Peer Consultation of Harmonized PBPK Model for Trichloroethylene
Background, Panel Members, and Disclosures
June 29, 2004

Background

Toxicology Excellence for Risk Assessment (*TERA*) is receiving funds from the U.S. Air Force (USAF) (through a subcontract with ManTech) to coordinate this peer consultation meeting on physiologically-based pharmacokinetic (PBPK) modeling of trichloroethylene (TCE) and its metabolites. This process is intended to assist in the protection of the public's health from exposure to this chemical by providing an open and transparent discussion of PBPK modeling issues.

Peer consultation is a process of seeking advice and input on a work product; this process could occur at one or more points during the development of a work product but often occurs at an early stage. The goal is to obtain information and analysis from experts, stakeholders, and/or members of the public to improve the work product. Peer consultation is different from peer review, which is a process of reviewing a final work product to determine if it is technically sound. Often a peer consultation panel is seeking individual opinions, which may or may not converge, while the peer review panel operates by consensus to reach a common opinion.

The outcome of this peer consultation will be used to make improvements to the harmonized TCE PBPK model; the model then will be made public to facilitate its use and consideration in risk assessments. *TERA* anticipates the results of the peer consultation and resulting harmonized model serve as important input into future TCE risk assessment efforts, including subsequent independent peer reviews and consultations.

Participants

The USAF and the U.S. Environmental Protection Agency (US EPA) are jointly sponsoring the scientific workgroup that has developed the harmonized PBPK model for TCE and its metabolites based on the full range of available science and data. The products from this joint workgroup will serve as important input to ongoing TCE risk assessment activities, including a planned multi-agency consultation with the National Academy of Sciences on TCE science issues as well as EPA's revised TCE human health risk assessment. This workgroup is composed of scientists from the USAF and EPA, with technical expertise from *TERA* and independent scientists. The participants from each organization are listed below:

U.S. Air Force (USAF)
Dave Mattie

U.S. Environmental Protection Agency (EPA)
Jerry Blancato
Weihsueh Chiu
John Lipscomb
Miles Okino
Fred Power

University of Georgia
Jeff Fisher*

ENVIRON
Harvey Clewell*
Tammie Covington*

Toxicology Excellence for Risk Assessment (*TERA*)
Michael Dourson
Eric Hack
Jay Zhao

* Participation sponsored by USAF

TERA's Disclosures as Peer Consultation Coordinator

TERA is a non-profit 501(c)(3) corporation that conducts research and documentation in risk assessment for public and private sponsors. *TERA* is currently working on other projects with author team organizations. For EPA *TERA* is preparing or peer reviewing several risk assessment documents and conducting issue-specific work (e.g., collecting physiological parameters for neonatal animals), and participating on the Candidate Contaminant List workgroup for the Office of Water. *TERA* has a cooperative agreement from EPA to develop and conduct peer consultations. None of the current or previous work for EPA is on TCE, but *TERA* has prepared drinking water criteria documents for EPA on dichloroacetic acid (DCA) and trichloroacetic acid (TCA). *TERA* also has worked jointly on projects with ENVIRON (and with the K.S. Crump Group while they were part of ICF Kaiser); a current project is to conduct Markov Chain Monte Carlo analysis of a PBPK model. *TERA* has collaborated with the USAF on research on health effects and assessment of perchlorate.

TERA is intentionally maintaining a separation in assigning work to our scientists working on the TCE issues and our peer consultation staff, in order to ensure the objectivity of the peer consultation process. Several *TERA* staff members have been facilitating these efforts on the harmonized PBPK model and other issues related to the scientific data for TCE. Different *TERA* employees have organized this peer consultation, including the selection of panel members, development of the charge for the panel, and drafting of the meeting report.

Selection of Panel

The primary criteria for selecting members for the TCE panel were knowledge and experience in PBPK modeling and TCE metabolism. This knowledge and expertise is essential for providing the authors with meaningful advice on the harmonized model at this stage of its development. Therefore, *TERA* concluded that the need for specific expertise outweighed potential concerns regarding bias that might arise from previous or current work related to TCE. The panel members selected do not have conflicts of interests (consistent with *TERA* policy on Conflict of Interest and Bias – http://www.tera.org/peer/COI.html), although most have done previous work on TCE and each brings a background and history of affiliation with various types of organizations. *TERA* has been careful to balance affiliations and backgrounds of these members (i.e., biases) to provide a wide range of views and perspectives. Members of this panel are from universities, government agencies, non-profits, and consulting agencies for government and industry.

