N.J.

9:45 - 10:10 Public Comment Period

10:10 - 10:25 BREAK

Morning Session II

10:25 - 10:30 Introduction
Stephen Schaub, Ph.D., U.S. Environmental Protection Agency, Office of Water, Washington, D.C.

10:30 - 10:55 Host Factors Affecting *C. parvum* Infection
John Balbus, M.D., Ph.D., George Washington University School of Public Health and Health Services, Center for Risk Science and Public Health and Department of Environmental and Occupational Health, Washington, D.C.

10:55 - 11:20 Genotyping *Cryptosporidium* for the identification of infection and contamination sources
Altaf Lal, Ph.D., Centers for Disease Control and Prevention, Division of Parasitic Diseases, Atlanta, Ga.

11:20 - 11:45 Host-Parasite Interactions
Honorine Ward, M.B.B.S., Tufts University School of Veterinary Medicine, Division of Infectious Diseases, and New England Medical Center, Division of Geographic Medicine and Infectious Diseases, Boston, Ma.

11: 45 - 12: 55 Lunch (on your own)

Afternoon Session I

12:55 - 1:05 Introduction
Peg Coleman, M.S., United States Department of Agriculture, Food Safety and Inspection Service, Washington, D.C.

1:05 - 1:35 Comparison of Cell Culture and Animal Assays for Measuring Infectivity of *Cryptosporidium parvum*
Ricardo De Leon, Ph.D., Metropolitan Water District of Southern California, Water Quality Laboratory, La Verne, Calif.

1:35 - 2:05 Cell Culture and Animal Models of *C. parvum* Infection
Theresa Slifko, University of South Florida, Department of Marine Sciences, Tampa, Fla.

2:05 - 2:20 Break

2:20 - 2:50 Dosage- and isolate-dependent response of IFN γ -knockout mice to *Cryptosporidium parvum* infection
Saul Tzipori, Ph.D., Sc.D., and Stephen Rich, Ph.D., Tufts University School of Veterinary Medicine, Division of Infectious Diseases, N. Grafton, Ma.

2:50 - 3:20 *Cryptosporidium parvum*: Infectivity in Healthy Volunteers and Laboratory Animal Models.
Cynthia Chappell, Ph.D., University of Texas School of Public Health, Center for Infectious Diseases, Houston, Tex.

Afternoon Session II: Panel discussion of dose-response modeling

3:30 – 5:00 *Panel members include Afternoon Session I speakers (Peg Coleman, Ricardo De Leon, Theresa Slifko, Saul Tzipori, and Cynthia Chappell),*

and panel discussants Jack Colford, M.D., Ph.D., University of California Berkeley School of Public Health, Department of Epidemiology, Berkeley, Calif.; Charles Haas, Drexel University, School of Environmental Science, Engineering, and Policy, Philadelphia, Pa.; and Mary Alice Smith, Ph.D., University of Georgia, Department of Environmental Health Sciences, Athens, Ga.

5:10 – 5:15 Conclusion and discussion

Session Chairs

Morning Session I Chair – Wes Long, Ph.D.

Dr. Long began his government career in 1991 in the Center for Food Safety and Applied Nutrition's Office of Premarket Approval. He has held numerous positions since then, including a brief stint with private industry. His current position is as the FDA Associate Scientific Director for the Joint Institute for Food Safety and Applied Nutrition (JIFSAN), with primary responsibilities for coordinating the development of collaborative programs between the University of Maryland and the FDA in the area of risk analysis. In addition, he chairs the Interagency Risk Assessment Consortium, composed of 18 federal agencies with food safety risk analysis responsibilities. Dr. Long received his Ph.D. in Inorganic Chemistry from Arizona State University.

Morning Session II Chair – Stephen Schaub, Ph.D.

Dr. Schaub has worked as Senior Microbiologist for the Office of Water, U.S. Environmental Protection Agency, since 1992. In this position, he provides expert scientific guidance and consultation on public health/environmental health microbiology issues related to the development and implementation of regulations for drinking water and ambient waters in the U.S. He also provides expertise for the establishment of EPA programs on recreational waters and shellfish-growing waters, and for water-related food safety and microbial risk assessment initiatives. In addition, he is co-lead for the Office of Water's pathogen strategy for the future. From 1972 to 1992, Dr. Schaub worked for the U.S. Army Office of the Surgeon General as a Water Supply Research Program Manager and Supervisory Research Microbiologist. In these positions, he led research activities aimed at protecting soldiers from microbial diseases associated with water supplies, determined pathogen treatment effectiveness of military water equipment, developed analytical methods for pathogens and indicators, and established current U.S. military/NATO combat drinking water standards. Dr. Schaub received a B.S. in Bacteriology and Public Health from Washington State University and an M.S. and Ph.D. in Microbiology from the University of Texas at Austin.

