Division of Science and Research

Research Project Summary

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NJRisk: Development of an Integrated Computational Tool to Support Prioritization of Chemicals of Emerging Concern

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Abstract

The objective of the NJRisk project is to develop, test, and deploy an integrated tiered system coupling computational platforms to support prioritization of Chemicals of Current and of Emerging Concern for assessment by the NJDEP. A nine-month pilot study was conducted from July 2013 to March 2014 in order to complete the necessary groundwork for the subsequent implementation. The full study, which began in April 2014, uses two operational computational platforms for hazard and exposure ranking, METIS (Metanomics Information System), developed by DuPont, and PRoTEGE (Prioritization and Ranking of Toxic Exposures with GIS Extension), developed by the Computational Chemodynamics Laboratory of the Environmental and Occupational Health Sciences Institute (EOHSI), respectively. This effort also takes advantage of, and incorporates in the development of the new system, current and anticipated outcomes of ongoing efforts by federal agencies, such as the USEPA. The goal is to implement an integrated software platform or "tool" (NJRisk) that will allow users to assess both hazard and exposure potentials of chemicals that are found (or could be introduced) in the New Jersey environment and/or biota, and to prioritize these chemicals for regulatory action based on tiered risk analysis.

Introduction

All regulatory agencies, nationally and internationally, face challenges in their efforts to address concerns regarding the rapid introduction of many "new" chemicals or the use of "old" chemicals in new products, resulting in "new types of exposures" for human populations and ecosystems. A variety of approaches are being developed to support these efforts; this effort directly addresses a critical State and National need.

A major attribute of the integrated NJRisk system is that, in addition to addressing chemicals of "current regulatory concern," it will also facilitate characterization of contaminants of "emerging concern." In general, the term "emerging contaminants" refers to hazardous materials or mixtures that may have:
  a. a perceived or real threat to human health, public safety or the environment;
  b. no published or evolving health standards or guidelines;
  c. insufficient or limited available toxicological information that is evolving or being re-evaluated; or
  d. significant new sources, pathways, or detection limits.

Some major classes of Chemicals of Emerging Concern (CECs) include pharmaceutical and personal care products (PPCPs); engineered nanomaterials (ENMs) such as silver nanoparticles and carbon nanotubes; plasticizers, flame retardants, protective coatings; home cleaning products; and food additives.

In the pilot phase of this project, METIS and PRoTEGE were employed to conduct a study involving hazard and exposure characterization applications for a broadly representative set of 15 chemicals of current and emerging concern, corresponding to various combinations of production volume, chemical properties, environmental distribution, usages, exposure pathways, etc. These case studies were analyzed and evaluated to identify optimal ways for linking and merging appropriate METIS and PRoTEGE components and corresponding data retrieval and calculation procedures, and to establish initial software requirements and specifications for NJRisk that will be incorporated through this and subsequent implementation phases. This pilot phase indicated that these independent databases could be merged to develop NJRisk that would become a valuable tool for the Department.

