

Greetings!

Calendar year 1997 was good for our *TERA*. We hired 3 individuals (Dr. Jay Zhao, Ms. Molly Lipstreu, and Ms. Carol Haynes), developed assessments for several chemicals, improved the existing *ITER* database, conducted 2 independent peer review meetings, published several papers, and donated 540 hours of time to State Hazard Evaluation Lending Program (State HELP) and scientific organizations. We also posted a modest gain of ~\$20,249. Our balance of work was 32% for government and other nonprofit organizations, 25% for industry and other profit organizations, 7% pro bono, 8% marketing, and 29% administrative (see table and figures in the administrative part of this report).

The enclosed agenda includes a number of important items for discussion at our upcoming annual meeting, including reports of various projects, a summary of our 1997 finances and presentation of our 1998 budget. We also need to expand of the Board of Trustees. We seek input on suggestions for appropriate individuals to replace our retiring members (Bingham, Culler and Keller). We would like our Board to be made up of a diverse group of individuals with experiences in either fundraising, marketing or business planning, in addition to technical skills and public participation from which our risk assessment group can draw.

We look forward to a productive meeting and value your contributions of time and talent!

Sincerely,

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

Annual Meeting Board of Trustees
Toxicology Excellence for Risk Assessment

April 26, 1998 2:00 pm
Agenda

- I. Call to Order and Approval of Agenda
Michael Dourson
- II. Introduction of New Staff
- III. Expansion of the Board of Trustees
Board of Trustees
- IV. Reports
TERA staff
 - A. *VERA* - Verifiable Estimates for Risk Assessment (page 3)
 - B. *ITER* - International Toxicity Estimates for Risk (page 5)
 - C. Peer Review Meetings (page 5)
 - D. Education and Outreach (page 6)
 - E. Research (page 8)
- V. Financial Report for 1997 and Proposed 1998 Budget (page 10)
Michael Dourson
Vote on 1998 Budget
Michael Keller
- VI. *TERA* Plans for the Future
All
- VII. Adjourn 4:00 PM

***VERA* (Verifiable Estimates for Risk Assessment)**

Under the *VERA* project, *TERA* scientists develop risk estimates for interested parties. Generally, risk estimates are developed for chemicals that have either not been evaluated by other agencies (e.g., U.S. EPA), or the available assessments are not up-to-date. The product of an assessment under *VERA* may take many forms, depending on the need of the sponsoring party. The assessment may be in the form of a report, a manuscript suitable for publication, or in the format used by U.S. EPA for their risk assessment files. Upon completion of a *VERA* assessment, the sponsor may opt to submit the new or updated assessment to a government agency (e.g., U.S. EPA) for their consideration, or may opt to bring the assessment to a *TERA*-sponsored peer review meeting for consideration of inclusion on our *ITER* database.

In 1997, several assessments were undertaken as a part of the *VERA* project:

- The inhalation cancer assessment done by *TERA* on acrylonitrile was presented and accepted at the December, 1996 peer review meeting. It was loaded onto the *ITER* database in March, 1997. In addition, a manuscript was submitted to Regulatory Toxicology and Pharmacology, accepted for publication, and published (see research report). This work was sponsored by an industry trade group.
- *TERA* conducted an evaluation of the toxicological data base for sodium chlorate. This included an evaluation of the data that are available to support an oral reference dose (RfD). This work was sponsored by a chemical industry.
- *TERA* conducted an evaluation of the toxicological database for chlorpyrifos, with an emphasis on noncancer effects following inhalation exposure. As part of this project, a preliminary reference concentration (RfC) was calculated. This work was done for another consulting firm, whose client was an internationally based industry.
- *TERA* conducted an evaluation of the noncancer health effects of acetonitrile. Preliminary RfDs and RfCs were calculated. This project was sponsored by an industrial client.
- Formaldehyde (inhalation, cancer): This is a collaborative effort with CIIT (Chemical Industry Institute of Technology), a non-profit research organization. The first draft of the assessment was completed in 1997. *TERA* gave several presentations on this research, including talks at the American College of Toxicology meeting (November, 1997) and the annual meeting of the Society for Risk Analysis (December, 1997). A revised draft of the document is scheduled for peer review by Health Canada and the U.S. EPA in March, 1998, with completion at some later point. *TERA*'s effort is sponsored by the Formaldehyde Epidemiology, Toxicology and Exposure Group, an industry trade group.
- *TERA* has recently been approved to expand an earlier project on acrylonitrile, which was completed in 1997. The original work focused on an assessment of carcinogenic risk to humans following inhalation of acrylonitrile. The additional work that has been authorized will involve an evaluation of cancer risk following oral exposure, as well as an evaluation of

noncancer risk following both oral and inhalation exposures. This work is being supported by an industry trade group.

