

Session 3: Tiered Evaluation Strategies

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- The categorization program for substances on the Canadian Domestic Substances List (DSL) includes over 20,000 chemicals, of which several thousand will be considered in screening assessments; fuller risk assessments will be completed on some.
- The Existing Substances Division is in the Healthy Environments and Consumer Safety Branch of Health Canada and addresses Health Canada's responsibilities for Existing Substances under the Canadian Environmental Protection Act (CEPA).
- CEPA is progressive legislation originally passed in 1988 (renewed in 1999) that encompasses information gathering/reporting, research, assessment/management, and enforcement. It is the primary authority to assess/manage risks posed by toxic substances in Canada. CEPA is administered by both Health Canada and Environment Canada and encourages public participation. For both assessment and management, there are mandated timelines within the legislation.
- Existing substances on the DSL are those that were produced or imported in Canada between 1/1/84 and 12/31/86 at over 100 kg/year.
- Under CEPA, the mandate for human health is to address exposure and effects to set priorities for risk management. The process is publicly accountable and transparent. CEPA '88 assessments focused on 69 Priority Substances that were data rich. CEPA '99 extended the mandate to the entire DSL and set a 7-year deadline for establishing priorities for assessment from among the 23,000 substances (*i.e.*, by September, 2006).
- Objectives of categorization (priority setting) of all existing substances and screening of priorities are both short- (systematic priority setting for data generation and assessment for both human health and ecological effects of all existing substances) and long-term (striving for greater consistency of consideration of New versus Existing substances – important because many of the New substances are used less and are less hazardous).
- The likely impacts of categorization and similar mandates elsewhere, such as the EU Registration, Evaluation and Authorization of Chemicals (REACH), include the development of information gathering and data repositories available to the public, development and refinement of predictive tools of exposure and effects, retrospective learning based on profiled substances, focused testing and research on priority chemicals, and an iterative approach to priority setting and assessment to increase efficiency.
- Tools developed for categorization and screening are iterative in nature. Substances have been categorized based principally using simple exposure and hazard tools that, in addition to identifying priorities, ranked chemicals for screening. More complex tools are then applied to additionally prioritize and screen. No more priority setting and assessment is conducted than is necessary to set aside a substance as a non-priority.

- Categorization has identified substances as priorities on the basis of their potential for exposure or weight of evidence determinations of hazard to human health.
- Considering priorities from among the 23,000 substances, many of which had limited available information, required considerable technical capacity to force the science to develop predictive tools relying on generic information to the extent possible. All technical components of developed methodology were peer reviewed and proposals for approaches to categorization were released for public comment. Following screening assessments, substances are considered to be priorities for risk management, set aside for no further action, or prioritized for in depth assessment.
- Simple and complex tools were developed to estimate exposure and hazard.
 - The simple exposure tool is a relative ranking tool based on the quantity of a substance produced, number of submitters, and use patterns, ranked in relation to their potential to contribute to human exposure. Results ranked a substance's potential for exposure as great, intermediate, or low.
 - The complex exposure tool is in development and will provide a quantitative plausible maximum estimate of exposure of individuals in the general population by age group for both consumer (near-field) and multimedia environmental exposure (far-field). Exposure is based on readily available generic data.
 - Experience with the simple and complex exposure tools indicates that early use profiling focuses resources and increases efficiency in identifying priorities for further consideration. Experience also indicates that volume is a poor surrogate for exposure – many high production volume chemicals have a low potential for exposure. Other observations included that priorities for environmental and human health often diverge and the chemicals identified as priorities were sometimes different than expected.
 - The simple hazard tool includes weight of evidence classifications of Health Canada and other agencies, based on clearly specified criteria and documented peer review.
 - The complex hazard tool is a hierarchical approach for considering information on multiple endpoints (qualitative and quantitative) in specified order and data sources, (reviews, original data, (quantitative) structure activity modeling, and analogues). It includes a secondary weight of evidence stage. If a chemical does not meet the criteria specified for degree of hazard (e.g., effect levels), it is not considered a priority. The first endpoint considered is cancer and then genotoxicity, where many substances are captured which are then considered in the weight of evidence approach. If they are determined not to be priorities on this basis, available data are considered against the criteria for other endpoints in hierarchical order, from developmental/reproductive toxicity through long term to short term repeated dose toxicity.
- For the results of (quantitative) structure activity modeling, detailed robust summaries of the input and results are produced to ensure transparency and contribute to capacity building, reuse, and interpretation of the models.

- While increased transparency in reporting is desirable to build capacity in model understanding and use, there is a need to integrate the expertise of toxicologists, risk assessors, and modelers in developing new models. QSAR has potential to contribute at all stages of priority setting and assessment, when data are limited and/or contradictory. To increase their robustness and application, there is a need for 1) transparency and public awareness of models (critical for model acceptance), 2) consistent consideration and transparent documentation of output for decision making, 3) capacity building and expert engagement to develop better models, and 4) consideration of coverage of appropriate “chemical space” (rather than the individual substance) in developing testing strategies to optimize efficiency and contribute to model development.
- A complete range of assessment products has been developed based upon the question asked and the decision that needs to be made. These products consider no more information than is needed to identify non-priorities and offer advice on priorities based on the issue at hand – screening tools are applied to non-priorities, a more in-depth focused screening assessment is applied to high-priorities.
- The implications of work conducted to date on the program include: 1) it is important to systematically consider all substances when setting priorities for testing and assessment, 2) profiling across compounds and applying predictive tools can obviate the need to fill data gaps, 3) it is desirable to develop integrated testing strategies that include consideration of potential for exposure and hazard 4) it is important to consider uncharacterized chemical space in testing rather than gap filling for individual chemicals, 5) risk management may be preferable to data generation in many cases, 6) the value of an iterative ‘fit for purpose’ approach to increase efficiency, and 7) the importance of international cooperation to increase efficiency in testing and assessment of existing chemicals.