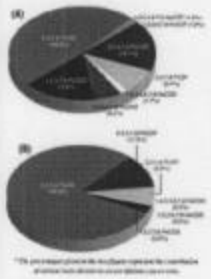
Environmental Bulletin Vol. 5/ No.2 - Fall 1995

Innovative SAIC Model Rights Imbalances in Dioxin Risk Assessment

Venkat Rao, Ph.D., an SAIC senior biochemist, and Alan Unger, Ph.D., an SAIC senior statistician, have reached a broad international audience with an innovative article on dioxin risk assessment. This publication, based on research conducted with SAIC IR&D funding, appeared in the May 1995 issue of Regulatory Toxicology and Pharmacology. By September 15, 1995, the two authors had received 61 requests for reprints and additional information on the project from environmental organizations in 18 countries, including Argentina, Canada, Croatia, Mexico, Sweden, and Taiwan.



Dr. Venkat Rao, an SAIC senior biochemist, and Dr. Alan Unger, an SAIC senior statistician, have estimated lifetime cancer risks from the ingestion of carp contaminated with dioxin residues. They used the standard EPA method (A), which takes a "one-chemical-at-a-time" approach to dose-response analysis, and an SAIC model (B), which concentrates on exposure to multiple dioxins. They found that the standard EPA approach tends to overestimate the combined risks for dioxins with low toxicity but may underestimate the risks of more toxic dioxins, particularly for TCDD.

These illustrations appeared originally in the May 1995 issue of *Regulatory Toxicology and Pharmacology* 21:108-116.
(Click on image to see 62k JPEG.)

In identifying the work that led to this article, Dr. Rao cited a 5-year (1985 to 1990), $1.2-million Toxicant Interaction contract with the EPA Office of Toxic Substances. The SAIC role in this contract was to assist the agency in developing scientific guidelines to assess the hazard of exposure to multiple carcinogenic chemicals. As principal investigator, Dr. Rao was instrumental in designing and developing the most comprehensive data base yet on binary combination effects of chemical carcinogens and tumor promoters. He also extensively analyzed the information in this data base, which included findings on the structure and activity relationships between carcinogens and tumor promoters.

Proceeding from the accomplishments of this project, Dr. Rao received $75,000 in SAIC IR&D funds over a 3-year period to develop new methods to assess the carcinogenic risks of exposure to dioxin mixtures.

Using the standard approach, EPA has relied on a conventional, "one-chemical-at-a-time" dose-response analysis that does not account for differences in the severity of the health hazards of dioxin mixtures and that results in estimates that are too high for the less toxic dioxins. This approach focuses on the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), expressing exposures to other dioxins as fractions of TCDD toxicity. The problem with this

method is that TCDD, while it is the most toxic dioxin, constitutes only a small fraction of the dioxins in the environment. SAIC addressed this crucial factor in its dioxin exposure assessment.

Working with Dr. Unger, Dr. Rao developed model algorithms that measured the binding of TCDD to Arylhydrocarbon (Ah) receptors in the presence of other dioxins. TCDD must form a complex with these receptors, which are proteins existing within the cell, to initiate toxic effects. The purpose of the modeling effort was to estimate probabilities for the initiation of toxicities of various dioxin molecules through this binding process. To compute carcinogenic risks and to compare the differences in the risks, Dr. Rao and Dr. Unger incorporated data into the algorithms from several case studies that measured dioxin binding to Ah receptors. Using the resulting model, they concluded that EPA's standard approach to dose-response analysis tends to overestimate the combined total risks for dioxins with low toxicity but may underestimate the risks of more toxic dioxins.

While this finding is still preliminary and will require additional study, it has significant potential. The SAIC model for dioxin mixtures, along with other new methods and technologies, is expected, Dr. Rao noted, "to improve risk assessment methods," which should result in a reduction in the "costs of complying with Federal and State regulations aimed at protecting the national environment." For additional information on this research, contact Dr. Rao at 301-698-5991.

PREVIOUS PAGE **CONTENTS PAGE** **NEXT PAGE**