



TERA

TOXICOLOGY EXCELLENCE FOR RISK ASSESSMENT

# ANNUAL REPORT

## 2010

### TERA: 1995 - 2010 FIFTEEN YEARS OF PROVIDING PUBLIC SERVICE THROUGH EXCELLENCE IN RISK ASSESSMENT

IN 1995, DR. MICHAEL DOURSON ORGANIZED TERA AS A NON-PROFIT AND INDEPENDENT CORPORATION WITH A MISSION TO SUPPORT THE PROTECTION OF PUBLIC HEALTH AND A VISION OF TOXICOLOGY EXCELLENCE FOR RISK ASSESSMENT. TERA FOCUSES ON HIGH QUALITY SCIENCE AND ON DEVELOPING PARTNERSHIPS AMONG ALL MEMBERS OF THE RISK ASSESSMENT COMMUNITY. TERA SUPPORTS THE PROTECTION OF PUBLIC HEALTH BY DEVELOPING AND COMMUNICATING RISK ASSESSMENT INFORMATION, SPONSORING PEER REVIEWS AND CONSULTATIONS, IMPROVING RISK METHODS THROUGH RESEARCH, AND EDUCATING INTERESTED PARTIES ON RISK ASSESSMENT ISSUES.

# LETTER FROM OUR PRESIDENT

Dear Colleagues:

TERA made excellent progress in 2010 addressing our mission to support the protection of public health by developing, reviewing and communicating risk assessment values and analyses; improving risk methods through research; and, educating risk assessors, managers, and the public on risk assessment issues. TERA's unique function, as a independent, neutral non-governmental organization, serves to protect human health by conducting scientific research and development on risk issues in a transparent and collaborative fashion and communicating the results widely.

The work of our scientific staff was widely recognized in 2010. Our director, Dr. Maier, accepted a role as a Toxicology Fellow via an Interagency Personnel Agreement with the Education and Information Division of the National Institute for Occupational Safety and Health (NIOSH). This work at NIOSH allows research to further develop methods in occupational risk assessment. TERA received the "Excellence in Risk Communication" award from the Alliance for Chemical Safety, for our work on the 2007 Air Toxics Report for the Hamilton County Department of Environmental Services. We shared this award with our partner on the project, EQM, and with the Hamilton County Department of Environmental Services.

A notable 2010 TERA publication was an assessment of diacetyl, the butter flavor implicated as a cause of lung effects in workers (e.g., popcorn workers' lung). TERA published an occupational exposure limit in Regulatory Toxicology and Pharmacology that was based upon our independent evaluation of the epidemiology and toxicology literature.

Two multi-stakeholder scientific workshops were conducted by TERA in 2010. TERA believes that risk assessment requires multiple and differing expert views in order to chart a credible path forward that adequately considers regulatory impact, as no one type of expertise, or group, can be expected to have all of the answers. A workshop series, under the aegis of the Alliance for Risk Assessment, was started in 2010 to build on the suggestions of the National Academy of Sciences report *Science and Decisions: Advancing Risk Assessment* (NAS 2009) and others. The workshop series intends to develop a practical guidance document of dose-response techniques to advance the field of risk assessment. A second effort resulted in a highly successful workshop held on the National Institute of Environmental Health Sciences campus in September to discuss mode of action and dose response for nuclear receptor mediated liver cancer and focused on the AHR, PPAR $\alpha$  and CAR/PXR receptors. These workshops bode well for future collaborative work.

TERA scientists presented at a variety of meetings, including scientific societies, public meetings, and peer reviews. We presented the results of our independent peer consultation panel's review of research needs and protocols to develop data to better understand hexavalent chromium's mode of action at EPA's listening session for its *Draft Toxicological Review of Hexavalent Chromium* in November. The peer panel redirected and improved the proposed research plan proposed and funded by an industry consortium. I traveled to Flin Flon, Manitoba in June to present the findings and results of yet another independent expert panel convened by TERA that had reviewed a human health risk assessment (HHRA) for the area surrounding the Hudson Bay Mining and Smelting Company facility in Flin Flon.