Methods

As stated earlier, the current effort utilizes components from two operational state-of-the-art platforms for hazard and for exposure characterization and ranking:
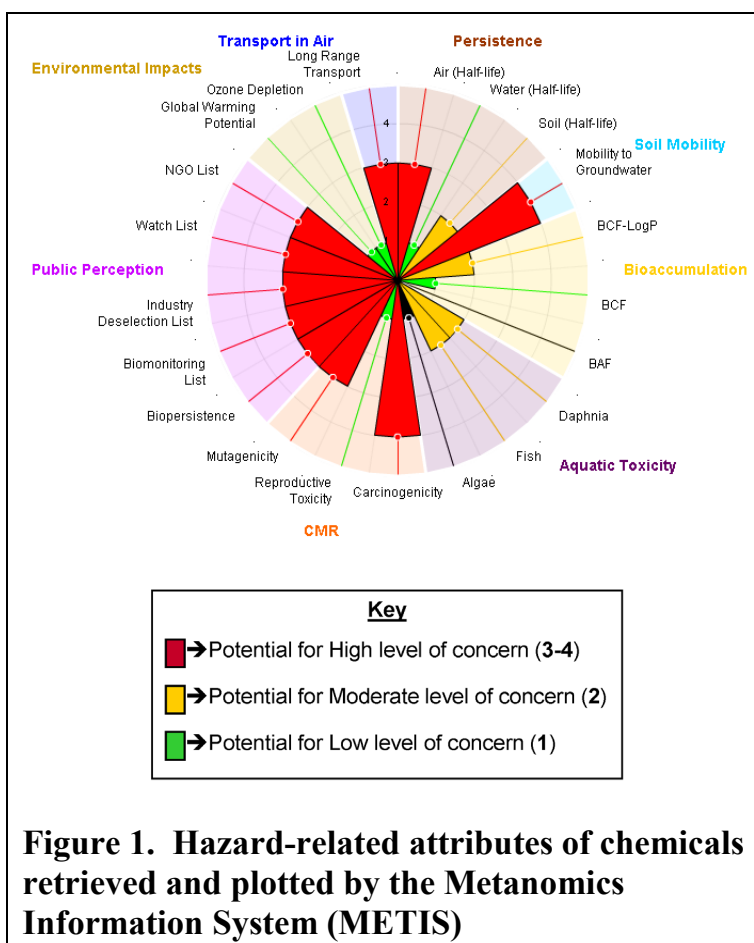
- METIS (Metanomics Information System), developed by DuPont, and

- PRoTEGE (Prioritization and Ranking of Toxic Exposures with GIS extension), developed by the Computational Chemodynamics Laboratory of EOHSI.

A brief description of each of these computational tools is described below.

METIS is a chemical informatics platform that provides a screening level view of potential environmental fate and effects, human health concerns, and societal perception issues associated with a chemical of concern. As an example, Figure 1 depicts "METIS attributes" that have been retrieved in a systematic manner from a variety of databases for a representative chemical. Typically, these attributes are:

- Environmental Persistence – indicates the predicted half-life in each environmental compartment,

- Soil Mobility – the potential for a chemical to migrate from soil into groundwater,

- Bioaccumulation – uses measured or estimated values to indicate the potential for a chemical to sorb to lipids,

- Aquatic Toxicity – the measured or estimated toxicity to aquatic organisms,

- CMR – indicates whether the compound is classified as known or suspected animal and/or human Carcinogen, Mutagen or Reproductive toxin,

- Public Perception – indicates that the chemical is present on a variety of regulatory, industrial and/or non-governmental lists that may influence how the public views a particular chemical,

- Environmental Impact – indicates the potential for the chemical to affect global warming and ozone depletion as compared to reference compounds,

- Long Range Transport (Air) – the potential for the chemical to travel long distances from its point of entry into the environment,

- Environmental Partitioning (Fugacity) – steady-state partitioning of a chemical in the environment (Air, Water, Soil, Sediment) based on different emission scenarios.

Figure 1. Hazard-related attributes of chemicals retrieved and plotted by the Metanomics Information System (METIS)

METIS has been built on open-source software that provides access to an aggregated database and estimation tool set. METIS retrieves and assembles information from over 1,400 publicly available databases (see Table 1 for a representative set of these databases). These data resources may contain, but are not limited to, physical and chemical properties, hazard, toxicological, environmental and regulatory information. The input for METIS is simply the chemical name, CAS #, or chemical structure. METIS retrieves information and assembles it together into a comprehensible view in seconds to minutes versus weeks to months that could be required, in some cases, by conventional searches.

PRoTEGE is an analysis and modeling platform that facilitates exposure calculations at multiple tiers, utilizing available data on:
- chemical production volumes,
- intrinsic properties that affect the environmental dynamics of the chemical (e.g. volatility, solubility, etc.),
- intrinsic properties (such as lipophilicity) that affect the biological dynamics (absorption, distribution, metabolism, elimination) of the chemical, and subsequent uptake/bioaccumulation by humans and wildlife,
- chemical transportation modes and amounts,
- chemical usage in industrial, agricultural, etc. applications,
- environmental release/disposal amounts and spatiotemporal pattern,
- chemical uses in consumer products and in foodstuffs,
- environmental concentrations of chemicals in multiple media (including food and beverages),
- age- and gender-specific population distributions of physiological and behavioral attributes.