TERA, as the independent group convening the peer consultation, was solely responsible for selection of panelists for the peer consultation of the TCE harmonized PBPK model. *TERA* did however ask the author team for suggestions of experts for *TERA* to consider and also to identify issues and questions for the charge.

TERA determined that in order to provide a complete and thorough review of the document it was important to locate scientists with experience in the following key subject areas:

- Metabolism of TCE
- PBPK modeling, evaluation of structure and extent to which model can describe the data sets with a consistent set of model parameters
- TCE metabolites and their effects
- Modeling of TCE and metabolites
- Use of PBPK in risk assessment
- Risk assessment

TERA's conflict of interest policy (see http://www.tera.org/peer/COI.html) identifies the following situations as examples of those that could create a real or perceived conflict of interest.

- Working for an organization that sponsors or contributes to the document to be reviewed,
- Having direct personal financial investments potentially benefiting from the outcome of the review, or
- Authoring or providing significant comments on the document.

Having defined COI generally in our policy, *TERA* then determines specific situations that could be considered a conflict for each individual meeting. Prior to selecting the TCE harmonized PBPK model panel members, *TERA* determined that the following would be conflicts of interest or sources of unacceptable bias and therefore reason to exclude a candidate from selection.

- Member of the author team.
- A significant contributor to the harmonized model. Providing data that are used in the model would not be a conflict.
- Individuals working in the same immediate office as the members of the author team (i.e., EPA/ORD/NCEA/NERL; USAF/AFRL/HEPB, ENVIRON, and the Department of Environmental Health Science, College of Agricultural and Environmental Sciences, University of Georgia) would not be allowed on the panel.
- Individuals with a financial stake in the results of the peer consultation. It is not practical and may not be possible to identify all the companies that manufacture TCE, use TCE currently or in the past, or have environmental liability regarding TCE and query candidates about their financial holdings or relationships with every party; therefore, *TERA* asked candidates directly if they have a financial stake in the outcome of the peer consultation.

The *TERA* COI policy also discusses bias. For these reviews, "bias" means a predisposition towards the subject matter under consideration that could influence the candidate's viewpoint. Examples of bias would be situations in which a candidate:

- Has previously taken a public position on subjects to be discussed, or
- Is affiliated with an industry, governmental, public interest, or other group with a partiality regarding the subjects to be discussed.

Most scientists with technical expertise in areas relevant to a risk assessment document will have existing opinions about some of the subject matter, and therefore, may be considered to have some degree of bias. These biases are considered in panel selection decisions to determine if they will interfere with the panel member's objectivity for the review. However, each panel member is representing his or her own personal views at the meeting and not that of an employer or other organization to which he or she may be affiliated.

Disclosures

None of the panel members has had direct involvement with the development of the harmonized PBPK model for TCE. However, the panel includes a number of experts in TCE metabolism and PBPK modeling who have been involved in development of previous models and some of the data used for this model. Each of the panel members has indicated that they are not aware of any personal financial holdings that have any connection to TCE (including manufacture, use, or environmental liability) or to the harmonized model, nor do they have any known financial stake in the outcome of this peer consultation. In addition each has certified that he or she does not believe he or she holds any personal values or beliefs that would preclude him or her from conducting an objective scientific evaluation of the materials to be reviewed and is not aware of any other factors that may create an actual or perceived conflict of interest or bias for his or her participation in this peer consultation.

The members of this panel were selected for their expertise in developing and evaluating PBPK models on TCE and other compounds, metabolism of TCE, kinetics of TCE and metabolites, and use of models in risk assessment. Each panel member brings his or her own perspectives

resulting from their employment, affiliations, and experience. *TERA* has attempted to balance potential biases by forming a panel with scientists from diverse backgrounds, including government, consulting for industry and non-industry, and academia. In addition, *TERA* selected scientists who have done research on TCE, as well as those who have not.

Individual panel biographical sketches and disclosure statements are found below.