TERA continues to train scientists on risk assessment techniques and methods. For example, we trained several dozen scientists from the US and elsewhere in our week-long Dose Response Boot Camp, providing them with enhanced skills to use in their government agencies, companies, universities, and non-profit organizations.

We look forward to continued work with a diverse set of colleagues as we strive to improve the protection of public health.

Sincerely,



Michael L. Dourson, Ph.D., DABT  
President



## TERA MISSION

Toxicology Excellence for Risk Assessment (TERA) is a non-profit and tax-exempt organization organized for scientific and educational purposes. Our mission is to support the protection of public health by developing, reviewing and communicating risk assessment values and analyses; improving risk methods through research; and, educating risk assessors, managers, and the public on risk assessment issues.

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## TERA BOARD OF DIRECTORS & CORPORATE OFFICERS 2010

*Year indicates ending year of current term.*

James D. Wilson (2010) CHAIR

Daniel Acosta, Jr. (2012) VICE CHAIR

Gail Charnley Elliott (2012)

Michael L. Dourson (perpetual)

Mike Fremont (2011)

Sam Kacew (2011)

Randall Manning (2011)

Gregery S. Romshe (2012)

Chad B. Sandusky (2010)

Jon L. Seymour (2011)

Philip E. Tobin (2010)

Chase D. Wright (2010)

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Michael Dourson, President

Jacqueline Patterson, Vice President, Corporate Secretary

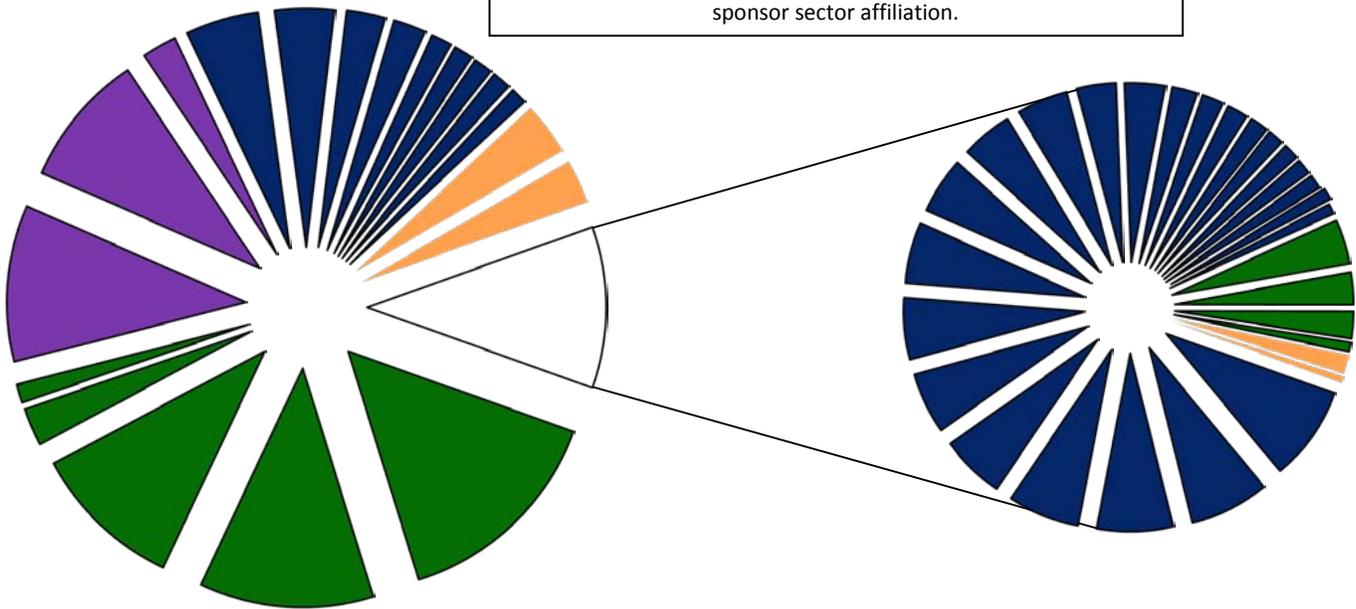
Andrew Maier, Treasurer

## FINANCES

TERA's 2010 income was \$2,359,938 and actual expenses totaled \$2,392,259. This resulted in a net loss of \$32,321.