Table 1. Selected databases accessed by METIS (hosted locally)

| Database	Expanded Name
BCF	Bio-concentration Factors Gold standard database (Cefic LRI, EURAS)
CDAT – CDR	Chemical Data Access Tool -Chemical Data Reporting
CCRIS	Chemical Carcinogenesis Research Information System
DIPPR	Design Institute for Physical Properties
ECOTOX	ECOTOXicology database
HSDB	Hazardous Substances Data Bank
MITI	Ministry of International Trade and Industry (Existing and New Chemical Substances List)
PHYSPROP	Physical Properties Database
PubChem	National Institutes of Health (NIH) open chemistry database
SRC BCF	SRC Bioconcentration Factor
ToxMiner	Links biological, metabolic, and cellular pathway data to genes and in vitro assay data
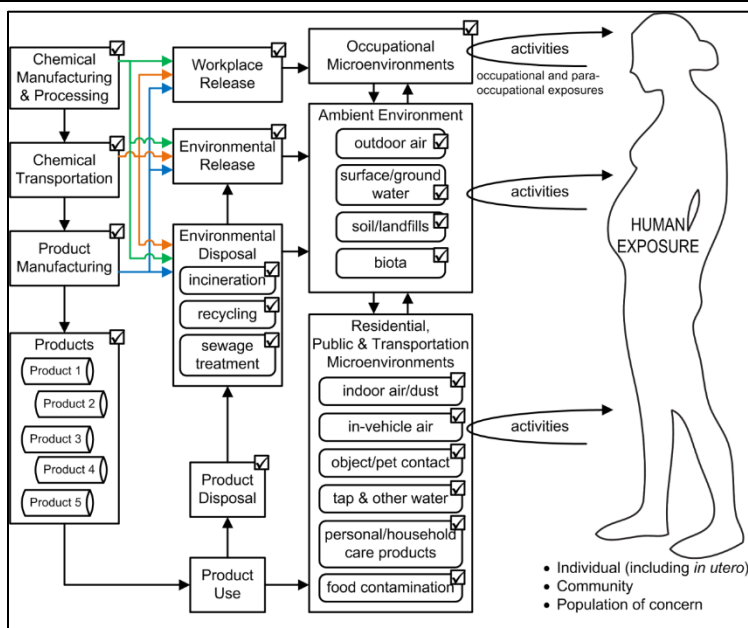
Figure 2. A schematic depiction of the conceptual framework of PRoTEGE (Prioritization and Ranking of Toxic Exposures with GIS Extension); this system uses a Life Cycle Assessment (LCA) approach to assess potential human exposures to chemicals that could take place during manufacturing, transportation, or using products containing these chemicals as well as following their environmental disposal.

The PRoTEGE approach takes advantage of, and integrates, both available measurements and model estimates to understand and quantify exposures of populations potentially at risk. Specifically, by utilizing over 50 available "information bases" of environmental releases, chemical production and usage, multimedia environmental concentrations, and age- and gender-specific population distributions of major physiological and behavioral patterns, the estimates of PRoTEGE provide a reasonably realistic assessment of exposures that could be experienced by the general population or by subpopulations of concern.

Results

In 2012 the New Jersey DEP's Science Advisory Board (SAB) issued a report to the Department suggesting strategies for the DEP to evaluate Contaminants of Emerging Concern. They suggested a tiered approach outlined in Figure 3.

NJRisk is the now the mechanism the Department can use to evaluate the Tier 2 approach. The SAB recognized that Tier 3 and 4 involved policy decisions by the DEP.

