

2003 Annual Report

Toxicology Excellence for Risk Assessment (*TERA*)

Cincinnati, Ohio

February 2004

TERA'S BOARD OF TRUSTEES

TERA's Board of Trustees consists of 8 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 was most recently elected to *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 April 18, 2003 to approve the 2002 Annual Report and the plans and budget for 2003. This meeting was held in Cincinnati, Ohio. The Board also held a conference call on September 5, 2003 to discuss *TERA's* progress.

Chairperson's Message

I again express pleasure in serving 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 2003 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 partnership with the National Library of Medicine (NLM) to add *ITER* to the TOXNET compilation of databases (<http://toxnet.nlm.nih.gov/>) in early 2004, and the launching of the Voluntary Children's Chemical Evaluation Program (VCCEP) peer consultations of chemical-specific assessments prepared by industry. Funding for *TERA*'s conduct of these peer consultations is from a cooperative agreement with the U.S. Environmental Protection Agency.

TERA research publications are well cited. Based on the latest identified percentiles of the Science Citation Index, nearly all of *TERA*'s publications fall into the top 25% of published papers, and many fall into the top 10%. *TERA* has also increased its project diversity in the Verifiable Estimates for Risk Assessment (*VERA*) program while maintaining core strength in developing comprehensive assessments.

The *TERA* Trustees offer their congratulations to Mike and his colleagues for a very successful 2003. 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.

International Toxicity Estimates for Risk (*ITER*) Database

The *ITER* Database had one of its most successful years during 2003. *TERA* and the National Library of Medicine (NLM) solidified a partnership to add *ITER* to NLM's TOXNET compilation of databases (<http://toxnet.nlm.nih.gov/>) in early 2004. *TERA* developed a partnership with NSF International to add its data to *ITER* during 2004. Additionally, over 80 chemical files were drafted with cancer classification information from IARC; this effort will be completed during 2004. *ITER* has also become more robust, as nearly all of the remaining RIVM and ATSDR data were added in 2003. Finally, because of *TERA*'s new partnerships with NLM and NSF International, *ITER* is now financially independent for the next several years.

Highlights for 2003

- The addition of *ITER* to TOXNET has resulted in an enhanced risk resource. For example, as part of TOXNET, *ITER* can now be searched by chemical synonym and via free text. Multi-file searching allows a single query to be run against multiple toxicological databases, including *ITER*, and links to TOXLINE allow users to obtain current literature references and abstracts on *ITER* chemicals.
- One of the goals of *ITER* was to provide a place for non-government organizations to provide their data to the public. NSF International is a non-profit, non-government organization that derives oral risk values. The addition of this data will help meet this goal and provide a new source of risk data.

Peer Consultation and Review Program

TERA's purpose for the Peer Consultation and Review Program is to provide sponsors with the opportunity for independent, expert scientific peer consultation and peer review of risk assessment related documentation through panel meetings or other venues. Most peer reviews and consultations are conducted through face-to-face group meetings, although we occasionally conduct a "paper" review through the mail. Our goal is a transparent and public process to facilitate maximum sharing of information and credibility of conclusions. *TERA*'s role is to manage all aspects of the peer consultation or review, including independent selection of the panel, identification and management of conflict of interest and bias issues, development of discussion items to focus panel deliberations (i.e., the Charge), conduct of meetings, all logistical and facility arrangements, and preparation of a meeting report.

Highlights for 2003

- During 2003 *TERA* organized and conducted peer consultations for assessments prepared under the Voluntary Children's Chemical Evaluation Program (VCCEP) and peer reviews for a number of risk documents prepared by industry sponsors. In addition, *TERA* scientists served as expert peer reviewers for others' documents and projects. *TERA* is applying peer consultation concepts and techniques to other projects, including our efforts to evaluate and characterize risks from non-lethal weapons and development of risk values.
- 2003 saw the start of Voluntary Children's Chemical Evaluation Program (VCCEP) peer consultations of chemical-specific assessments prepared by industry. Funding for *TERA*'s conduct of these peer consultations is from a 5-year cooperative agreement with the U.S. Environmental Protection Agency

2003 Peer Consultations

- **VCCEP Vinylidene chloride**
Dow Chemical Company
- **VCCEP Decabromodiphenyl ether - ACC Brominated Flame Retardant**
Industry Panel
- **VCCEP Octabromodiphenyl ether**
Great Lakes Chemical Company
- **VCCEP Pentabromodiphenyl ether**
Great Lakes Chemical Company
- **VCCEP Acetone**
ACC Acetone Panel
- **NLW Electromuscular disruption device (TASER)**
DoD
- **NLW Riot Control Agent**
DoD

(EPA). These are public meetings and observers are provided the opportunity to present comments for the panel's consideration. Approximately 15 additional chemicals will undergo peer consultation in the VCCEP program over the next 3 years.

