

Conflict of Interest and Panel Biographical Sketches

This document discusses the measures taken by Toxicology Excellence for Risk Assessment (*TERA*) to evaluate potential conflict of interest and provides brief biographical sketches for each of the panel members. Monsanto and Dow AgroSciences, LLC requested that this project be done under the auspices of the Alliance for Risk Assessment (*ARA*). This project was accepted by the *ARA* steering committee in April 2009. The sponsors then contracted with *TERA*, through the *ARA*, to independently organize and conduct this independent peer expert workshop. *TERA* is being paid for labor and the direct expenses related to this workshop under a contract with Monsanto.

TERA has no current financial relationship or other work supported by the Monsanto or Dow AgroSciences, LLC (beyond this peer workshop) or any current financial relationships with any of the competing pesticide producers, or companies intending to produce acetochlor or alachlor. *TERA* is not doing any work on acetochlor or alachlor for any other sponsor. In the past decade, *TERA* has provided technical review on projects to Dow AgroSciences, LLC and Monsanto, but none of this work was related to evaluating acetochlor, alachlor or the associated degradates.

In selecting panel members, *TERA* carefully screens candidates for potential conflicts of interest and biases that might interfere with an expert's objectivity in evaluating the subject materials. *TERA* follows the U.S. National Academy of Sciences (NAS) guidance on selection of panel members to create panels that have a balance of scientific viewpoints on the issues to be discussed. As a result, the expert panels have a broad and diverse range of knowledge, experience, and perspective, including diversity of scientific expertise and affiliation. Panel members serve as *individuals*, representing their own personal scientific opinions. They do not serve as representatives of their companies, agencies, funding organizations, or other entities with which they are associated. Their opinions should not be construed to represent the opinions of their employers or those with whom they are affiliated.

The selected panel members have a variety of relevant expertise and affiliations to provide a range of opinions and perspectives on the subject document. The panel members of the peer workshop are experienced in the review of toxicology studies, and development of Reference Doses (RfDs) or similar health-based guidance values, particularly for use in setting water standards.

An essential part of panel selection is the identification of potential conflicts of interest and biases or the appearance of conflicts or biases. Prior to selecting the panelists, each candidate completed a questionnaire to identify their activities, financial holdings or relationships, or affiliations that could pose a real or perceived conflict of interest or bias. To facilitate the evaluation of potential conflict of interest and bias situations for the part of peer expert candidates, *TERA* identified a list of potentially affected or interested parties for this independent peer expert workshop and asked the candidates to consider these parties and information when completing their forms. The completed questionnaires were reviewed by *TERA* staff and discussed further with panel candidates as needed. *TERA* used the information collected to identify potential conflicts and/or biases and

evaluate whether these situations would hinder the candidate from objectively participating in the peer workshop discussions. (See www.tera.org/peer/COI.html for *TERA*'s conflict of interest and bias policy and procedures for panelist selection).

The key question when evaluating candidates for conflict of interest is whether a candidate's participation can have a direct and predictable effect on his or her finances or financial relationships with the parties affected or involved in the matter. Direct means a close causal link between any decision or action taken in the course of the independent peer expert workshop and a predictable effect on the financial interests of the candidate. There must be an actual, as opposed to speculative, possibility that the matter will affect the financial interest to be a real conflict of interest.

TERA has selected members for the panel that are free from conflict of interest and are able to objectively participate and contribute to this independent peer expert workshop. None of the panel members works for, or is doing work for, Monsanto, Dow AgroSciences, LLC or the other identified parties. None of the panel members has a financial interest that can be affected by the work of the panel or the outcome of this independent peer expert workshop. In addition, none of the panel members was an author of, or contributor to, the data under deliberation.

Every scientist and expert has biases resulting from his or her education, training, and experience. *TERA* sought to identify sources of biases and evaluated these to determine if the biases would interfere with the peer expert's ability to objectively participate in the discussions and peer workshop. Evaluation of bias included consideration of candidates' relationships with affected parties and public positions on the chemicals or key issues.

A brief biographical sketch of each panel member is provided below. In the interests of transparency, as appropriate, a short disclosure statement is provided.