Dr. Hugh A. Barton

Dr. Hugh A. Barton received his Ph.D. in Applied Biological Sciences from the Toxicology Program at MIT in 1988. He is currently a toxicologist, and formerly Branch Chief, in the Pharmacokinetics Branch of the Experimental Toxicology Division of the US EPA's National Health and Environmental Research Laboratory in Research Triangle Park, NC. He is an adjunct Assistant Professor in the Curriculum in Toxicology at the University of North Carolina at Chapel Hill. Dr. Barton develops models and supporting data on tissue dosimetry and mode of action for use in biologically based dose-response analyses for chemical toxicity. He specializes in the use of state-of-the-art techniques, including physiologically based pharmacokinetic (PBPK) and pharmacodynamic modeling, to address the low dose, interspecies, and inter-route extrapolations that critically determine the development of chemical-specific dose-response values used for estimating risks. Recently, he has used modeling for evaluating noncancer toxicities, including reproductive and developmental effects, and for assessing dose-response and mechanisms of endocrine active compounds. Pharmacokinetic modeling to which he has contributed include: vinyl chloride, trichloroethylene, dichloroacetate, bisphenol A, and acetate esters and their metabolites (e.g. butyl acetate, butanol, butyraldehyde, and butyric acid). Pharmacodynamic models were developed for the male and female central hormonal axis (e.g. feedback between testosterone/estradiol and LH/FSH) and estrogen receptor-mediated gene regulation in the uterus.

Upon completion of his Ph. D., Dr. Barton worked at ENSR Consulting and Engineering where he planned and implemented risk based environmental management for toxic chemicals at contaminated waste disposal sites and manufacturing facilities. He was an Adjunct Assistant Professor at Boston University School of Public Health, from 1990 - 1993, teaching Principals of Toxicology. In 1991 he joined the Toxic Hazards Research Unit of ManTech Environmental Technology, Inc. at the Air Force Toxicology Division, Wright-Patterson AFB. There he directed research in xenobiotic metabolism, trichloroethylene carcinogenicity, PBPK modeling of mixtures, and risk assessment for total petroleum hydrocarbons (TPH). From 1995 - 1999 he was Principal Toxicologist with the K.S. Crump Group of ICF Kaiser where he developed pharmacokinetic and pharmacodynamic models focusing on issues of dose response for endocrine active compounds. He has published more than 25 articles in the scientific literature on xenobiotic metabolism, PBPK and PD modeling, endocrine disruption, dose response assessment, and risk assessment, with approximately 10 publications in peer-reviewed literature on TCE kinetics, modeling, and cancer and noncancer risk assessment.

Disclosures

Dr. Barton is currently employed by the US EPA. Dr. Barton has informally provided comments and discussed TCE issues with other offices at EPA as requested, but he is not formally part of the EPA group working on the TCE risk assessment. He formerly worked for ManTech Environmental as a contractor to the USAF and for ICF Kaiser as a member of the group currently at ENVIRON. He has conducted research on TCE, TCA, and DCA pharmacokinetics or pharmacokinetic modeling in relation to cancer and noncancer dose-response analysis while with ManTech Environmental. He participated in meetings of the TCE Issues Group and the 1995 Williamsburg meeting on TCE while with ManTech. While with ICF Kaiser, he

participated in a TCE literature review for a law firm. In October of 2001, while employed by EPA, Dr. Barton provided public comments to the EPA Science Advisory Board (SAB) on EPA's Draft Trichloroethylene Health Risk Assessment document (dated August 2001). The main focus of Dr. Barton's personal comments on the EPA document was that use of a combined point of departure would make it difficult to use a mode of action approach and pharmacokinetic modeling in a non-cancer analysis.

Dr Barton has developed models for TCE (Barton et al., 1995, Toxicol Appl Pharmacol 130: 237-247) and DCA (Barton et al., 1999, Toxicol Lett 106:9-21). He has also utilized the Clewell et al. model for dose response analyses (e.g., Barton and Clewell, 2000, Environ Health Perspect 108(Suppl 2):335-342).

Dr. Barton was selected for the panel for his experience in developing PBPK models, including models for TCE and metabolites.

Dr. Richard J. Bull

Dr. Richard J. Bull has a Ph.D. in Pharmacology from the University of California, San Francisco Medical Center. For 34 years, he has been involved in research related to environmental health. His field of study is toxicology and he has been most heavily involved with human health effects of drinking water contaminants. He has published extensively on the modes of action of halogenated solvents and byproducts of the disinfection of drinking water.