- In addition to the reviews mentioned above, *TERA* also assisted government and private sponsors by reviewing the technical basis for chemical analyses, exposure assessments, methodological approaches, and computer software. Examples include serving on government committees or peer reviews for the World Trade Center cleanup, EPA's Candidate Contaminant List (CCL), Homeland Security, EPA Toxicological Reviews.

2003 Peer Reviews

- **Cancer mode of action for Captan**
The Captan Task Force: Arvesta Corporation, and Makhteshim-Agan of North America Inc.
- **Reference dose (RfD) for resorcinol**
Beazer East, Inc
- **Assessment of acrylonitrile**
The Acrylonitrile Group
- **Water treatment process**
Progress on Previous Peer Review Recommendations

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. A significant percentage of the research program continues to be risk characterizations of nonlethal weapons. This work included the development and application of new risk assessment approaches to complex problems, and bringing the NAS risk assessment paradigm to nonchemical agents, such as electromagnetic disruptors. Other *TERA* research projects include improving evaluations of children's risk, analysis of the methods used to evaluate risk from short-term exceedances of drinking water guidance levels, and improvement of methods for hazard screening and ranking large numbers of chemicals.

Highlights for 2003

- ***Nonlethal weapons health effects and effectiveness risk characterizations*** - completed the characterization of the risks from two weapon systems. Developed a generalized risk characterization model that can be adapted to include a variety of weapon systems, in collaboration with LINEA, Inc. Began two new risk characterizations. Implemented a modified approach

2003 Research Projects

- Nonlethal weapons risk characterizations:
 - CS gas (o-chlorobenzylidene malonitrile), a riot control agent
 - Advanced tactical laser (ATL) system
 - Electromuscular disruptors (e.g., TASER)
 - OC gas (oleoresin capsicum), a riot control agent
- Screening and ranking methods for Health Canada's Domestic Substances List (DSL)
- Physiological parameters for neonatal animals
- Analysis of, and improvements to, methods for evaluating Unreasonable Risk to Health (URTH) for short-term exceedances of drinking water guidance levels.
- Copper nausea threshold – phase II
- Integrating excess and deficiency in evaluation of copper exposures
- Completed project on dose-response assumptions

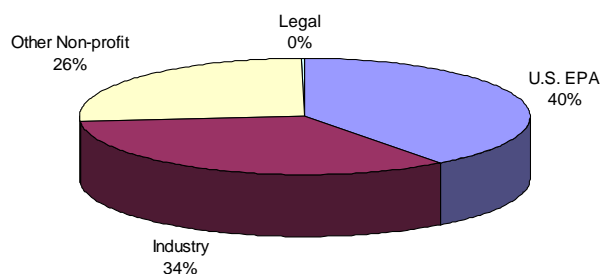
for the characterizations to include a data sharing workshop and a peer consultation on interim work, in addition to the already-existing peer review of the completed document.

- **Children's risk** - continued work in collaboration with Environ, 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 dose to children (and thus potentially higher risk) than to adults. Presented to EPA's Science Advisory Board regarding EPA's draft methods for evaluating cancer risk to children.

Verifiable Estimates for Risk Assessment (VERA) Program

The *VERA* program's mission is to develop state-of-the-science risk assessments that protect human health through the best use of toxicity data. Our *VERA* project work continued to provide value to sponsors in need of neutral guidance and a high degree of technical expertise. The *VERA* program also ensures that *TERA* staff remains current on important issues encountered in the practical application of toxicology to risk assessment, enhancing our ability to identify research needs and conduct high quality peer reviews and consultations.