Afternoon Sessions I and II Chair – Peg Coleman, M.S.

Peg Coleman has found fascinating challenges in dose-response modeling and predictive microbiology applied to food safety hazards concerning the USDA Food Safety and Inspection Service (FSIS) for the past eight years. She has had a number of opportunities to publish and speak about her collaborative work in dose-response modeling for bacterial pathogens at national and international fora. Peg's professional activities include service as current President of the Dose-Response Specialty Group of the Society for Risk Analysis, as the FSIS representative on the Risk Assessment Consortium and its Dose-Response Working Group, and as a journal reviewer for Quantitative Microbiology. Her academic credentials include two M.S. degrees (Medical Microbiology, University of Georgia; Biology/Biochemistry, Utah State University) and a B.S. degree (Biology/Chemistry, State University of New York, College of Environmental Science and Forestry at Syracuse). nonetheless

The Importance of Dose-Response Modeling to the Public

William K. Hallman, Ph.D., Department of Human Ecology, Rutgers University, New Brunswick, N.J.

Dr. William Hallman is an Associate Professor in the Department of Human Ecology at Rutgers University where he teaches courses on risk perception, risk communication, research methodology, and the politics of environmental issues. He received his M.A. and Ph.D. in Psychology from the University of South Carolina and was honored with the Dissertation of the Year award from the Division of Community Psychology of the American Psychological Association for his work. Dr. Hallman has written more than twenty-five papers, articles, and book chapters concerning public perceptions of risks, risk communication, and the ways that individuals and communities cope with perceived environmental threats. He is a member of the American Psychological Association, the American Evaluation Association, and the Society for Risk Analysis, and has served as a consultant to state and federal agencies, utilities, industry associations, private corporations, and non-profit groups.

Dose-response calculations play an important part in determining regulatory policies. However, determining appropriately protective dose levels is a difficult task, and regulatory decisions involving dose-response models must also take into consideration available technologies, likely impacts on health and the environment, regulatory and economic burdens, unintended consequences, and ultimately, public understanding, acceptance, and approval. As such, communicating about dose-response relationships with the public is an important part of the process. Key to communicating about the potential impacts of microbial risks is to understand what people already know, how they know it, and what they want to know. Successfully incorporating new information depends a great deal on whether one has an appropriate context in which to fit new ideas. Studies suggest that much of the public has a difficult time understanding chemical dose-response relationships and that much of what they know about microbiology is rooted in popular culture. Studies also suggest that many in the public have difficulties understanding quantitative and probabilistic data. Because of this, explaining microbial dose-response faces significant barriers. Nonetheless, communicating about dose-response with the public is possible, necessary, and important to ensure that people have the tools they need to understand and participate in regulatory decisions that may affect them.

Host Factors Affecting *C. parvum* Infection

John Balbus, M.D., Ph.D., George Washington University School of Public Health and Health Services, Center for Risk Science and Public Health and Department of Environmental and Occupational Health, Washington, D.C.

John Balbus is currently Director of the Center for Risk Science and Public Health and an Associate Professor of Environmental and Occupational Health at the George Washington University School of Public Health and Health Services. Dr. Balbus is a physician boarded in both Internal Medicine and Occupational and Environmental Medicine. He received his M.P.H degree from the Johns Hopkins School of Hygiene and Public Health, his M.D. degree from the University of Pennsylvania, and his undergraduate degree in biochemistry from Harvard University. Dr. Balbus is the Principal Investigator on a cooperative agreement with the U.S. Environmental Protection Agency's Office of Water, which focuses on a number of issues related to risk assessment for drinking water contaminants. Projects under the cooperative agreement include a survey of drinking water beliefs and practices in the metropolitan Washington, D.C., area, characterization of susceptibility factors for microbial and chemical exposures, definition of outcomes of waterborne microbial infections, and study of calicivirus infections among children in Washington, D.C. Dr. Balbus' research interests also include lead neurotoxicity and health effects of global climate change. He has served as technical consultant and author for the health sector for both the United Nations Environmental Programme project on global climate change and the United States Country Studies program.