- *TERA* in association with the U.S. Air Force, U.S. EPA, the Perchlorate Study Group and others has helped develop protocols for several studies on perchlorate that will fill in data gaps that currently exist in the database. The protocol review panel reviewed all of the protocols before studies were initiated. The following studies are currently in progress and will be incorporated into a reassessment of the perchlorate RfD that will take place in the fall of 1998.

90-day bioassay in rats. Conducted by Springborn Laboratory, Ohio. Funded by the U.S. Air Force. The 90-day study was designed to identify the threshold for thyroid effects of perchlorate, address the potential for toxicity of other organs, and to produce results suitable for benchmark modeling. The final protocol for this study is available on the homepage.

Neurobehavioral Developmental Study in rats. Conducted by Argus Research Laboratory, Inc. in Horsham, Pennsylvania. Funded by the U.S. Air Force. The neurobehavioral developmental study was designed to address the potential for perchlorate to affect neurological development and learning after fetal/neonatal exposure. The final protocol for this study is available on the homepage.

Segment II study (and dose range-finding study) in rabbits. Conducted by Argus Research Laboratory, Inc. in Horsham, Pennsylvania. Funded by the Perchlorate Study Group. This study will evaluate the potential for perchlorate to cause developmental effects and was designed to meet U.S. EPA testing guidelines and reduce uncertainty associated with an incomplete database. The protocol for the dose range-finding study is available on the homepage and the protocol for the full study will be available when it is finalized.

Two-generation reproduction study in rats. Conducted by Argus Research Laboratory, Inc. in Horsham, Pennsylvania. Funded by the Perchlorate Study Group. This study will evaluate the potential for perchlorate to cause reproductive effects and was designed to meet U.S. EPA testing guidelines and reduce uncertainty associated with an incomplete database. The protocol for this study is available on the homepage.

Immunotoxicity Assay. Conducted by the Medical University of South Carolina. Funded by a research grant from the U.S. Army. The immunotoxicity study is also in progress and will help address questions regarding the potential for perchlorate to alter the immune system.

- *TERA* completed an Occupational Hazard Profile on Perchloroethylene in 1997; this work was done for NIOSH. The document includes a description of physical and chemical properties, regulatory information, and a brief summary of the toxicological database for perchloroethylene. Following completion of this document, NIOSH approved additional

work for *TERA* to write Hazard Profiles for 10 additional chemicals. This work will be completed in 1998.

***ITER* (International Toxicity Estimates for Risk)**

During 1997, *TERA* explored the possibility of forming a partnership with one or more other organizations to further develop the *ITER* database. The previous strategy had been to pursue direct funding from corporate or government sources. This had not been very successful, but we found a number of groups interested in working together on *ITER*. *TERA* discussed possibilities with several for-profit and not-for-profit organizations and in mid-1997 signed a Memorandum of Understanding (MOU) with Concurrent Technologies Corporation (*CTC*) of Johnstown Pennsylvania to enhance and expand the *ITER* database.

CTC is a non-profit research and development corporation. Their mission is to improve the Nation's industrial competitiveness through effective development and transfer of leading edge technologies, such as *ITER*. *CTC* has agreed to make enhancements to the database and develop a web enabled data entry interface, as well as compile and load information on over 70 additional chemicals for *ITER*. *CTC* is funding this work through DOD contracts to provide DOD with easy access to high quality risk values for a variety of DOD needs. Under subcontract to *CTC*, *TERA* will provide quality control of data compilation and will write the synopsis paragraphs which explain the differences between the organizations' values. This task is currently being performed with the additional chemicals to be completed by early summer 1998. In addition, Syracuse Research Corporation (*SRC*) is providing some informal assistance to add the remaining risk values from EPA's IRIS to the system by the end of this year.