Dr. Bull worked with the Environmental Protection Agency's Health Effects Research Laboratory in Cincinnati, Ohio for fourteen years, where he directed the Toxicology and Microbiology Division at Cincinnati and was in charge of the EPA's health research programs in water. He joined Washington State University as a professor/scientist in the College of Pharmacy in 1984. In 1994, he accepted a position at Pacific Northwest National Laboratory (PNNL). At both institutions his research focused on establishing the mechanisms of action of environmental chemicals data in ways that will facilitate accurate across-species and low-dose extrapolation of health effects data, with an emphasis on mechanisms of carcinogenesis by halogenated solvents. Dr. Bull left PNNL in 2000 to return to Washington State University to work with the Department of Energy on their Low-Dose Radiation Research Program. As of May of 2003, Dr. Bull devotes all his time to his company MoBull Consulting.

Dr. Bull has served on numerous committee and advisory bodies, including those for the World Health Organization, International Agency for Research on Cancer, EPA's Science Advisory Board, Santa Anna River Water Quality and Health Science Advisory Panel, and National Research Council (NRC) Committees. Dr. Bull had conducted research and published over 40 articles on trichloroethylene and its metabolites. He was a state of the science author commissioned by the U.S. EPA and wrote a paper entitled "Mode of action of liver tumor induction by trichloroethylene and its metabolites, trichloroacetate and dichloroacetate" (2000, Environ Health Perspect 108(Suppl 2):241-59). Dr. Bull is on the editorial board of *Toxicology*.

Disclosures

Dr. Bull worked for the U.S. EPA from 1970 to 1984. Dr. Bull has worked with Irvin Schultz, who is also a kineticist, while at Pacific Northwest National Laboratory and together they have informally collaborated with Jeff Fisher on projects. While he and Dr. Schultz have published pharmacokinetic data on trichloroethylene and metabolites, he does not suggest that they have a competing model to the two models being evaluated and used in the harmonized model. Both the models have however, depended to varying degree on data generated in Dr. Bull's laboratory and that of Irvin Schultz. Dr. Bull worked as a consultant (now terminated) to a law firm to whom he provided literature on the health effects of TCE and provided guidance to the lawyers taking a deposition. He did not serve as an expert witness, nor make public statements.

In addition to the state of the science article in *Environmental Health Perspectives*, Dr. Bull has published extensively in the scientific literature on a variety of topics directly or indirectly related to metabolism of TCE and the effects of a number of its metabolites. He has also participated in a number of workshops and symposium addressing issues related to risk assessments for TCE. Dr. Bull has noted that "in the course of my career, I have probably made statements that support positions taken by the USAF while at other times supported the views of EPA."

Dr. Bull was selected for the panel because of his expert knowledge of the metabolism of TCE.

Hisham El-Masri, Ph. D

Dr. Hisham A. El-Masri is the director of the Computational Toxicology Laboratory at the Agency for Toxic Substances and Disease Registry (ATSDR) in Atlanta, Georgia. He has held this position since 1999. He received his M. Sc. degree in Environmental Engineering from California State University in 1989. He was awarded a Ph. D. degree in Environmental Health from Colorado State University at Fort Collins in 1994. After graduation, he joined the Computational Biology and Risk Analysis Laboratory at the National Institute of Environmental Health Sciences as a research fellow. Upon completion of his fellowship at NIEHS, Dr. El-Masri had worked as a biomathematical modeler for Novigen Sciences, Inc. before joining ATSDR. Dr. El-Masri's research and publications are in the area of computational toxicology to further advance methods for risk analysis and help in investigations of chemical mixture toxicity. He had served in several scientific advisory boards as an expert in biologically-based computational methodologies.

Disclosure

Dr. El-Masri works for ATSDR. Dr. El-Masri holds an unpaid adjunct faculty position at the University of Georgia, where he teaches 5-6 lessons for one course which is offered every other year. While he was at Colorado State University he developed a model for the interaction between TCE and 1,1-DCE in the mid-1990s (funded by the USAF). He also presented a poster at a Society of Toxicology meeting, which looked at the application of default uncertainty factors as applied to some solvents, including TCE.

Dr. El-Masri was selected for the panel for his expertise in PBPK modeling and Markov Chain Monte Carlo techniques.