Genotyping *Cryptosporidium* for the identification of infection and contamination sources

Altaf Lal, Ph.D., Centers for Disease Control and Prevention, National Center for Infectious Diseases, Division of Parasitic Diseases, Atlanta, Ga.

Dr. Lal is chief of the Molecular Vaccine Section of the Immunology Branch of the CDC's Division of Parasitic Diseases, which conducts laboratory and field studies on important issues of parasitic diseases and the interaction between HIV/AIDS and parasitic diseases. He received his B.S. in Botany from the University of Kashmir (India), his M.S. in Biochemistry from Lucknow University (India), and his Ph.D. in chemistry from Kanpur University/Central Drug Research Institute (India). He was subsequently a Fogarty International Visiting Fellow at the Laboratory of Cell Biology in the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH), and a Rockefeller Foundation Fellow/Visiting Associate at the Laboratory of Parasitic Diseases at NIH's National Institute of Allergy and Infectious Diseases. He has been at the CDC since 1989. Dr. Lal has numerous publications and international collaborations, including projects in Papua New Guinea, Brazil, India, Kenya, Gabon, Thailand, Cameroon, and Venezuela.

To clarify the taxonomy and public health significance of *Cryptosporidium* parasites and to develop molecular tools for the diagnosis of *Cryptosporidium* oocysts in clinical and environmental samples, we conducted multilocus genetic characterizations of *Cryptosporidium* isolates from humans, farm animals, companion animals, and wildlife. Sequence analyses of the SSU rRNA, HSP70, COWP, and actin genes have supported the presence of multiple *Cryptosporidium* species, such as *C. parvum*, *C. felis*, *C. saurophilum*, *C. baileyi*, *C. serpentis*, and *C. muris*. Several previously unnamed species (*Cryptosporidium* spp in snakes, tortoises, finches, geese, etc.) were also found. These studies also revealed the presence of numerous host-adapted *C. parvum* genotypes (human, monkey, bovine, mouse, pig, ferret, marsupial, opossum, dog, fox, bear, skunk). These *C. parvum* genotypes were closely related to *C. wrairi*, *C. meleagridis*, and *C. felis*, and were members of a larger *C. parvum* group.

These molecular studies have led to the development of various *Cryptosporidium* diagnostic tools at species, genotype, and subgenotype levels. A TRAP-C2-based PCR-RFLP technique was first developed for the differentiation of human and bovine genotypes of *C. parvum*. Subsequently, an SSU rRNA-based PCR-RFLP tool was developed to differentiate various *Cryptosporidium* species and *C. parvum* genotypes. Several confirmation tests were also developed for species differentiation and genotyping based on sequencing analysis of HSP70, COWP, and actin genes. More recently, sequence analyses of the HSP70 and double-stranded RNA have led to the development of subgenotyping techniques for human and bovine genotypes of *C. parvum*.

These species-differentiation, genotyping, and subgenotyping tools have been used

extensively in the analysis of clinical samples from the United States and abroad. The TRAP-C2 technique was used in the identification of two transmission cycles of human cryptosporidiosis. The use of the SSU rRNA-based PCR-RFLP has led to the identification of non-*C. parvum* *Cryptosporidium* parasites (*C. meleagridis* and *C. felis*) in AIDS patients in the United States, Switzerland, and Kenya. More recently, these non-*C. parvum* *Cryptosporidium* spp and the dog genotype of *C. parvum* have also been found in HIV-negative Peruvian children. These genotyping and subgenotyping tools have also been successfully used in the investigation of foodborne and water-borne outbreaks of cryptosporidiosis. Results of these studies have helped to clarify the public health significance and transmission dynamics of different *Cryptosporidium* parasites.