As an example, we can evaluate 1,4-Dioxane. 1,4-Dioxane is a compound that has been added to chlorinated solvents to enhance their performance and help to stabilize the solvents during storage and use. It is now a contaminant of emerging concern across the country. Figure 4 is the NJRisk report on 1,4-Dioxane.
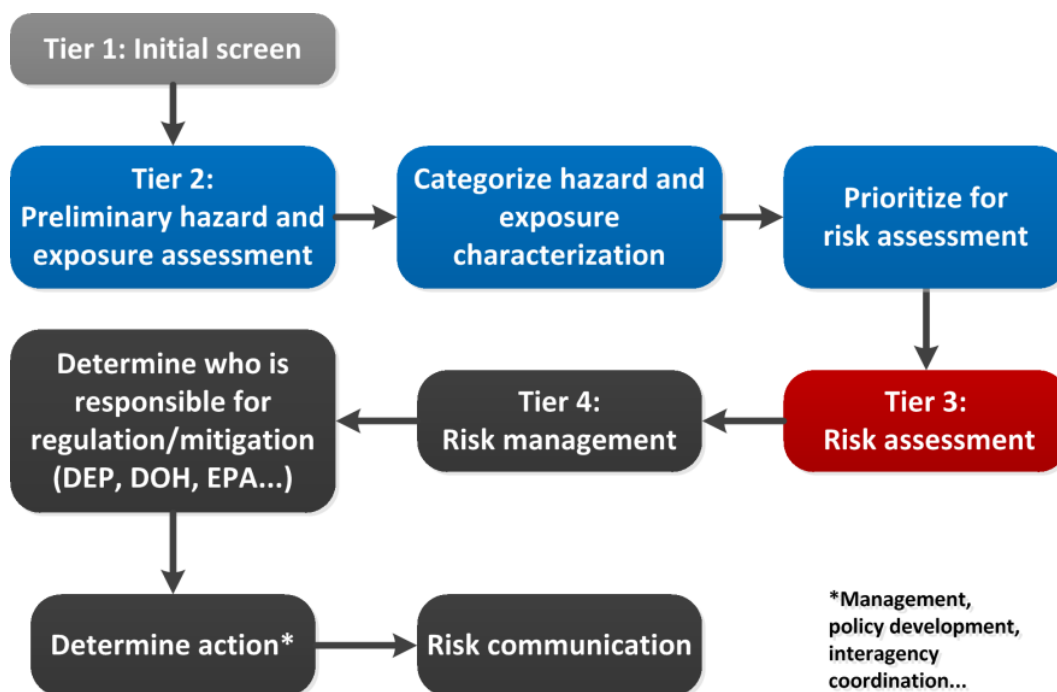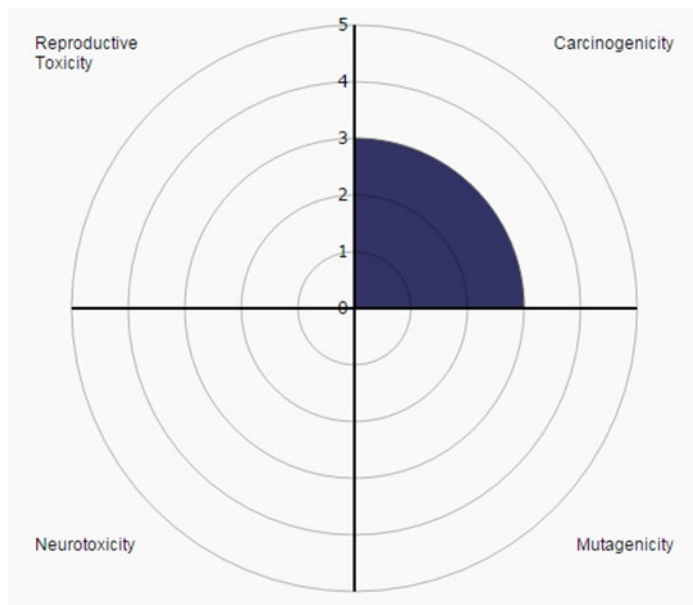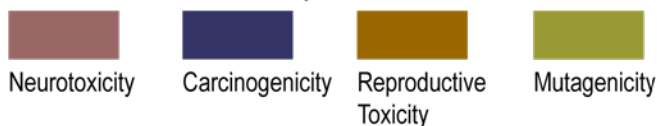