Michael L. Gargas

Dr. Michael L. Gargas, Ph.D., is a toxicologist Managing Principal of *The Sapphire Group*™, with over 26 years of related environmental experience. Dr. Gargas oversees and prepares human health risk assessments, conducts toxic tort support investigations, serves as an expert witness, interacts with regulatory agencies, and addresses critical toxicological issues through applied and basic research on behalf of clients. His clients include private industry, trade associations, law firms, regulatory agencies, and private citizens. Dr. Gargas' area of expertise is in human health risk assessment and biochemical toxicology research with emphasis in the areas of inhalation toxicology, chemical metabolism, physiologically based pharmacokinetic (PBPK) modeling, and chemical dosimetry, with specific application of these approaches to risk assessments. Prior to joining *The Sapphire Group*™, Dr. Gargas served as a Principal Health Scientist with ChemRisk (a risk assessment and toxicology consulting firm), a senior research scientist at the Chemical Industry Institute of Toxicology (CIIT), and as a toxicology research scientist with the U.S. Air Force (as a civilian) and the U.S. Navy (on active duty).

Dr. Gargas received his doctorate in Biomedical Sciences (Toxicology Specialty) from Wright State University. Dr. Gargas has been honored by the Society of Toxicology with the Frank R. Blood Award, the Department of the Air Force Invention/Patent Award (Co-Inventor) for an *In Vivo* Dermal Absorption System for Rats, Invention No. 15, 859 (U.S. Patent Number: 4,582,055) and the Outstanding Technical Civilian of the Year Award, from the Air Force Aerospace Medical Research Laboratory. Dr. Gargas has served on the editorial board of *Toxicology and Applied Pharmacology*. Dr. Gargas has been invited to present numerous guest lectures on toxicology and risk assessment topics and is an Adjunct Assistant Professor of Toxicology at Wright State University, serving as director for a graduate course in biokinetics and toxicology. He has published numerous book chapters and publications on a wide range of health and toxicologic topics.

Disclosures

Dr. Gargas worked for the USAF as a civil servant from 1981-89 conducting toxicological research at Wright Patterson Air Force Base, including studies with TCE. He has conducted research and published papers with Fisher and Clewell regarding metabolism and pharmacokinetic modeling of trichloroethylene. He currently consults to a confidential (industrial) client on TCE issues. His task is to keep them informed of progress on the U.S. EPA reassessment of TCE. He also conducted a comparison of risk values for the same client that included TCE (2000-2001). Dr. Gargas consulted to the Trichloroethylene Users Group in the mid-1990s on a project that used a PBPK model to recalculate the U.S. EPA cancer potency factor. Dr. Gargas is currently working on a project on chloroethane PBPK modeling for the EPA, but he is not aware of any other project the Sapphire Group is working on for EPA, USAF, ENVIRON, or *TERA*. He has previously served on *TERA* panels, most recently receiving an honorarium for his VCCEP acetone panel participation.

Dr. Gargas was selected for the panel for his extensive experience in PBPK modeling and familiarity with TCE.

Lynne T. Haber

Dr. Lynne Haber is Research Program Manager for Toxicology Excellence for Risk Assessment (*TERA*). She received her Ph.D. in Molecular Biology from the Massachusetts Institute of Technology in 1990. She has more than 12 years of experience in developing risk values for government agencies and industry and conducting research related to risk assessment methods. She has developed more than 20 noncancer and cancer assessments for EPA's Integrated Risk Information System (IRIS) for EPA program offices (including ones using PBPK models), for other government agencies, and for private sponsors. Her current interests are in the application of mechanistic information in risk assessment and in methods for extending the dose-response curve to low doses. Other recent work includes research on children's risk issues, consideration of mode of action in cancer risk assessment, incorporating data on polymorphisms into risk assessment, and development of scientifically-based occupational exposure limits. Dr. Haber was the coauthor for an analysis of the effect of genetic polymorphisms on human variability in dose, using PBPK and Monte Carlo modeling. Dr. Haber worked for ICF Kaiser/Clement from 1991-1998 and as a Staff Scientist for the Illinois Legislative Research Unit. Dr. Haber has served on National Academy of Science panels and has served on peer review panels for EPA, the Department of Defense, and the Ontario Ministry of the Environment.

Disclosure

Dr. Haber works for Toxicology Excellence for Risk Assessment (*TERA*), but has not been involved in the efforts to develop the harmonized PBPK model. While with *TERA* and with ICF Kaiser/Clement she helped develop risk assessment documents for the U.S. EPA, including drinking water criteria documents on DCA and TCA. While with ICF Kaiser she served as the contract manager for work performed by Clewell and colleagues on TCE that became part of the 2000 EHP volume, but she had minimal technical involvement. She has worked on a joint project with scientists of the K.S. Crump Group for the U.S. EPA collecting physiological parameter data for neonatal animals.