# 2010 REVENUE BY SPONSOR

Each "slice" represents an individual sponsor; shading represents sponsor sector affiliation.



- Government
- Training
- Coalition
- Industry
- Other (each is less than 1% of work)

TERA provides independent scientific services to a broad range of sponsors, including government agencies, industry, non-governmental organizations, and consultants. By collaborating with many types of organizations, TERA gains an appreciation and understanding of the range of scientific perspectives. We utilize this understanding and the resulting relationships to identify and encourage collaboration among parties to improve risk assessment and protection of public health. In addition to the programmatic work for sponsors, TERA contributes between 11 and 21 percent more hours of professional and donated time, including serving as officers in scientific societies. In addition, TERA as a corporation performs *pro bono* work associated with state, tribal and provincial unmet needs under the State Hazard Evaluation and Lending Program (State HELP) and the Alliance for Risk Assessment (ARA).

## HIGHLIGHTED SPONSORS BY SECTOR AFFILIATION

- Coalition**
- Alliance for Risk Assessment (ARA)
  - Beyond Science and Decisions Coalition
  - Nuclear Receptor MOA Coalition

- Training**
- African Society for Toxicological Sciences
  - Concurrent Technologies Corporation
  - Dose Response Assessment Boot Camp
  - International Toxicity Estimates for Risk (ITER)

- Industry**
- American Chemistry Council
  - CEFIC - The European Chemical Industry Council
  - American Petroleum Institute
  - American Cleaning Institute
  - Halogenated Solvents Industry Alliance Inc.
  - Methanol Institute
  - Nickel Producers Environmental Research Association (NiPERA)

- Government**
- Environmental Protection Agency
  - Food and Drug Administration
  - Health Canada
  - National Institute for Occupational Safety and Health
  - National Library of Medicine
  - New Zealand Ministry of Health
  - TERA State HELP Program
  - Texas Commission on Environmental Quality

# PROGRAMS

## APPLICATION OF CUTTING EDGE SCIENCE FOR HUMAN HEALTH RISK ASSESSMENT.

TERA has an active slate of diverse projects developing and applying cutting-edge approaches for human health risk assessment. We have coauthored assessments and toxicology reviews for U.S. EPA (drinking water criteria), NIOSH (IDLH support documents), and private sponsors. We published an occupational assessment of the butter flavor diacetyl (Maier et al. 2010) and published oral reference doses for pesticide degradates derived using an expert workshop approach (Gadagbui et al. 2010). We are also developing and reviewing documentation required under the EPA eHPV and EU REACH Programs for private sponsors. To meet our objectives in technology leadership



we have continued to be active in developing risk assessment methods. One area of emphasis centered on the use of early effects and systems biology to support dose-response assessment based on the concept of biologically-informed empirical models. Our methods development work also includes novel techniques related to modeling chemical mixtures, assessment of children's risk assessment issues, and application of mode-of-action, dose-response, and weight-of-evidence tools.

**PEER REVIEW AND CONSULTATION.** Engaging experts in development and review of toxicological and risk assessments is essential to ensure high quality results. Since 1995, we have provided private and public sponsors with high quality expert review and input, designing the most effective approach for the type of work product, stage of development, and purpose for engaging experts. Peer input, peer consultation, and peer review are three approaches we use, all of which follow the principles that are the cornerstone of our program – selection of appropriate expertise, scientific robustness, and transparency. The fourth principle, independence, is essential for all peer reviews and an important consideration for peer input and consultation efforts.

