

2002 Annual Report

**Toxicology Excellence for
Risk Assessment
(*TERA*)**

Cincinnati, Ohio

February 2003

TERA'S BOARD OF TRUSTEES

TERA's Board of Trustees consists of 9 members who serve 3-year rotating terms. The Board has elected officers, as listed below. Michael Dourson, Director of *TERA*, serves on the Board. Listed below are *TERA's* Board members for 2003. The date in parenthesis indicates the year each member joined *TERA's* Board of Trustees.

Chair: Roger McClellan, Independent Advisor and Chemical Industry Institute of Toxicology (President Emeritus) (2000)

Vice-Chair: Steven Lewis, ExxonMobil Biomedical Sciences (2001)

Daniel Acosta, Jr., University of Cincinnati, College of Pharmacy (2002)

Gail Charnley, HealthRisk Strategies (2002)

Robin Corathers, Mill Creek Restoration Project (2002, resigned mid-year)

Michael Dourson, Toxicology Excellence for Risk Assessment (indefinite)

Elaine Dorward-King, Rio Tinto plc (2001)

Jennifer Orme-Zavaleta, U.S. Environmental Protection Agency (2001)

James Wilson, Resources for the Future (2000)

The Board of Trustees held a meeting on February 13, 2002, to discuss the 2001 Annual Report and the plans and budget for 2002. This meeting was held in Cincinnati, Ohio and convened at 10:00 am Eastern. The Board also held a conference call meeting later in the year to discuss *TERA's* progress. On April 7, 2003, the Board met for a retreat with *TERA* staff, followed by its annual meeting on April 8, 2003, to discuss the 2002 Annual Report and the plans and budget for 2003. Both the retreat and the annual meeting were held in Cincinnati, Ohio, and the annual meeting convened at 8:30 am Eastern.

Chairperson's Message

It is a pleasure to serve as Chair of *TERA*'s Board of Trustees. *TERA* is a remarkable non-profit organization dedicated to promoting the best use of scientifically sound toxicity data for risk assessment purposes. It was created in 1995 by Dr. Michael Dourson to fill a critical need that was not being met by government, industry, environmental or academic organizations. *TERA* works with groups and individuals from all sectors of society to find a common ground through application of science-based data in risk assessments that address important societal issues.

The year 2002 was one of substantial accomplishments for *TERA*. It secured a record level of funding balanced between government and industry sponsors allowing further growth in staffing. The staff continued to grow professionally and, most importantly, demonstrated through individual efforts and effective teamwork a remarkable level of productivity. *TERA* continues to gain in both national and international reputation with recognition for its science-based orientation to risk assessment and its independence. This was exemplified by *TERA*'s receipt of an award from the State of West Virginia for leadership in developing a risk assessment for perfluorooctanate using a multi-party, multi-stakeholder approach.

At year-end, it was announced that Dr. Michael Dourson would receive the Society of Toxicology's Arnold J. Lehman Award. This prestigious award is given annually to an individual in recognition of their contributions to risk assessment and/or regulation of chemicals including pharmaceuticals. I join with my fellow Trustees and many others in extending congratulations to Mike for an award that not only recognizes his professional contributions over the past two decades, but also his founding of *TERA* and its remarkable achievements of the *TERA* staff since its founding.

The *TERA* Trustees offer their congratulations to Mike and his colleagues for a very successful 2002. We also renew our commitment to work with the *TERA* staff and sponsors to continue a remarkable record of achievement built on applying scientifically sound data in an impartial manner to important societal issues.

/s/

Roger O. McClellan, DVM, DABT,
DABVT, FATS

INTRODUCTION

Toxicology Excellence for Risk Assessment (*TERA*) is a growing scientific and educational organization that strives to protect public health by studying the toxicity of environmental contaminants and developing corresponding risk values. Through research and publication, our organization seeks to improve the methods by which these risk values are derived and made available. *TERA* helps environmental, industry, and government groups find common ground through the application of good science to risk assessment. In fostering successful partnerships, improvements in the science and practice of risk assessment will follow. *TERA*'s work on such partnerships provides us with a good appreciation for the diversity of scientific judgments on different issues. In addition, our peer review program and on-line database enable *TERA* to provide scientists and the general public with the most accurate and reliable source of published risk values. *TERA*'s mission is to improve risk assessment through the best use of toxicity data. *TERA* is a non-profit and tax-exempt 501(c)(3) organization under the U.S. Internal Revenue Service Code. *TERA* is independent and not associated with any organization, government, or industry.