TERA is excited to have established a formal relationship with *CTC* and we are exploring opportunities to collaborate on future research and development projects. Future projects with *CTC*, to market the database and establish a fee system, which will cover maintenance and updates, are being explored.

Peer Review Meetings

TERA's peer review program continues to provide industry, government and others with high-quality independent peer reviews. Two meetings were held in 1997. In March, assessments for dichloromethane (methylene chloride), cadmium, and perchlorate were reviewed by a panel of risk assessment experts. In September, assessments for phenol and acetaldehyde were reviewed. The dichloromethane, acetaldehyde and phenol assessments were prepared and presented by Health Canada. The cadmium RfC was presented by U.S. EPA's Region 8, while perchlorate was developed by *TERA*.

These peer review meetings provide a forum for public and private organizations to have their chemical-specific assessments and other risk-related documentation undergo an independent scientific peer review. The peer review panels consist of experts in risk assessment from government, industry, academia and other groups. These individuals volunteer their time and

talents to help improve the science and practice of risk assessment. All meetings are open to the public.

Sponsors of the assessments have been very pleased with the high quality reviews they have received. Health Canada has appreciated the risk assessment expertise of the panels and has scheduled two additional chemicals for review during 1998.

A number of issues related to this program have been identified. These include the inclusion of specific expertise, management of conflict of interest and quantity of review materials. For example, the review of the perchlorate RfD (reference dose) has caused *TERA* to consider the issue of our organization setting up the peer review and also having prepared the chemical assessment. While *TERA* has been very careful to keep staff working on an assessment from participating in the selection of peer reviewers and running of the peer review meeting, there are still some people who feel there is an appearance of a conflict of interest in this situation. In the case of perchlorate, the peer review panel demonstrated its independence of *TERA* as it disagreed with the RfD and rendered the opinion that more animal studies were needed before the data would be adequate to derive an RfD. This conclusion of the panel has resulted in the U.S. Air Force and the Perchlorate Study Group (a coalition of companies) to have several animal toxicity studies performed to address the weaknesses in the perchlorate database.

Education and Outreach

As a non-profit organization, *TERA* is committed to working with the public to improve knowledge and understanding of risk assessment issues. In 1997, *TERA* expanded its education program to accomplish these goals. *TERA* has worked with industry, the legal community, the academic community, and a local environmental group in this area. Some specific projects are listed below:

Training Activities

- Volunteered time to University of Cincinnati Graduate program in Toxicology to coordinate and help teach a graduate level risk assessment course.
- Volunteered time to University of Cincinnati Medical School to teach noncancer and cancer risk assessment to Occupational Medicine residents.
- Developed and presented a one-day training course in noncancer risk assessment to U.S. EPA's Office of Toxic Substances.
- Developed and presented lectures in Toxicology and Risk Assessment given at the Manager Training program sponsored by the EPA Office of Personnel Management.
- Developed and presented a one-day training course in cancer risk assessment for a private physician.

- Participated in AIHC/EPA Workshop on use of innovative risk assessment methods in Superfund site remediation.

Legal Activities

- Reviewed the effect of incorporating EPA's new PCB cancer potency value into a Superfund risk assessment. *TERA's* written comments were incorporated into the Public Comments on the site Consent Decree that were submitted to U.S. EPA Region III.
- On behalf of attorney for a citizen's group in California, *TERA* reviewed the data related to a delisting petition for a chemical.
- Provide risk assessment support and expert testimony on dioxin toxicity to an attorney for a cost-recovery suit.

Public Involvement

- Volunteered time to a local comparative risk project, the Hamilton County Environmental Priorities Project.
- On behalf of an industry partner, planned and facilitated a public meeting in California on the health effects of perchlorate in drinking water.
- Served as a resource for citizens in California and Nevada to obtain information on perchlorate, by phone and email.

State HELP

In keeping with our mission, *TERA* has a project called "State Hazard Evaluation and Lending Program (State HELP) under which each state, including local government or public/non-profit entities within a state, can receive annually up to 10 hours of technical support from *TERA* scientists free of charge. In 1997, the States of Oregon, Vermont, Ohio, California, New York and Michigan took advantage of this project by requesting either technical support for risk assessment problems over the telephone, by email, or requesting a written review of one of their States' risk assessments.

