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Canada's Chemicals Management Plan

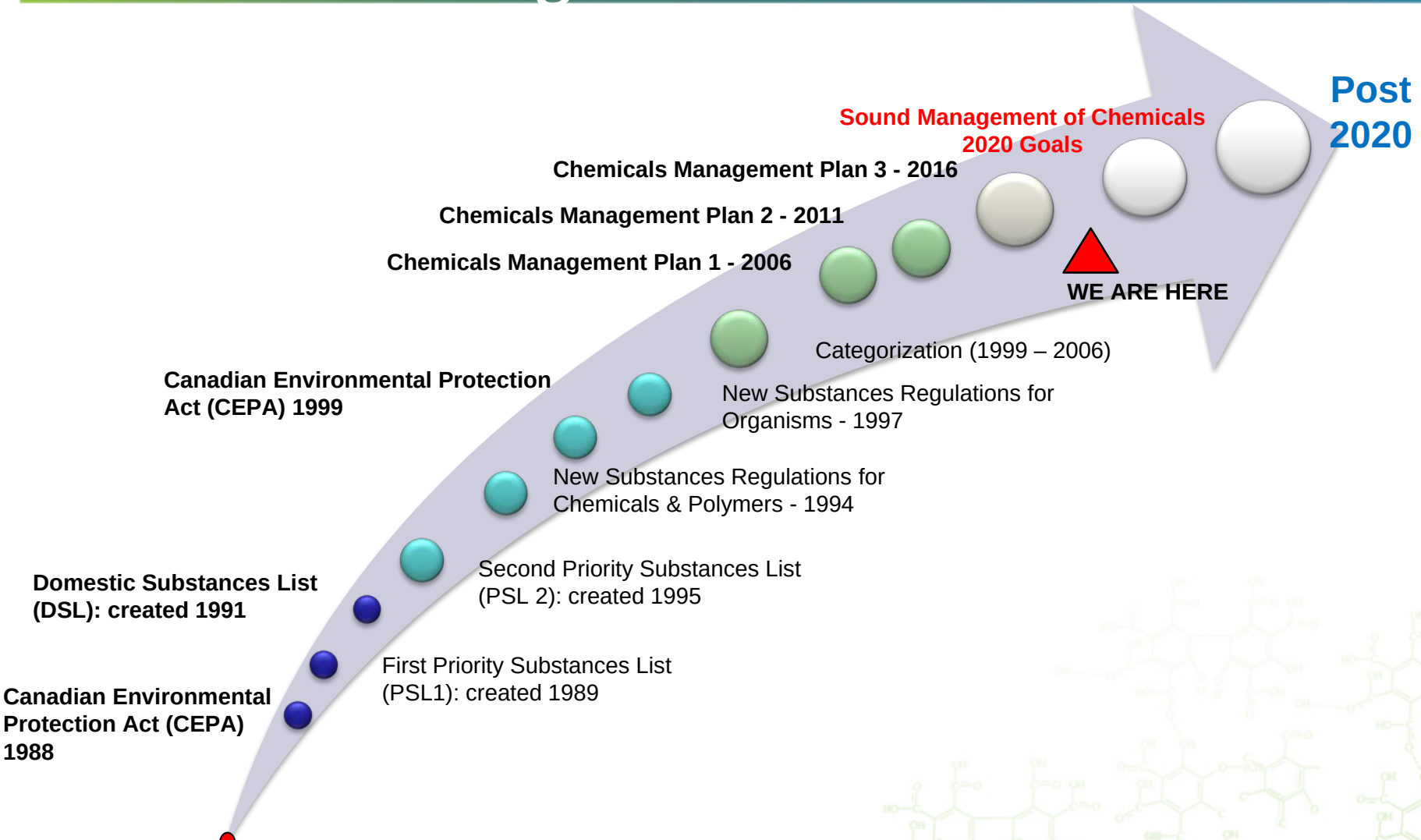
Approaches to Prioritization and to Streamlined Assessments