TERA's staff has exceptional scientific credentials. Several staff members either served on EPA's RfD/RfC workgroup (two as co-chairs), or provided contractor support. Collectively, *TERA* staff have reviewed or developed hundreds of RfDs and RfCs, and *TERA* scientists have been at the forefront of research related to the application of uncertainty factors. *TERA* scientists were also among the first contractors to develop chemical assessments under EPA's IRIS pilot program, and then later under the implementation of the revised IRIS process resulting from that pilot program. Our scientists have developed (in whole or in part) at least five IRIS toxicological support documents under the revised IRIS program, are very familiar with the format and data requirements for these documents and the related IRIS cover sheets. *TERA* scientists have extensive experience in the development of RfCs under EPA's 1994 methodology. We are knowledgeable in the methods of making dosimetric adjustments between animals and humans, and have authored several RfCs for respiratory irritants. This experience is enhanced by the experience of *TERA* staff who have conducted research in respiratory toxicology.

Highlights of *TERA*'s programs are on the following pages.

VERA (VERIFIABLE ESTIMATES FOR RISK ASSESSMENT)

The mission of *TERA*'s *VERA* program is to develop state-of-the-science risk assessments that protect human health through the best use of toxicity data and exposure factor values. *TERA* scientists continue to develop comprehensive assessments, such as those for IRIS, while also increasing our activity in several other types of assessment. In 2002, *TERA*'s *VERA* program saw the continuation of work on numerous assessments that were initiated in 2001. For example, we continued support of Drinking Water Criteria Document development for disinfection byproducts and IRIS assessments for phenol, soluble nickel, and tetrahydrofuran. We also facilitated the development of an RfD and RfC for ammonium perfluorooctanoate for the State of

West Virginia using a cooperative process that allowed for input by multiple stakeholders. We will be encouraging this multi-stakeholder process for new assessments in 2003. In addition to the comprehensive assessments that have been the core of our work activity, we broadened the scope of our projects beyond traditional EPA chemical hazard and dose response assessments in 2002. For example, *TERA* engaged new sponsors in project areas, including determining clearance values for product residuals on equipment, deriving occupational exposure limits, conducting screening level exposure assessments, and conducting cancer mode of action assessments.

***ITER* DATABASE (INTERNATIONAL TOXICITY ESTIMATES FOR RISK)**

Develop and maintain a comprehensive database that provides risk assessors tools to help protect public health through the use of the best toxicity and exposure information.

- Obtained funds for reviewing, updating and expanding *ITER*.
- Goal to finalize addition of RIVM data by 12/31/02. We have submitted 21 chemicals to RIVM for final review, are finalizing 4 more, need to finalize about 75 more chemicals.
- We have completed addition of ATSDR data to 57 chemicals (30 of which are new to *ITER*). We have drafted and need to finalize about 20 more.
- We have kept our existing data current, including *ITER*'s "What's New" page, and updated information pages on *ITER* (such as Glossary, Methods, Sponsors, etc.) as needed.
- We have begun sending list of recent *ITER* What's New items to several individuals who asked to be on mailing list
- Partnership with National Library of Medicine (NLM) to add *ITER* to the TOXNET system. With this arrangement, *ITER* would be available in its current location and also on NLM's TOXNET compilation of databases.
- Conducted a study of *ITER* to evaluate which and how many organizations have derived risk values for the chemicals on *ITER*. Presented posters with results of this study at SOT 2002 meeting, a multi-agency risk assessment conference in Spring 2002 in Cincinnati, and presented the results at the Midwest States Risk Assessment Symposium in July.

PEER CONSULTATION AND REVIEW PROGRAM

Our purpose for the Peer Consultation and Review Program is to provide scientists and others with the opportunity for expert independent peer consultation and peer review of risk assessment related documentation through panel meetings or other venues.

We have provided this service to the risk assessment community since 1996, having organized and conducted over two dozen panel reviews and numerous paper reviews. Meetings are generally conducted in a transparent fashion and open to the public. *TERA* manages all aspects of the peer consultation or review including: the selection of the panel, identification and management of conflict of interest and bias, development of issues to focus panel discussions, conducting meeting, all logistical and facility arrangements, and preparation of a meeting report.

In October, we conducted a very significant review of toxicity benchmark values for use in the World Trade Center clean up. An expert panel was assembled in Manhattan to conduct a scientific peer review of a document entitled, "World Trade Center Indoor Air Assessment: Selecting Contaminants of Potential Concern and Setting Health-Based Benchmarks." The document was developed by U.S. federal, state, and local agencies involved in the World Trade Center cleanup. The panel engaged in detailed discussions regarding key aspects of the documents including selection of contaminants of concern, suitability of selected toxicity benchmark values, and appropriateness of the sampling techniques and exposure analysis. Over 25 members of the public who were provided the opportunity to present comments to the panel attended the open and public meeting.

In March, *TERA* organized an independent panel of expert scientists, including skin penetration researchers and dermal exposure and risk assessors, to meet in Ottawa to review an early draft of dermal exposure guidance being developed by Health Canada's Existing Substances Division, Safe Environments Programme, for assessment of existing substances under the Canadian Environmental Protection Act (CEPA, as amended in 1999). The expert panel members provided advice to Health Canada on their approach.