TERA engaged experts in 2010 to evaluate and review a variety of topics and work products, including a workshop to discuss a proposed hypothesis for lung tumor induction after inhalation exposure to nickel substances; peer review of support documents on nickel and arsenic for the Texas Commission on Environmental Quality's effects screening levels; letter reviews of Health Canada screening assessments for their Chemical Management Program; a workshop on nuclear receptor mediated liver cancer; a science advisory board to provide guidance on the design and conduct of a series of studies investigating the mode of action by which hexavalent chromium is carcinogenic; and completion of a peer review of a community-wide human health risk for Flin Flon, Manitoba.



**GLOBAL RISK RESOURCES.** *International Toxicity Estimates for Risk (ITER)* - Contains chronic human health risk assessment data from organizations around the world (660+ chemicals). [www.tera.org/iter](http://www.tera.org/iter) or <http://toxnet.nlm.nih.gov/>.

*Risk Information Exchange (RiskIE)* - Current human health risk assessment projects (over 4700) from 35 organizations in 13 countries. [http://www.allianceforrisk.org/ARA\\_tools.htm](http://www.allianceforrisk.org/ARA_tools.htm). This tool makes risk information readily available to help risk assessors collaborate during the risk assessment process.

*Alliance for Risk Assessment (ARA)* - A collaboration of organizations dedicated to supporting public health protection by working together on projects to improve the process, efficiency, and quality of risk assessment. ARA also provides up to 10 hours free technical support to each state and tribe annually through the State Hazard Evaluation Lending Program (StateHELP). [www.allianceforrisk.org](http://www.allianceforrisk.org)

# PROJECT HIGHLIGHTS

TERA scientists worked on dozens of technical project in 2010 for a variety of sponsors. TERA works collaboratively with scientists from all sectors to bring the best science and analysis to a project. Highlights and copies of project reports are available on the TERA web site. Below are a few examples of 2010 accomplishments.

**NUCLEAR RECEPTOR MEDIATED MODES OF ACTION WORKSHOP.** A workshop was held September 27-29, 2010 at the National Institute for Environmental Health Sciences (NIEHS) campus in Research Triangle Park to evaluate the current state of the science on nuclear receptor-mediated toxicities. The workshop was highly interactive with plenary sessions and case-study panel discussions. Participants included invited experts in nuclear receptor biology, toxicology, and risk assessment with additional experts from industry, academia, government, and non-profits. Case study panels evaluated mode of action and dose response data for the AHR, CAR/PXR, and PPAR $\alpha$  receptors. The workshop will result in peer-reviewed publications of the deliberations. For more information, see <http://www.tera.org/peer/nuclearreceptor/>.



**DOSE RESPONSE ASSESSMENT BOOT CAMP.** TERA's Dose-Response Assessment Boot Camp is an intensive hands-on training course in hazard characterization and dose-response assessment. Beginners through expert toxicological risk assessors will learn advanced methods, as well as enhance their understanding and skills in the basics.

Participants learned to derive and evaluate risk values and supporting documentation for both non-cancer and cancer risk assessments. Five Certification Management (CM) points are available from the American Board of Industrial Hygienists (ABIH), and the course is endorsed by both the Society of Toxicology (SOT) and the Society of Risk Analysis (SRA). We plan to offer this course at least annually. See <http://www.tera.org/Global/Bootcamp/> for the current offerings.

**BEYOND SCIENCE AND DECISIONS - DOSE RESPONSE WORKSHOPS.** TERA initiated a series of workshops in 2010 under the aegis of the Alliance for Risk Assessment ([www.allianceforrisk.org](http://www.allianceforrisk.org)). Sponsored by nearly 40 different organizations (including government agencies, industry groups, scientific societies, non-profit organizations/consortia, and consulting companies), this workshop series seeks to build on the suggestions of the National Academy of Sciences report *Science and Decisions: Advancing Risk Assessment* (NAS 2009) and other publications and panels, with the goal of developing a practical guidance document of dose-response techniques to advance the field of risk assessment. Two workshops were held in 2010 and a final workshop is scheduled for May 2011. The second workshop in October 2010 was held in tandem with the Federal & State Risk Assessment & Toxicology Committee.