VERA Hours by Sponsor Category



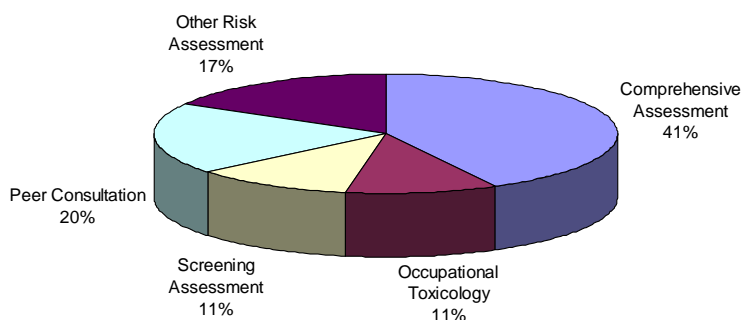
Highlights for 2003

- **Increased project diversity** - Maintained core strength in developing comprehensive assessments, while expanding into growth areas such as hazard screening and new chemical assessments under U.S. EPA's Sustainable Futures Initiative.

- **High impact projects** - Last year, *TERA* announced the initiation of a peer consultation process on risk assessment issues for trichloroethylene (TCE) at the request of the United States Air Force.

The purpose of this project is to develop the science for issues of shared interest to the Air Force and EPA. The resulting science (documents, models, databases, or analyses) will be available for any interested party for incorporation into their own TCE risk assessment efforts. Initial work was started on the development of a harmonized TCE PBPK model, and may be followed by consultation meetings for other key issues.

VERA Hours by Project Area



Comprehensive Assessments: Atrazine, Cyanide, Nickel, Tetrahydrofuran
Occupational Toxicology: Occupational exposure limits; Job Safety Analysis
Screening Assessments: EPA Sustainable Futures Initiative
Peer Consultation: Trichloroethylene
Other Risk Assessment: Perchlorate, Disinfectant By-products Children's Risk

Financial Report

TERA's 2003 income was \$1,865,674, including Combined Federal Campaign donations of \$1,304 and interest earned of \$3,128. Actual expenses totaled \$1,868,751. This resulted in net loss of \$3077. Seventy-nine percent of *TERA* work was for governments and other non-profits, and 19% for the private sector. The figures below summarize *TERA's* program activity during 2003.

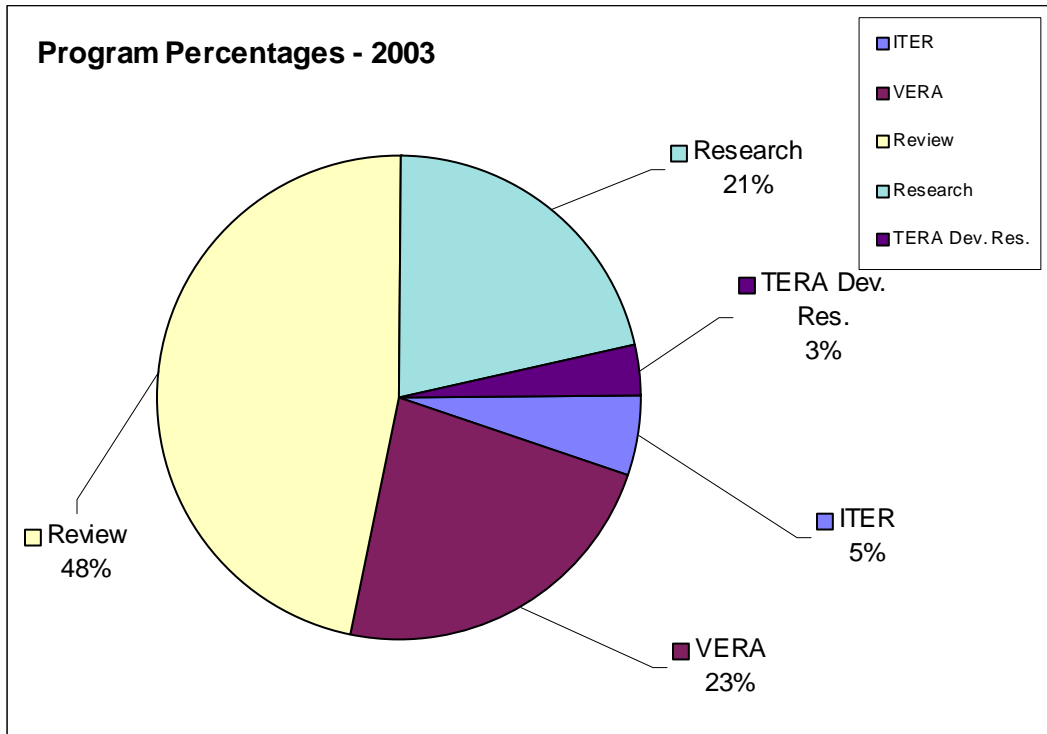


Figure 1. Percentage of *TERA* effort by program area for 2003.