TERA has continued to develop our program in the area of peer consultation, utilizing a five-year cooperative agreement from the U.S. Environmental Protection Agency (EPA) and individual project funding. Issues regarding identification and management of conflict of interest and bias, format and scope of meeting reports, public participation at meetings, and communicating review materials and results with participants and the public, have been explored and procedures developed. These policies and procedures will be tested in various peer consultations planned over the next several years, including those for the Voluntary Children's Chemical Evaluation Program (VCCEP).

TERA scientists continue to provide review and comment on risk documentation for both government and private-sector sponsors. These include serving as expert peer reviewers for EPA Integrated Risk Information System (IRIS) documents, and assisting government and private sponsors by reviewing the technical basis for chemical analyses, exposure assessments, methodological approaches, and computer software.

We shared our work in this area primarily by posting information and documents on our website (www.tera.org/peer). In addition, a poster exploring the similarities and differences between peer review and peer consultation was presented at the 2002 Annual Meeting of the Society for Risk Analysis.

RISK ASSESSMENT RESEARCH PROGRAM

The mission of *TERA*'s Research Program is to move the science of risk assessment forward by improving the application of current methods, developing and defining new methods, obtaining the data to support such applications, and educating the scientific community and the general public about advances in risk assessment research.

TERA scientists have led efforts in the development of many of the methods currently used by risk assessors, and we continue to conduct research in these areas. In 2002, our research program published four papers (Haber & Maier, 2002; Araya et al., 2002; Gentry et al., 2002; and Haber et al. 2002) with additional manuscripts nearing publication. In work that is likely to ultimately have a substantial impact on how risk assessments for children are done in the future, *TERA* collaborated with scientists from the Environ Corporation in collecting and analyzing data on physiological parameters for neonatal animals. This work will aid in determining whether a given exposure will result in a higher tissue or lower dose to children (and thus potentially higher risk) than to adults. We also published two other papers on issues related to children's risk (Dourson, et al., 2002 and Scheuplein et al., 2002). In another collaboration with Environ, we published an approach for evaluating the impact of polymorphisms in metabolic enzymes on tissue dose. *TERA* has also published research on ways to improve the development of occupational exposure limits. We have been developing hazard evaluation frameworks for considering the risk to human health from occupational exposure to chemicals and physical agents, and risks from diverse non-lethal weapons technologies.

- **Non-lethal weapons.** *TERA* (for the Department of Defense, under subcontract with Veridian Engineering) has developed a proposed framework for risk characterization of non-lethal weapons. This framework was applied to characterize the risks from the 66mm Non-Lethal Grenade and CS gas (o-chlorobenzylidene malonitrile), and work was begun on the advanced tactical laser (ATL) system. *TERA* held five workshops with experts and DoD personnel to develop the framework and these assessments. This work has been presented at several meetings and conferences.
- **Genetic polymorphisms.** In collaboration with Environ, *TERA* completed two case studies (for warfarin and parathion) evaluating how polymorphisms in metabolic enzymes affect tissue dose. Implications for determination of chemical-specific adjustment factors (CSAFs) were discussed. Results of the analysis were published in 2002. This work was funded by a competitive grant from the American Chemistry Council.
- **Hazard evaluation frameworks.** Chemical and physical hazard evaluation frameworks were completed for Applied Biosystems, and a poster describing some of the work received the "Outstanding Risk Assessment Poster" award at the 2002 American Industrial Hygiene Conference & Expo (AIHCE). These projects included frameworks for: 1) evaluating the human health risk from occupational exposure to a chemical, making maximum use of the available toxicity and exposure data, and 2) assessing the physical hazards of new chemicals intended for R&D usage. In a related project for another company, *TERA* is comparing selected hazard and risk ranking methods for evaluating the relative hazard and risk profiles of the chemicals used in facilities and products.
- **Parameters for neonates.** Under contract to EPA and in collaboration with Environ, *TERA* compiled data on physiological parameters for neonatal animals. The ultimate goal of this project is to develop a set of parameters for physiologically-based pharmacokinetic (PBPK) modeling of neonates, to aid in determining how the tissue dose of neonates compares with that of adults, thus aiding in the evaluation of children's risk. The results of this analysis will be submitted for publication early in 2003.
- **Copper.** *TERA* continued its support to the International Copper Association for laboratory studies being conducted to determine the acute nausea threshold for copper. A manuscript was submitted in 2002, and the manuscript revised in response to the peer review comments will be submitted in early 2003.

- **Scientific Criteria for the Development of OELs.** *TERA* published a paper surveying the methods used by a number of organizations to develop limits on occupational exposure (also known as occupational exposure limits, or OELs) for metals, metal compounds, and other compounds related to mining operations. Differences and commonalities in OELs were highlighted, and research and other actions to address outstanding issues were recommended. This work was presented to the European Union committee on OELs.

Financial Report

Our income for 2002 was \$1,661,822. Our budgeted expenses were \$1,706,600. This resulted in a loss of \$44,779 on our budget. However, with the inclusion of other income and expense, our overall net revenue was \$13,609.