**DIACETYL.** TERA prepared a toxicology review and issues analysis related to the availability of data to support development of an occupational exposure limit for diacetyl. Diacetyl, and several related chemicals, are used as butter flavors. These chemicals have been implicated as a cause of lung effects in microwave popcorn and flavor manufacturing workers (i.e., popcorn workers lung). Issues related to interspecies extrapolation and effects of peak versus cumulative exposure were evaluated and results were published (Maier et al., 2010) to document an OEL recommendation. The results were presented to science staff off various stakeholders, including regulatory agencies (U.S. OSHA and California OSHA) and organized labor organizations (e.g., the United Food and Chemical Workers Union). This issue has highlighted the need to consider occupational health issues for food ingredients and flavors, even where dietary exposures show little potential for harm. Using this work as a foundation, TERA continues to work with food companies to develop occupational health hazard characterization methods that are being applied for health risk prevention.

**SEARCH.** TERA and the Alliance for Risk Assessment partnered with a graduate student at Cleveland State University to reach out to state risk assessors. A comprehensive survey of the states uncovered a need for a centralized source of state agency contact information. The result, the State Environmental Agency Risk Collaboration for Harmonization (SEARCH) database of risk contacts for each state, was created. SEARCH is intended to help the flow of information across organizational boundaries. SEARCH is available at <http://www.allianceforrisk.org/SEARCH/index.html>.

## PUBLIC SERVICE



TERA staff continued to dedicate significant effort providing support to local communities and governments, as well as, supporting scientific development through *pro bono* activities and our TERA Corporate Development fund. Highlights of the *pro bono* efforts of the staff for 2010 are provided below.

**PROFESSIONAL SOCIETIES.** Many TERA staff hold office or leadership positions in professional societies, including the Society for Toxicology (SOT), the Society of Risk Analysis (SRA), and the American Industrial Hygienist Association (AIHA). During 2010, TERA scientists served as officers for the Mixtures Specialty Section of the Society of Toxicology (SOT), Chair of the AIHA Workplace Environmental Exposure Levels Committee, Member of the Science Symposium Committee, Member of a special AIHA Task Force on Guideline Values, Co-chair of the subcommittee that organizes continuing education workshops at the Society for Risk Analysis (SRA) Annual Meeting, Chair-elect of the Dose-Response Specialty Group of the SRA, Secretary of the Ohio SRA, councilor of the Ohio Valley Chapter of SOT, and an Executive Committee member of SOT Toxicologists of African Origin (TAO) specialty group.

**COMMUNITY SERVICE & OTHER ACTIVITIES.** TERA prides itself on being involved with our local communities. TERA staff volunteer their time and have been elected or appointed to local community organizations involved in public health, environmental and community issues. These include the City of Cincinnati's Environmental Advisory Committee, Oxbow Inc. board (a local land conservancy group), and local community councils. TERA also enjoys being involved with local activities, such as Earth Day. TERA staffed a booth at Cincinnati's Earth Day Celebration that focused on educating the public on toxicology and risk assessment and how it relates to their daily lives. Children's activities were also provided. Staff members also volunteer in local schools and serve as judges for science fairs and scholarship competitions. TERA is an organizational member of the Cincinnati Alliance for Chemical Safety (ACS), and has given lectures at their monthly meetings. Our scientists have given guest lectures at local universities on toxicology, risk assessment, and systematic approaches for evaluating the quality of epidemiological and clinical studies. Our Director serves as an Adjunct Associate Professor in the University of Cincinnati's Department of Environmental Health, providing lectures to graduate students and serving as a member of the Advisory Committee for the Biological Monitoring Core.

TERA scientists have given invited lectures to local and regional risk assessment meetings, to the National Library of Medicine, to the Commissioners of the Consumer Product Safety Commission, and at an African Society of Toxicological Sciences workshop in Nigeria. TERA scientists serve as expert peer reviewers on standing panels such as the expert science panel for NSF International, as well as served as peer reviewers for government agencies, such as the U.S. EPA.

# PUBLICATIONS

TERA staff have authored and co-authored a number of journal articles and book chapters in 2010. A full list of TERA's publications can be found on our website at <http://www.tera.org/Publications/Publications.html>. TERA scientists serve as peer reviewers for many journals.