Health Canada and
Environment and Climate Change Canada

December 11, 2017

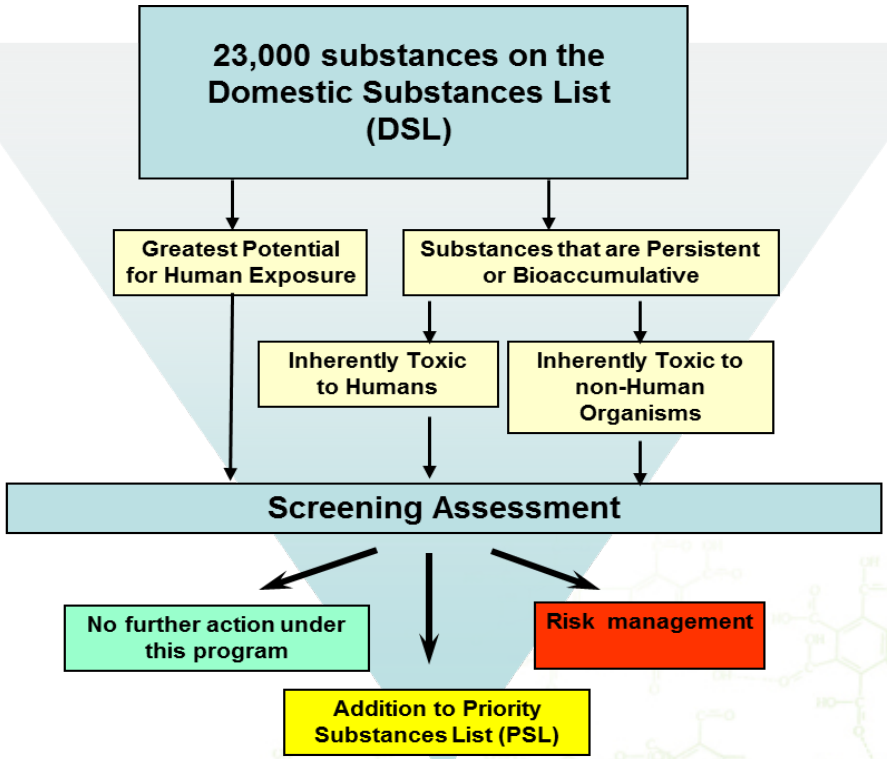
Canada

Chemicals Management in Canada

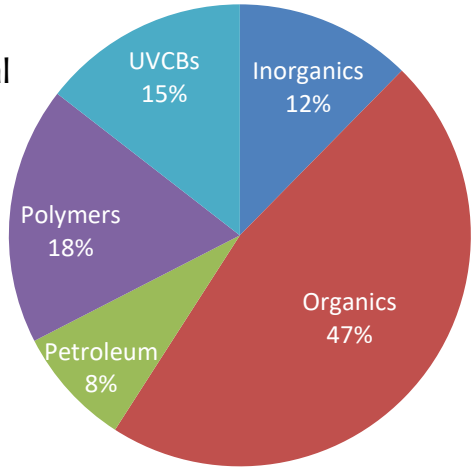


Categorization/Prioritization

- Categorization was a prioritization exercise from 1999-2006 which examined Canada's entire Domestic Substances List (DSL)
  - Used criteria for persistence, bioaccumulation and inherent toxicity to humans and non-human organisms, or greatest potential for human exposure
- Outcome of Categorization was identification of approximately 4300 substances requiring further consideration
  - Led to the creation of the CMP, under which the majority of risk assessment work is focused

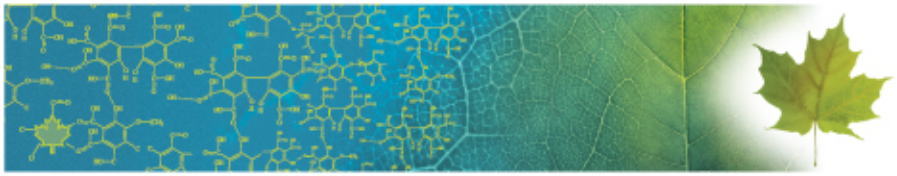


Broad Chemical Groupings of the 4300 Categorized Substances



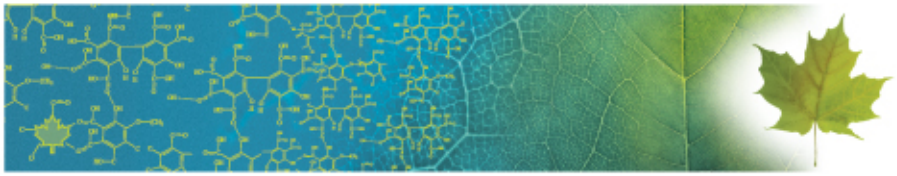
Categorization: Lessons Learned

- Categorization decisions were based on hazard and human exposure data available up to 2006
  - Used inventory data from 1984-86
  - Categorization decisions triggered legal obligations to conduct risk assessment
- Categorization using ecological criteria lead to <10 % of substances concluded as toxic when the risk assessment was undertaken
  - Lack of exposure considerations for ecological receptors
  - Not weight of evidence driven (i.e., used pass/fail decision-making)
- Unable to model Persistence and Bioaccumulation properties for substances with challenging chemistries
  - *e.g.*, ionizing chemicals, persistent/mobile/ toxic chemicals, Unknown or Variable Composition, Complex reaction products, and Biologicals (UVCBs).