Biographical Sketches and Disclosures of Panel Members

John Christopher, DABT
Ph.D., Biological Science Oregon State University
Department of Toxic Substances Control
California Environmental Protection Agency

Dr. Christopher is a staff toxicologist with the Department of Toxic Substances Control (DTSC), California Environmental Protection Agency. In this position he reviews, critiques, and approves assessments of risk to human health and ecological risk assessments at military facilities and other hazardous waste sites and permitted facilities in California. He constructs multi-pathway risk assessments to identify numerical criteria for classifying hazardous levels of metals and organic chemicals in waste. He also uses Monte Carlo methods in various exposure settings to identify levels protective of human health. He has received a significant grant for research on *in vitro* and *in vivo* bioavailability of arsenic at mine-scarred lands from the US EPA Brownfields Program and was a peer reviewer of the Integrated Risk Information System (IRIS) risk assessment of tetrahydrofuran. Dr. Christopher recently received a Lifetime Achievement Award for contributions to site cleanup at the 15th International Conference on Soils, Sediment, and Groundwater. Prior to his current position with the State of California, Dr. Christopher conducted risk assessments for ICF Kaiser Engineers and IT Corporation. He also worked for contract research laboratories where he conducted and managed animal studies.

Dr. Christopher received his Ph.D. in Biological Science from Oregon State University in 1979. He earned a B.S in Biology from Georgetown University, in 1971 and a M.A. in Pharmacology from Stanford University in 1967. Dr. Christopher is a Diplomat of the American Board of Toxicology and a former member of this Board.

He has served as President and held several other offices in the Risk Assessment Specialty Section of the Society of Toxicology and also in SOT's Northern California Chapter. He is a peer reviewer for *Toxicological Sciences*, *Risk Analysis*, *Human and Ecological Risk Assessment*, and *CRC Critical Reviews in Toxicology*.

Disclosure: Dr. Christopher is employed by the Department of Toxic Substance Control of the California EPA. Dr. Christopher notes that the California Department of Toxic Substances Control regulates transport, disposal, and cleanup of hazardous waste. At times, the parties responsible for creating and disposing of hazardous waste will pay fees or other monies to the Department to defray regulating costs. It is possible that some of the private sector entities are now, or have been in the past, party to "Voluntary Cleanup Agreements" with his employer. He does not have specific knowledge of any such agreements that are currently in place with any of the private sector entities, nor does he have any knowledge of agreements in the past. TERA has determined that Dr. Christopher has no conflicts of interest with participation in this independent peer expert workshop.

**Michael L. Dourson, DABT, FATS
Ph.D., Toxicology, University of Cincinnati
Toxicology Excellence for Risk Assessment (TERA)**

Dr. Dourson is the President of Toxicology Excellence for Risk Assessment (*TERA*), a nonprofit corporation dedicated to the best use of toxicity data in risk assessment. Before founding *TERA* in 1995, Dr. Dourson held leadership roles in the U.S. Environmental Protection Agency as chair of US EPA's Reference Dose (RfD) Work Group, charter member of the US EPA's Risk Assessment Forum and chief of the group that helped create the Integrated Risk Information System (IRIS).

Dr. Dourson received his Ph.D. in Toxicology from the University of Cincinnati. He is a Diplomate of the American Board of Toxicology and a Fellow of the Academy of Toxicological Sciences.

Dr. Dourson has served on or chaired numerous expert panels, including peer review panels for US EPA IRIS assessments, US EPA's Risk Assessment Forum, *TERA*'s International Toxicity Estimates for Risk (*ITER*) independent peer reviews and consultations, FDA's Science Board Subcommittee on Toxicology, the NSF International's Health Advisory Board, and SOT's harmonization of cancer and non-cancer risk assessment. He served as Secretary for the Society for Risk Analysis (SRA) and has held leadership roles in specialty sections of SRA and SOT. He is currently on the editorial board of three journals. Dr. Dourson has published more than 100 papers on risk assessment methods, has co-authored over 100 government risk assessment documents, and has made over 90 invited presentations. Dr. Dourson was selected for the panel for his expertise in toxicology and risk assessment, as well as his experience in chairing expert panels.

Disclosure: Dr. Dourson works for Toxicology Excellence for Risk Assessment (*TERA*). *TERA* has no current financial relationship or other work supported by the Monsanto or Dow AgroSciences, LLC (beyond this peer workshop) or any current financial relationships with any of the competing pesticide producers, or companies intending to produce acetochlor or alachlor. *TERA* is not doing any work on acetochlor or alachlor (or degradates) for any other sponsor. In the past decade, *TERA* has provided technical review on projects to Dow AgroSciences, LLC and Monsanto, but none of this work was related to evaluating acetochlor, alachlor or the associated degradates. As an US EPA employee, Dr. Dourson chaired an US EPA workgroup that reviewed the toxicity of acetochlor and alachlor for entry into IRIS. *TERA* has determined that Dr. Dourson has no conflicts of interest with participation in this independent peer expert workshop.