Cain, WS; Dourson, ML; Kohrman-Vincent, MJ; Allen, BC. (2010) [Human Chemosensory Perception of Methyl Isothiocyanate: Odor and Chemesthesis](#). *Reg. Toxicol. and Pharmacol.* 58(2):173-180.

Chambers A, Krewski D, Birkett N, Plunkett L, Hertzberg R, Danzeisen R, Aggett PJ, Starr TB, Baker S, Dourson M, Jones P, Keen CL, Meek B, Schoeny R, Slob W. 2010. [An exposure-response curve for copper excess and deficiency](#). *J Toxicol Environ Health B Crit Rev.* 2010 Oct;13(7-8): 546-78. (Linked paper is a pre-print)

Dourson, M and Haber, L. (2010) Linear Low-Dose Extrapolation. In: *Cancer Risk Assessment*. Ching-Hung Hsu and Todd Stedeford, ed. John Wiley & Sons.

Dourson, ML; Kohrman-Vincent, MJ; Allen, BC. (2010) [Dose response assessment for effects of acute exposure to methyl isothiocyanate \(MITC\)](#). *Reg. Toxicol and Pharmacol.* 58(2):181-188.

Dourson, ML. (2010) [U-shaped dose-response curves: implications for risk characterization of essential elements and other chemicals](#). *J Toxicol Environ Health A.* 2010;73(2):181-6.

Gadagbui, B; Maier, M; Dourson, M; Parker, A; Willis, A; Christopher, JP; Hicks, L; Ramasany, S; Roberts, SM. (2010) [Derived Reference Doses \(RfDs\) for the Environmental Degradates of the Herbicides Alachlor and Acetochlor: Results of an Independent Expert Panel Deliberation](#). *Regulatory Toxicology and Pharmacology* 57:220-234.

Gadagbui, B; Rak, A; Patterson, J; Kutzman, R; Reddy, G. (2010) Development of a Relative Source Contribution Factor for Drinking Water Criteria: The case of Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX). Accepted for publication in *Human and Ecological Risk Assessment (HERA)*.

Haber, LT; Maier, MA; Hack, CE; Shulte, P; Fowler, B; Lotz, WG; Savage, RE Jr. (2010) [A Method for Biomarker Validation and Biomarker-Dose Response: A Case Study with a Bayesian Network Model for Benzene](#).

Hack, CE; Haber, LT; Maier, A; Schulte, P; Fowler, B; Lotz, WG; Savage, RE. (2010) A Bayesian Network Model for Biomarker-Based Dose Response. *Risk Anal.* 30(7): 1037-51.

Hasegawa, R; Mutsuko, HK; Dourson, ML; Parker, A; Sweeney, LM; Nishikawa, A; Yoshida, M; Ono, A; Hirose, A. (2010) [Proposal of new uncertainty factor application to derive tolerable daily intake](#). *Regul. Toxicol. Pharmacol.* 58(2): 237-242.

Maier, AM; Kohrman-Vincent, M; Parker, A; Haber, LT. (2010) [Evaluation of concentration-response options for diacetyl in support of occupational risk assessment](#). *Reg. Toxicol. and Pharmacol.* 58(2): 285-296.

Nance, P; Kroner, O; Haber, L; Dourson, M. (2010) Assessing Risks to Human Health. In: *Comprehensive Toxicology*, 2nd Ed., Charlene A. McQueen, ed.

Sweeney, LM; Kirman, CR; Gargas, ML; Carson, ML; Tardiff, RG. (2010) Development of a physiologically-based toxicokinetic model of acrylamide and glycidamide in rats and humans. *Food Chem Toxicol.* 48:668-85.

Zhao, QJ ; Haber, L ; Kohrman-Vincent, M ; Nance, P ; Dourson, M. (2010) Quantitative modeling in noncancer risk assessment. In: *Quantitative Modeling in Toxicology*, John Wiley, K. Krishnan and M.E. Andersen, ed.