Dr. Haber was selected for the panel for her experience in applying PBPK models and data to risk assessments and chairing expert panel meetings.

Gregory L. Kedderis

Dr. Gregory L. Kedderis is currently a consultant in biochemistry, pharmacology, and toxicology. He received his Ph.D. degree in biochemistry in 1982 from Northwestern University Medical and Dental School, Chicago, IL. He was a postdoctoral fellow at the Chemical Industry Institute of Toxicology (CIIT) in Research Triangle Park, NC from 1982 to 1984 and subsequently joined Merck Sharp & Dohme Research Laboratories in Rahway, NJ as a senior

research biochemist. Dr. Kedderis returned to CIIT as a staff scientist in 1988, where he was Director of the Chemical Carcinogenesis Research Program (since 1998) and the Division of Biochemistry and Molecular Genetics (since 2000) until 2002. He is also a Visiting Research Professor in the Nicholas School of the Environment and Earth Sciences and in the Integrated Toxicology Program at Duke University, Durham, NC. Dr. Kedderis is author or co-author of 67 publications. He has served on the editorial boards of *Fundamental and Applied Toxicology*, *Drug Metabolism and Disposition*, *Cell Biology and Toxicology*, *Chemico-Biological Interactions*, *Archives of Toxicology,* and the *Journal Pharmacology and Experimental Therapy*. His research interests include the relationship between chemical dosimetry and biological effects, mechanisms of toxicity of drugs and xenobiotics, and mechanisms of genotoxicity and chemical carcinogenesis. Dr. Kedderis is a member of the Society of Toxicology, the Chemical Substances Threshold Limit Values Committee of the American Conference of Governmental Industrial Hygienists, and the National Occupational Research Agenda Cancer Research Methods Team.

Disclosure

Dr. Kedderis was a coauthor of a recent paper (Lipscomb et al., 2003) that addresses interindividual variability in metabolic capacity using TCE as an example. Their modification of the Fisher model was to use better estimates of metabolic capacity and a statistical distribution of that activity. This work was supported by funding from a cooperative agreement with EPA (2000-2003), that was entitled "Development of Chemical-specific Human Physiologically Based Pharmacokinetic Models for Adults and Children" with TCE and chloroform as examples. The objective of the work was to evaluate the impacts of interindividual differences in bioactivation and adult-child differences in bioactivation on internal dosimetry using PBPK models.

Dr. Kedderis was selected for the panel because of his expertise in pharmacokinetics and enzyme kinetics on multiple chemicals.

Dr. Kannan Krishnan

Dr. Kannan Krishnan is Professor of Occupational and Environmental Health at the University of Montreal where he is also the Director of the Human Toxicology research group (TOXHUM). He was a Post Doctoral Research Fellow at the Chemical Institute of Toxicology (CIIT) from 1990-1992. He has been the leader of the risk assessment methodologies theme team of the Canadian Network of Toxicology Centres (1994 – 2001), and Vice President of the Biological Modeling Specialty Section of the Society of Toxicology (2001-2002). Dr. Krishnan is a member of the U.S. National Academy of Sciences (NAS) Sub-committee on Acute Exposure Guideline Levels (2001-2004). He is currently a temporary advisor for the World Health Organization for developing a document on the scientific principles for the health risk assessment for children. His primary expertise is in the areas of pharmacokinetics, PBPK modeling, risk assessment methods, Quantitative Structure Activity Relationship (QSAR) modeling and mixture toxicology. He has been a peer reviewer of several IRIS updates, risk assessments, mixture risk assessment supplemental guidance and efforts on interactions for US

EPA and on toxicological profiles of chemicals, interaction profiles involving Environmental contaminants and mixture risk assessment guidelines for ATSDR. Dr. Krishnan received his P.D. in Public Health from the University of Montréal. He has been on the editorial boards of *Toxicological Sciences*, *International Journal of Toxicology*, *Journal of Applied Toxicology*, and the *Journal of Children's Health*.

Disclosure

Dr. Krishnan has applied a published human PBPK model (Lapare and coworkers at the University of Montreal) to derive the fraction of TCE absorbed following dermal and inhalation exposures of adults and children of various age groups (6, 10 and 14 years) for the Drinking Water Division of Health Canada. He is currently receiving funding from the U.S. EPA to develop a document on the appropriate use of PBPK models in risk assessment.

Dr. Krishnan was selected for the panel for his expertise in pharmacokinetics and PBPK modeling for multiple chemicals.