Lebelle Hicks, DABT
Ph.D., Food and Nutrition Sciences, University of Maine,
Maine Board of Pesticides
Department of Agriculture

Dr. Lebelle Hicks is a pesticide toxicologist for the State of Maine, Department of Agriculture since 1989. Where, in addition to addressing pesticide concerns from the general public, her responsibilities include written and oral presentation of hazard reviews and risk assessments for a variety of pesticide active ingredients relating to human health or environmental exposure. Dr. Hicks' duties also cover a range of pesticide and non-pesticide food safety issues. Prior to joining the State of Maine in 1989, she was a pesticide toxicologist for the State of Massachusetts, Department of Agriculture.

She received her Ph.D. in Food and Nutrition Sciences from the University of Maine in 1999, and her masters degree in Biology/Toxicology from Northeastern University in 1983. Dr. Hicks has been a Diplomate of the American Board of Toxicology since 1991.

Dr. Hicks is a member of the Society of Toxicology (SOT) and has served on several committees, including Kennebec County Local Emergency Planning Committee, Medical Advisory Committee, Environmental Risk Advisory Committee of the Board of Pesticides Control Activities, Technical Committee on Drift Issues (chair), Stakeholder Committee on Drift Issues, and Technical Committee reviewing Bt-Corn registrations.

Disclosure: Dr. Hicks works for the State of Maine as a pesticide toxicologist. She previously served in a similar role for Massachusetts. She has reviewed numerous active pesticide ingredients, including alachlor (in the 1980s). She has made presentations on pesticides in general, but not on these specific herbicides or their degradates. She provided expert testimony in two legal cases in the early 1990s, but neither case involved these herbicides or their degradates, nor were the pesticide manufacturers parties in the cases. She is not currently working on alachlor, acetochlor or their degradates and has no position on the toxicity of these substances. TERA has determined that Dr. Hicks has no conflicts of interest with participation in this independent peer expert workshop and does not believe her current position or previous work will interfere with her objective evaluation or participation on this panel.

Santhini Ramasamy, DABT
Ph.D., Biochemistry, University of Madras, India
MPH, Emory University, Georgia
Office of Water
US Environmental Protection Agency (US EPA)

Dr. Ramasamy is a senior toxicologist with the Environmental Protection Agency (US EPA) since 2000. She currently works in US EPA's Office of Water (OW) in Washington DC. She conducts human health risk assessment of many chemical contaminants under the Safe Drinking Water Act (SDWA) and Clean Water Act (CWA). She is US EPA's chemical manager for the inorganic arsenic risk assessment under IRIS (Integrated Risk Information Systems) and has given several invited speeches on inorganic arsenic risk assessment. She represents OW in many US EPA workgroup activities such as genomics task force, research planning and coordination, and in 21st century toxicity testing.

Before working with the OW, she worked in US EPA's Office of Pesticide Programs (OPP) where she conducted both human and environmental risk assessments of many pesticides for both registration and re-registration purposes under Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and Food Quality Protection Act (FQPA). She has received several science achievement awards and bronze medal awards from the US EPA. Prior to joining the US EPA she worked as a Senior Scientist for an environmental consulting company in Silver Spring, Maryland and was an Assistant Professor at Emory University School of Medicine.

Dr. Ramasamy received her Ph.D. in biochemistry from University of Madras, India (1986) and Masters in Public Health (Environmental and Occupational Health) from Emory University, Atlanta, GA (1999). She served as a postdoctoral fellow at the University of Kentucky, working on endothelial cell dysfunction and oxidative stress upon exposure to polyunsaturated fatty acids. Dr. Ramasamy is a Diplomate from American Board of Toxicology since 1997. She is one of the senior fellows in a leadership program organized by Council for Excellence in Government (Partnership for Public Service).

Disclosure: Dr. Ramasamy currently works for the US EPA Office of Water and previously was with the US EPA's Office of Pesticide Programs. She has not worked on alachlor, acetochlor or their degradates and has no position on the toxicity of these substances. *TERA* has determined that Dr. Ramasamy has no conflicts of interest with participation in this independent peer expert workshop.

Stephen Roberts
Ph.D., Pharmacology, University of Utah
Center for Environmental & Human Toxicology
University of Florida

Dr. Roberts is Director of the Center for Environmental and Human Toxicology at the University of Florida. Dr. Roberts was a professor in the same department before being named director in 1995 and is still active in teaching and research. Prior to his position at the University of Florida Dr. Roberts was an assistant professor in pharmacology and toxicology at the University of Arkansas for Medical Sciences and the University of Cincinnati Medical Center.

