United States
Environmental Protection
Agency

QSAR/VFAR Workshop

SPONSORED BY EPA's

National Homeland Security Research Center

AND

National Risk Management Research Laboratory

Hilton Netherland Hotel, Cincinnati, Ohio

June 20 – 21, 2006

To register for this **free** workshop, contact Jennifer Legge at ***jennifer.larkin.legge@saic.com***

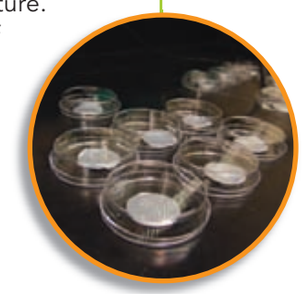
What is QSAR/VFAR?

The health risk assessment process, as defined by the National Academy of Sciences (NAS, 1983), includes four components: hazard identification, dose-response or toxicity assessment, exposure assessment, and risk characterization. Risk assessment is often conducted using limited experimental data. In such instances, the ability to accurately and quickly predict potential health hazards from chemical exposure would save time and valuable resources that could be more wisely invested. When data are limited, it is necessary to develop and apply special techniques to aid in the risk assessment process.

One viable option is the use of non-empirical parameters that can be calculated directly from a chemical structure. This approach is available through the application of Quantitative Structure Activity Relationship (QSAR) models, which have already proven to be both appropriate and useful for chemicals having large quantities of known physical or chemical data. QSARs can relate a chemical's biological activity, such as Lowest Observed Adverse Effect Level (LOAEL), Effective Concentration (EC_{50}), and carcinogenicity, to its structural components (physicochemical properties).

In addition to QSAR methodology, a new and evolving methodology called Virulence Factor Activity Relationship (VFAR) is emerging for estimating the health hazards posed by biological organisms. The concept of VFAR was developed as a way to relate the architectural and biochemical components (such as biotoxins) of a microorganism to its potential to cause human disease.

For Workshop Goals, Logistics, and additional background information on NHSRC and NRMRL, please go to page 2.

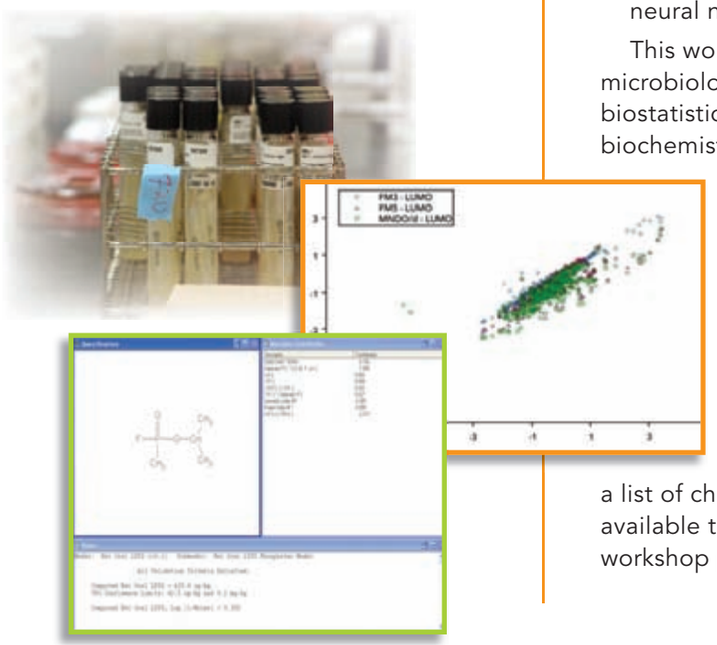


$$T = s(d)+C$$

T = the biological or toxicological endpoint
d = the descriptors computed for each molecule of interest
s = the coefficient associated with the descriptors
C = a constant

Workshop Goals

- Identify data needs for the development of quantitative non-cancer and cancer models, including models that are capable of predicting benchmarks such as LOAELs , LD50s, LC50s, Bench Mark Dose (BMD), Bench Mark Dose Levels (BMDLs), Bench Mark Concentration (BMC), and Bench Mark Concentration Levels (BMCLs) for various exposure durations.
- Predict benchmarks and health effects associated with acute and short-term exposure to chemical and biological agents.
- Explore the feasibility of developing and applying hybrid QSAR models.
- Explore the development and application of VFAR models to estimate the activity of biological toxins.



- Explore incorporation of genomic, proteomic, and metabolomic data into QSARs in order to link the mode or mechanism of action (MOA) into QSAR models.
- Assess the development of models capable of predicting the chemical nature, rate of production, and in vivo stability of metabolites resulting from P450 metabolism.
- Assess the development of models for predicting the relative toxicity of the parent compound and metabolites for identification of the ultimate chemical effector.
- Discuss computational approaches such as various regression methods, genetic algorithm descriptor selection techniques, data clustering methods, neural networks, and expert systems.

This workshop will convene toxicologists, microbiologists, chemists, engineers, biostatisticians, pharmacologists, biochemists, and risk analysts. Expert panel members include Drs. Mark Cronin, Andrew Worth, Kannan Krishnan, William Welsh, Andy Maier, Joan Rose, and Syed Hashsham. The workshop also includes scientists within the Agency with expertise in the development and application of QSARs and VFARs. To facilitate discussion at the workshop, a list of charge questions will be made available to the expert panel and the workshop participants.

Workshop Logistics

A block of rooms at the government rate has been reserved for this workshop. In order to obtain the government rate, please call 1-800–HILTONS (1-800-445-8667). You must mention the "*US EPA QSAR/VFAR Workshop*" in order to receive the group rate of $88.00 plus 17.0% tax per night. Reservations must be made by May 30, 2006, in order to receive this rate. If you are unable to get reservations at the group or government rate, please contact Jennifer Legge of SAIC at *jennifer.larkin.legge@saic.com*. Workshop registration is limited to 50 participants. Risk assessors, toxicologists, microbiologists, statisticians, biomathematicians, chemists, and persons interested in QSAR and VFAR methodology from the government, academia, and private industry are encouraged to attend.

Background Information on NHSRC

EPA's National Homeland Security Research Center, headquartered in Cincinnati, Ohio, was formed in 2002 to advance our nation's security through science. A part of the Office of Research and Development, it manages and supports a variety of research and technical assistance efforts. NHSRC focuses on enhancing our ability to detect, contain, mitigate the effects of and clean up after significant emergency events or terrorist attacks. Its scientists and engineers seek to identify or develop affordable, effective technologies and methods for addressing the risks posed by chemical, biological, and radiological agents.

Background Information on NRMRL

The mission of EPA's National Risk Management Research Laboratory is to develop ways to prevent and reduce pollution of air, land, and water. This mission plays a critical role in the U.S. EPA's goal of achieving sustainability; several methodologies have been developed within NRMRL to quantify the potential environmental harm of chemical releases.