Figure 3. Overview of the Chemicals of Emerging Concern (CEC) evaluation process [1]
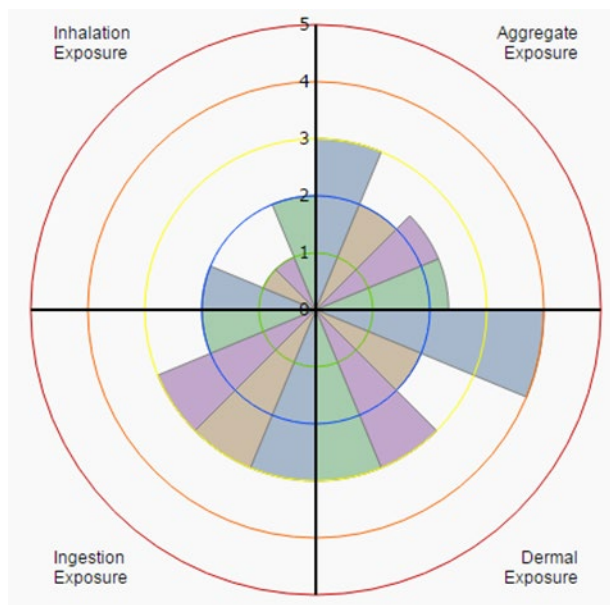
Figure 4. NJRisk Results for 1,4-Dioxane
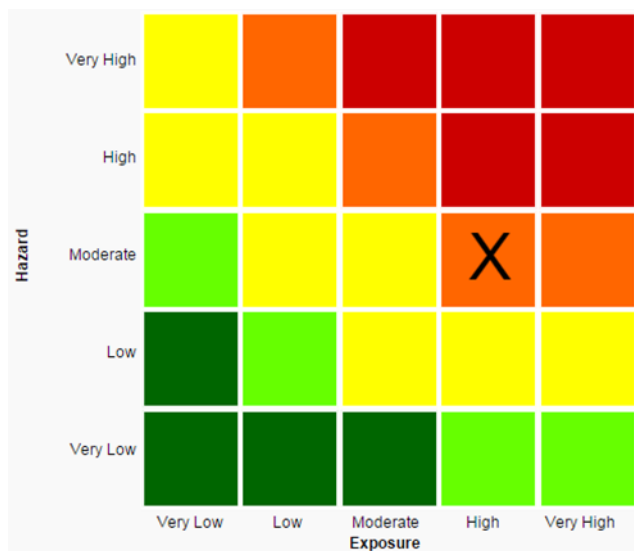
(a) Human Hazard Rose

Human Hazard Rose Color Key

Neurotoxicity | Carcinogenicity | Reproductive Toxicity | Mutagenicity

(b) Human Exposure Rose

Human Exposure Rose Color Key

Pervasiveness | Persistence | Severity | Efficacy

(c) Human Health Risk Grid

Human Health Risk Grid Color Key

Very Low Risk | Low Risk | Moderate Risk | High Risk | Very High Risk

(a) Human Hazard
Estimated ranking of human hazard risk from 1,4-Dioxane, in terms of neurotoxicity, carcinogenicity, reproductive toxicity, and mutagenicity.

(b) Human Exposure
Estimated human exposure ranking based on semi-quantitative metrics of pervasiveness, persistence, severity, and efficacy of 1,4-Dioxane.

(c) Human Health Risk
Estimated human health risk from 1,4-Dioxane, based on calculation of exposure values from PRoTEGE combined with hazard values from METIS.

NJRisk identifies 1,4-Dioxane as a high-risk compound alerting the Department to begin Risk Assessment and Risk Management Strategies.

Conclusions

NJRisk is now available for the NJDEP to use to evaluate contaminants of emerging concern. It can provide results in minutes on the hazard and exposure of the contaminant that in the past may have taken days or longer to assemble.

References

[1] NJDEP SAB. 2012. Proposed CEC Framework. Trenton, NJ: NJ DEP Science Advisory Board CEC Workgroup. https://www.nj.gov/dep/sab/Appendix%20A_Final%20Workbook%20CEC%20Framework_August8_2012.pdf

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