Dr. Roberts is interested in mechanisms of drug- and chemical-induced toxicity. His active research includes: 1) absorption, distribution and elimination of nanomaterials in the body and potential adverse health effects of nanomaterials; 2) identification of mechanism(s) by which exposure to certain chlorinated pesticides accelerates the development of systemic lupus erythematosus; 3) examination of the potential approaches for mitigation of adverse effects of drugs and chemicals by upregulating stress proteins; 4) measurement of arsenic bioavailability from various types of contaminated soils in support of an effort to develop a rapid and inexpensive test to ascertain arsenic bioavailability at arsenic contaminated sites.

Dr Roberts received his Ph.D. in pharmacology from University of Utah in 1977 and a Bachelors in Pharmacy from Oregon State University in 1973. He was a NIH post-doctoral Fellow at the State University of New York during 1977-1980.

Dr. Roberts is a member of the Society of Toxicology (SOT), Society for Risk Analysis, and International Society of Regulatory Toxicology and Pharmacology. He serves on numerous committees including the Science Advisory Board for the U.S. Food and Drug Administration's National Center for Toxicological Research; member of the Science Advisory Board for the U.S. EPA; and was previously Chair of the US EPA's FIFRA Scientific Advisory Panel. He has over 100 peer reviewed, abstract, and letter publications, and is active in advising graduate and post-doctoral students.

Disclosure: Dr. Roberts works for the University of Florida and notes that through a contract between the University of Florida and the Florida Department of Environmental Protection, he provides advice to the state on risk issues, including the development of soil and groundwater criteria for alachlor. He has not worked on these degradates and has no position on the toxicity of these substances. If the State decided in the future to develop criteria for the degradates, his group at the University would be responsible for that development. *TERA* has determined that Dr. Roberts has no conflicts of interest with participation in this independent peer expert workshop and does not believe his previous work on alachlor will interfere with his objective evaluation or participation on this panel.

CONFIDENTIALITY AGREEMENT

I, _____, request access to the confidential study reports on acetanilide degradates for purposes of the Expert Panel Workshop. I agree to not copy nor distribute this information or utilize the information for any purpose other than this workshop. I have listed below the documents I examined and I agree to return all materials to *TERA* before the end of the workshop. I understand I shall not be restricted in using any material which is publicly available, already in my possession or known to me without restriction, or which is rightfully obtained by me from sources other than *TERA* or Monsanto.

List of documents examined:

Signature

Print Name

Date

Overview of the Acetanilide Degradates Peer Workshop Process

Background

This independent peer expert workshop has been organized by Toxicology Excellence for Risk Assessment (*TERA*) under the auspices of the Alliance for Risk Assessment (*ARA*). *TERA* is an independent non-profit organization with a mission to protect public health through the best use of toxicity and exposure information in the development of risk assessments. *ARA* is a collaboration of organizations that fosters the development of technical chemical risk assessment products and services, through a collaborative effort of specialists and organizations. *ARA* is dedicated to protecting public health by improving the process and efficiency of risk assessment, and to increasing the capacity for developing risk values to meet growing demand. *ARA* provides a unique venue for governmental, industrial, environmental, and non-profit organizations to collaborate to produce high quality risk assessment science (see <http://www.allianceforrisk.org/>). *TERA* has organized and conducted peer review, consultation and workshop meetings for private and public sponsors since 1996 (see www.tera.org/peer for information about the program and reports from meetings).

The subject of this independent peer expert workshop is to review pertinent toxicology data for the derivation of Reference Doses (RfDs) for the following alachlor and acetochlor degradates: 1) alachlor t-ESA, 2) alachlor t-OXA, 3) acetochlor t-ESA, and 4) acetochlor t-OXA. The data package was prepared by Dr. Bernard Gadagbui of *TERA* with assistance from Dr. Andy Maier and Ms. Alison Willis, also of *TERA*.

Monsanto and Dow AgroSciences selected and contracted with *TERA* to independently organize and conduct this peer workshop. *TERA* is being paid for labor and the direct expenses related to this independent peer expert workshop under a contract with Monsanto.

This independent peer expert workshop is organized for the purpose of providing expert input and advice regarding the determination of the critical effect of each acetanilide degradate, appropriate NOAEL/LOAELs/BMDs, and recommended uncertainty factors. The objective of this peer workshop is for a diverse group of appropriate experts to review the toxicity data on alachlor t-ESA, alachlor t-OXA, acetochlor t-ESA, and acetochlor t-OXA to develop RfDs. The independent peer expert workshop seeks to gain the opinions of technical experts with a variety of perspectives and backgrounds.