More recently, we have used the SSU rRNA-based PCR-RFLP technique in conjunction with immunomagnetic separation to identify species and sources of *Cryptosporidium* oocysts present in water samples. The identification of *Cryptosporidium* oocysts in environmental samples is traditionally made by the use of immunofluorescent assay (IFA). Because IFA detects oocysts from almost all *Cryptosporidium* parasites, the species distribution and source of *Cryptosporidium* parasites in environmental samples is unclear. Analysis of storm water samples collected at one New York site with the SSU rRNA-based PCR-RFLP technique revealed the presence of a total of 12 wildlife *Cryptosporidium* genotypes, only four of which could be attributed to sources. In contrast, four common genotypes (*C. parvum* human and bovine genotypes, *C. andersoni*, and *C. baileyi*) were found in surface water samples and 7 genotypes were found in raw wastewater samples. The most common *Cryptosporidium* were the *C. parvum* human and bovine genotypes and *C. andersoni* in surface water, and *C. andersoni* in wastewater. Mixed genotypes were present in some storm and surface water samples.

In summary, molecular studies have helped to clarify the taxonomy of *Cryptosporidium* parasites and have increased our understanding of the epidemiology and transmission of *Cryptosporidium* parasites. These studies received collaborative support from several investigators working on epidemiology and laboratory aspects of cryptosporidiosis, and were jointly funded by CDC, EPA, and USDA. The combination of efforts of different investigators and the joint funding of the projects by several agencies has increased our understanding of the nature of the pathogen and has led to the development of diagnostic tools that are required for epidemiological studies and for monitoring pathogens in water. As we proceed, the following research areas need attention. (1) Further molecular studies need to be conducted to assess the public health importance of animal *Cryptosporidium* parasites. This requires the characterization of *Cryptosporidium* parasites from additional animal species and analysis of large numbers of *Cryptosporidium* samples from humans in different regions. (2) There is a need to examine the species structure, public health importance, and contamination sources of *Cryptosporidium* oocysts in water. This requires molecular characterization of *Cryptosporidium* oocysts in various waters (e.g., storm water, source water, finished water, wastewater) in various geographic locations, and systematic characterization of *Cryptosporidium* dispersal in different environmental settings (i.e., feral, rural, urban). (3) There is a need to examine the transmission dynamics of human cryptosporidiosis by systematic analyses of *Cryptosporidium* in humans, animals, and the environment in a given location, using species-differentiation, genotyping, and subgenotyping tools. Molecular tools now exist to answer each of these questions.

Host-Parasite Interactions

Honorine Ward, M.B.B.S., Tufts University School of Veterinary Medicine, Division of Infectious Diseases, and New England Medical Center, Division of Geographic Medicine and Infectious Diseases, Boston, Ma.

Dr. Honorine Ward is an Assistant Professor of Medicine at the Division of Geographic Medicine and Infectious Diseases at the New England Medical Center, Tufts University School of Medicine, and at the Division of Infectious Diseases, Tufts University School of Veterinary Medicine. She has an M.B.B.S. (U.S. equivalent M.D.) from Christian Medical College, Vellore, India. Her publications and presentations at scientific meetings have been on host-parasite interactions involved in the pathogenesis of intestinal protozoal infections, particularly those caused by Giardia lamblia and C. parvum.

Host-parasite interactions occur at a number of stages during the process of infection with Cryptosporidium. The initial host-parasite interactions of attachment and invasion are crucial primary steps in the pathogenesis of cryptosporidiosis. Ultrastructural studies have shown that sporozoites attach to host cells by their anterior pole. Attachment is followed by invagination of the host cell's plasma membrane, which extends along the surface of the sporozoite and eventually completely surrounds it, leading to formation of a parasitophorous vacuole where the parasite undergoes further development in a unique intracellular but extracytoplasmic location. Using *in vitro* models of sporozoite attachment to epithelial cells, studies have shown that attachment is dose- and time-dependent, is influenced by pH, divalent cations, and the degree of differentiation of host cells. In addition, sporozoite motility and invasion have been shown to be dependent on parasite and host cell cytoskeletal elements. However, although ultrastructural details and various factors affecting attachment and invasion have been characterized, little is known about the molecular basis of these initial host-parasite interactions or of the specific parasite and host molecules that mediate them. Knowledge of such molecules is crucial for understanding the pathogenic mechanisms involved in the host-parasite interaction and for designing preventive and interventional strategies to combat cryptosporidiosis. A few *C. parvum* surface proteins have been implicated in attachment and invasion and are the subject of ongoing investigation. Similarly, a few host surface molecules have also been postulated to play a role in these processes. This presentation reviews the existing knowledge of the molecular basis of these host-parasite interactions and of specific molecules that may be involved in them.