The project with the Oregon Department of Health was of particular interest because it was the first StateHELP project to ultimately produce income. Under the StateHELP program, ODH originally requested that *TERA* provide a written review of a risk assessment it had performed on

microcystin toxin in blue-green algae tablets. As a follow-up, ODH hired *TERA* to provide written response to public comments on the risk assessment.

Research

TERA scientists, through sponsored projects and *TERA* efforts, investigate new risk methods and improvements on existing methods. *TERA* has worked on projects such as data-derived uncertainty factors, comparative dietary risk for fish advisories, chromium contamination of soils, route-to-route extrapolation of methyl tert-butyl ether, and probabilistic RfDs with researchers from government, industry, university and other research organizations. Each of these projects has (or will) result in the publication of peer-review manuscripts, a listing of which can be viewed at www.tera.org/research. Specific activities for 1997 follow.

- *TERA* conducted research on route-to-route extrapolation for cancer endpoints, with a focus on the use of oral toxicity data to determine carcinogenic hazard following dermal exposure of consumer products to humans. This work was performed for an industrial client.
- *TERA* evaluated the kinetics of nicotine in humans for a Washington, DC - based consulting firm. This involved drawing conclusions as to the systemic uptake of inhaled nicotine, and the biological half-life of the absorbed dose. On a related project, *TERA* also evaluated the kinetics of ethylene glycol. This involved evaluating urinary data from exposed workers and reviewing the literature to see whether sufficient information was available to determine what dose would have led to the urine output levels. This also determined whether it was likely that the absorbed dose was a function of inhaled or dermally-absorbed ethylene glycol.
- *TERA* published research on route-to-route extrapolation for the chemical MTBE. [**Dourson, M.L. and S.P. Felter. 1997. Route-to-route extrapolation of the toxic potency of MTBE. Risk Analysis. 17(6):717-726**]. This work was done for a Washington, DC - based consulting firm.
- *TERA* published research on the risk assessment of chromium contaminated soils [**Felter, S.P. and M.L. Dourson. 1997. Hexavalent chromium contaminated soils: Options for risk assessment and risk management. Reg. Tox. Pharmacol., 25(1):43-59**]. This work was done for the City of Kearny, New Jersey.
- A recent publication by *TERA* staff [**Dourson, M.L., S.P. Felter, and D. Robinson. 1996. Evolution of science-based uncertainty factors in noncancer risk assessment. Regulatory Toxicol. Pharmacol. 24, 108-120**] highlighted available data for each of several areas of scientific uncertainty, and show examples from U.S. Environmental Protection Agency and Health Canada where data have been used to support the selection of uncertainty factors values other than default. Work is continuing on this project in the development of a 2-day workshop on issues raised by this paper. The workshop will be sponsored in part by the International Society for Regulatory Toxicology and Pharmacology.

- Published a paper with scientists from ChemRisk and the U.S. EPA [**Price, P.S., R.E. Keenan, J.C. Swartout, C.A. Gillis, H. Carlson-Lynch, and M.L. Dourson. 1997. An approach for modeling noncancer dose responses with an emphasis on uncertainty. Risk Analysis. 17(4):427-438**] that gives another approach to estimating risks above the RfD. This paper won a recent award at the annual SOT meeting in 1998. *TERA's* efforts on this paper were sponsored by *TERA*.
- *TERA* is working on a cooperative agreement with the U.S. Environmental Protection Agency (EPA) on Comparative Dietary Risk. The project goals are to:
 1. develop knowledge of problems and solutions on comparative risks posed by dietary changes as a result of fish consumption advisories,
 2. construct a conceptual framework on the potential health risks and benefits of consuming fish, specifically the potential health outcomes of not consuming fish, and the potential health risks from chemically-contaminated fish, and to
 3. show the impacts of fish consumption advisories on individual's and communities' diets and health.

Diverse research and advisory groups have been formed to help *TERA* with this task. Members of these groups include native Americans, states, federal agencies, industry, environmentalists, consultants and academics.

Financial Report for 1997

A budget summary report for fiscal 1997 (same as calendar 1997) is attached. *TERA* earned ~\$432,177 reflecting an ~\$67,823 shortfall in projected income. This shortfall in projected income was offset by actual expenses that were ~\$57,012 less than budgeted and actual transfers to back salary, loan principal, and operating reserve that were ~\$31,060 less than budgeted. The net profit for *TERA* was thus ~\$20,249.