Independent Expert Panel

The independent panel is made up of scientists with expertise in the key disciplines necessary to evaluate the proposed approach. Dr. Michael Dourson of *TERA* will chair the panel. Each panelist is a well-respected scientist in his or her field. The panel members of the peer workshop are experienced in the review of toxicology studies, and development of Reference Doses (RfDs) or similar health-based guidance values, particularly for use in setting water standards.

TERA independently identified candidates for the panel and was solely responsible for the selection of the panel members. *TERA* offered to cover travel expenses and offered an honorarium to partially compensate panel members for their time to review the materials and participate in the meeting.

Each panel member has disclosed information regarding potential conflicts of interest and biases related to the proposed approach and its sponsors. *TERA* carefully evaluated these disclosures when selecting panel members as discussed below. Short biographical sketches and disclosure statements for panel members are provided to all meeting participants and will be part of the final meeting report.

Review Materials and Charge to Peer Experts

The panel received the review package a few weeks prior to the meeting to allow review of the data package and preparation for the meeting discussions. The review package included key data summary tables, critical endpoint summary tables, benchmark dose modeling results, potential RfD summary tables, and copies of key references. Based on the data package, *TERA* prepared a “charge” document outlining the key questions and scientific issues that will focus the panel’s discussions.

Meeting Procedures

The meeting has been organized to make the best use of the time available to hear and discuss the opinions of the panelists regarding the assessment and answers to charge questions. The meeting will begin with brief panel introductions and a disclosure of conflict of interest and bias issues. Dr. Gadagbui will then present background information and a brief summary of the critical endpoints followed by clarifying question from the panel. To start each discussion section, comments from observers will be presented, followed by panel discussion of the relevant charge questions. The panel discussion will address several areas of the assessment: adequacy of the data, critical effects, mode of action, uncertainty factor selection, and derivation of reference values.

Observers

This meeting is open to the public; interested persons were invited to attend the meeting either in person or observe via a real-time Internet webcast. Observers were provided the opportunity to provide written technical comments or present brief oral comments at the meeting. No written comments were submitted prior to the meeting.

Meeting Report

TERA will prepare a meeting manuscript from the results of this workshop. Written or oral public comments will be briefly summarized and included in this text.

Biographical Sketches of Presenter

Bernard Gadagbui, Ph.D., DABT
Toxicology Excellence for Risk Assessment (TERA)

Dr. Gadagbui has over 12 years of research and teaching experience in environmental health, experience in evaluating human health risks posed by chemicals including pesticides, experience in reviewing human health risk assessment documents, and experience in the application of current risk assessment methods in the development of RfDs and RfCs.

Dr. Gadagbui received his Ph.D. in Environmental Health and Aquatic Toxicology, a M.Sc. in Biochemistry from the University of Bergen, Norway, and a B.Sc. in Biochemistry with Chemistry from the University of Ghana.. Prior to joining *TERA* in 2004, Dr. Gadagbui held a toxicologist position at the Florida Department of Agriculture and Consumer Services (FDACS) and the University of Florida (UF). At FDACS, he served as the Scientific Evaluation Section Staff Coordinator for the Bureau of Pesticides, where he conducted and coordinated toxicological reviews and assessments of data submitted for the support of pesticides registration relative to their potential impact on human health, animal and plant species, including endangered species.

At *TERA*, Dr. Gadagbui is involved in many projects that require an in-depth understanding of mechanisms of toxicity, current methods for assessing toxicology outcomes, and appropriate interpretation of toxicology and human health data for deriving risk assessment values. He has co-authored several toxicological assessments (e.g., for U.S. EPA's Integrated Risk Information System and U.S. EPA's Office of Water) that typically draw on a detailed critical examination of all types of epidemiology and toxicology studies. Dr. Gadagbui also applies current risk assessment methods in the development of skin notations for diverse groups of chemicals, provisional health-based groundwater and surface water criteria for several data-poor chemicals or mixtures of chemicals and has a broad understanding of the use of animal and human databases to derive human health risk assessments.

Dr. Gadagbui is interested, among others, in the use of mode of action and mechanisms of toxicity of occupational and environmental toxicants and carcinogens in risk assessment. He is a Diplomate of the American Board of Toxicology.

Additional Authors and Contributors

Dr. Andy Maier and Ms. Alison Willis contributed to the review and assimilation of toxicology data for the workshop.

**Peer Workshop on Toxicological Assessment and Development of RfDs
for Acetanilide Degradates
Attendees**

May 11-12, 2009

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* Attending meeting via web cast