**Comparison of Cell Culture and Animal Assays for Measuring Infectivity of
*Cryptosporidium parvum***

Ricardo De Leon, Ph.D., Metropolitan Water District of Southern California, Water
Quality Laboratory, La Verne, Calif.

Dr. De Leon is the Principal Microbiologist for the Metropolitan Water District of Southern California, a position he has held since 1994. He was previously an assistant professor in the Department of Environmental Analysis and Design, University of California at Irvine, and a Research Assistant Professor in the Department of Environmental Sciences and Engineering, University of North Carolina at Chapel Hill. He received both a B.S. and a Ph.D. in Microbiology from the University of Arizona in Tucson. His publications are in the area of detection of viruses and parasites in water supplies.

***Cryptosporidium parvum*:**
Infectivity in Healthy Volunteers and Laboratory Animal Models

Cynthia Chappell, Ph.D., University of Texas School of Public Health, Center for Infectious Diseases, Houston, Tex.

Cynthia Chappell is an Associate Professor of Parasitology at the University of Texas School of Public Health in Houston and an Associate Professor in the Department of Internal Medicine (Division of Infectious Diseases) at the University of Texas Medical School. She is also Director of the School of Public Health's Center for Infectious Diseases. Her previous positions include Assistant Professor in the Department of Microbiology and Immunology at the Baylor College of Medicine. Her B.S. and M.S. degrees are from Middle Tennessee State University and she received a Ph.D. in Microbiology and Immunology from Baylor, where she also did postdoctoral work. She has published extensively in the area of Cryptosporidium research.

Cryptosporidium parvum causes infection in humans and animals and has been associated with many community outbreaks of disease. Currently developed animal models fall short of providing good surrogates for cryptosporidiosis in healthy adults due to differences in GI anatomy, physiology, and/or maturity. In addition, many models require immunosuppression and are inadequate for studying the normal immune response to the disease. Studies in healthy volunteers compared three *C. parvum* genotype 2 isolates (IOWA, UCP, TAMU) for their infectivity and virulence. Dose response studies revealed that the ID₅₀ for these isolates varied from 9 (TAMU) to 87 (IOWA) to 1042 (UCP) oocysts. These data provide an opportunity to evaluate animal and *in vitro* systems for their utility as human surrogates. The present study was designed to test the infectivity of these same *C. parvum* isolates in CD1 neonatal mice and HCT-8 cells. Dose response studies of 4- to 6-day-old mice yielded ID₅₀'s from 30 oocysts to 99 oocysts. Although the ID₅₀'s did not vary dramatically in mice, the TAMU dose-response curve was lower than the curves for the other two isolates, which grouped together. The relationship to human infectivity was examined by plotting mouse ID₅₀'s against the human ID₅₀'s ($r^2 = 0.548$). The resulting curve illustrated the inability of the mouse model to differentiate well between two of the isolates, even though these two isolates showed more than a 10-fold difference in humans. In comparison, isolate infectivity for HCT-8 cells varied from 24.7 \forall 1.6% to 59.5 \forall 7.1% with TAMU being significantly higher than the other isolates studied ($p \neq 0.01$). Further, a highly significant ($r^2 \ni 0.933$) correlation was seen in infectivity between HCT-8 cells and healthy volunteers, suggesting that this human enterocyte cell line may serve as a useful and sensitive surrogate model for human *C. parvum* infection.

Dosage- and isolate-dependent response of IFN γ -knockout mice to *Cryptosporidium parvum* infection

Saul Tzipori, Ph.D., D.Sc., and Stephen Rich, Ph.D.

Dr. Tzipori is Professor and Division Head in Infectious Diseases, Department of Biomedical Sciences, Tufts University School of Veterinary Medicine, N. Grafton, Ma. He is also Professor, Division of Geographic Medicine and Infectious Diseases, New England Medical Center, Boston, Ma. He received his D.V.M. and Ph.D. degrees from Queensland University in Australia, and a D.Sc. from Melbourne University in Australia. In 1990, he was made a Fellow of the Royal College of Veterinary Surgeons in London for meritorious contribution to learning.

Cell Culture and Animal Models of *C. parvum* Infection

Theresa Slifko, University of South Florida, Department of Marine Sciences, Tampa, Fla.

Theresa Slifko is a graduate student in the laboratory of Joan Rose in the Department of Marine Sciences, University of South Florida, Tampa. She has won several awards for her research on cell culture methodology and has more than 20 publications. She will be working with Orange County Utilities in Florida after graduation.

Panel Discussants

Jack Colford, M.D., Ph.D., is a graduate of the Johns Hopkins School of Medicine. He completed a residency in Internal Medicine and a fellowship in Infectious Diseases at the University of California, San Francisco. He was Chief Resident in Medicine at Stanford University Hospital. He received a Ph.D. in Epidemiology from the University of California Berkeley School of Public Health, where his primary appointment is now as Assistant Professor of Epidemiology. He is the sole instructor in graduate level courses on epidemiological methods, clinical/intervention trial design, and meta-analysis at UC Berkeley. He has also taught as visiting faculty at the University of Michigan and the University of Zurich. He has a joint appointment as an Attending Physician at the UCSF/San Francisco VA Medical Center Infectious Diseases Clinic.

His research interests include the health effects of drinking water and the methodologies employed in the study of waterborne infectious diseases such as cryptosporidiosis. He is the Principal Investigator of four federally-funded, randomized, placebo-controlled trials evaluating in-home drinking water interventions. These trials (WET, or Water Evaluation Trials) include studies in both immunocompetent populations--PILOTWET in Walnut Creek, Calif., (CDC/EPA), and BIGWET (CDC/EPA) in Davenport, Iowa--and immunocompromised populations--HIVWET (Univ. of CA/CDC/EPA) in San Francisco, Calif., and the elderly in SonomaWET (NIH/NIA) in Sonoma, Calif.

Panel Discussants

*Charles N. Haas is the L.D. Betz Professor of Environmental Engineering at Drexel University, where he has been on the faculty since 1991. He has over 20 years of experience in environmental engineering and science. Professor Haas received his B.S. in Biology and his M.S. in Environmental Engineering from the Illinois Institute of Technology, and his Ph.D. in Environmental Engineering from the University of Illinois at Urbana-Champaign. He has received a number of honors, including the Ellet and Chanute awards from the Western Society of Engineers, and he is a Fellow of the American Academy of Microbiology. Professor Haas has served on three committees of the National Research Council, on potable water reuse, on the New York City water supply, and (currently) on priority setting for drinking water contaminants. He is the Chairman of the US Committee of the International Water Association, and the founding editor in chief of Quantitative Microbiology. He is a past member of the editorial board of Applied and Environmental Microbiology. He has received funding from a variety of government (federal, state, and local) agencies, and from the private sector. His primary research interests are in the quantitative risk assessment of public health threats (especially microorganisms), and in the control of microbial exposures by disinfection, and water and waste treatment processes. He has also performed research in hazardous and industrial waste treatment. He is the author of ten books and over 150 papers. He was the major co-author of *Quantitative Microbial Risk Assessment*, which was published by Wiley in May, 1999, and is the first comprehensive treatment of its subject.*

Panel Discussants

*Mary Alice Smith is an Associate Professor in the Department of Environmental Health Science at the University of Georgia. She graduated with a B.S. degree in biology education from Auburn University, an M.A.T. degree in science education and an M.S. degree in Developmental Biology from Emory University, and a Ph.D. degree in Toxicology from the University of Arkansas for Medical Sciences. Dr. Smith conducts research on the effects of chemical and microbial exposures during reproduction and development. Her focus is on understanding and predicting biological and chemical hazards during development, and she is currently developing a dose response model for *Listeria monocytogenes* exposure during pregnancy. Dr. Smith teaches courses in environmental toxicology and risk assessment. She holds an appointment in the College of Pharmacy at the University of Georgia, and she is a Collaborative Scientist in the Division of Research Resources at the Yerkes Regional Primate Research Center, Atlanta, GA. Before coming to the University of Georgia, Dr. Smith worked in private industry as a consultant in toxicology and risk assessment and as a high school biology teacher. Dr. Smith is a member of the Society of Toxicology, Society of Risk Analysis, and the Teratology Society. She has served as a peer reviewer for health assessments conducted by the Agency for Toxic Substances and Disease Registry in Atlanta, Ga.*

Acknowledgements

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