Categorization: Lessons Learned Cont'd

- Additional streamlined approaches were still required
  - E.g. rapid screening for low volume chemicals
- Need for ongoing investment in development of efficient/novel ways to facilitate prioritization and assessment
  - E.g. advancement of QSAR tools
- Strong stakeholder engagement, starting early on
  - Earlier buy-in to approaches adopted, especially non-traditional and group approaches
  - Stakeholder engagement played an essential role in developing information gathering approaches and strategies; evidence provided by stakeholders is critical
  - Early sharing of preliminary decisions



Evolution of the CMP

- The CMP has been rolled out in 3 phases, with each phase building on lessons learned in the previous phase

Phase 3: 2016-2020

Remaining Priorities

- Range of data availability (data rich to **data poor**)
- Many with limited data sets
- Opportunity to integrate emerging data (i.e. NAM) & novel approaches

Streamlined Approaches

- ERC, TTC, Rapid Screening IV, Polymer Rapid Screening II, Biomonitoring approaches, etc.

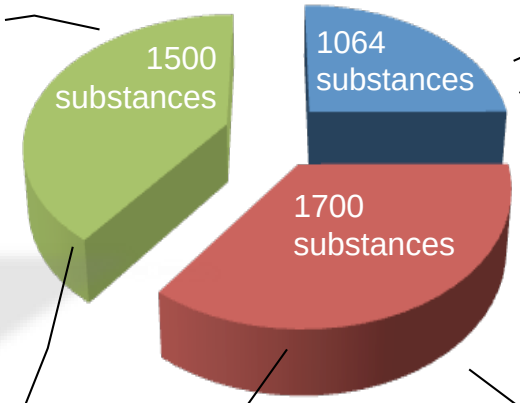
Phase 1: 2006-2011

Challenge Initiative

- Substance by substance risk assessment
- Used best available traditional toxicity data and QSAR modeling
- Limited use of alternative approaches

Streamlined Approaches

- Rapid Screening: substances of low concern



Phase 2: 2011-2016

Streamlined Approaches

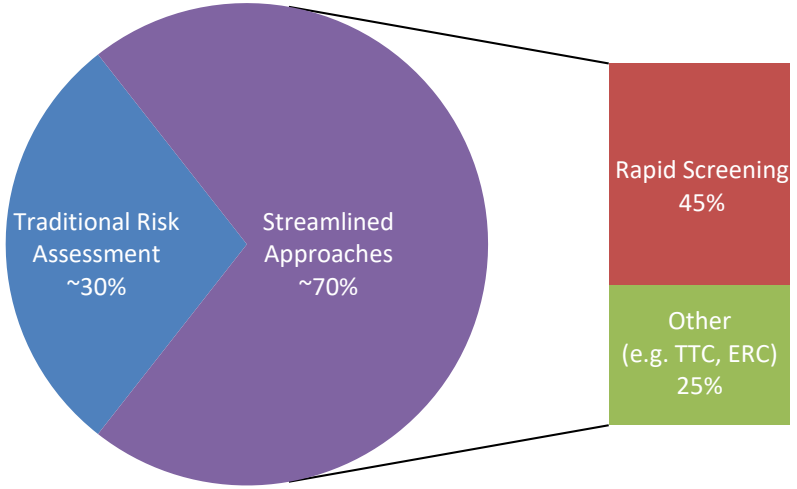
- Rapid Screening I, II, III and Polymer Rapid Screening I

Substance Groupings Initiative

- Used best available traditional toxicity data
- Expanded use of alternative approaches
  - *In silico*
  - Read-across
- Aromatic Azo & Benzidine-based substances, Phthalates, moiety based approaches (Selenium) etc.

Streamlined Assessment Approaches

- Were critical for meeting commitment to assess all priorities within 2020 timelines
- Proved highly useful for identifying and rapidly assessing low priorities with less effort and less time
  - Allowed focus of resources on higher priority substances
- All approaches were externally peer reviewed and also open for public comment



* Accounts for, at minimum, one department utilizing a streamlined approach
** For both departments utilizing a streamlined approach on the same set of substances, proportion is ~ 50 % streamlined approaches vs. ~ 50 % traditional risk assessments

Streamlined Assessment Approaches

Rapid Screening

- Approach developed early in CMP and reused as inventory information was updated
- Included substances with low volumes in commerce in Canada
- Included substances with uses that were not expected to lead to general population exposure (e.g., research and development, site-limited industrial use)
- Applicable to all substances , including inorganics, UVCBs and polymers
- Approach has been applied 6 times to date, resulting in conclusions on more than 1900 substances

Human Biomonitoring

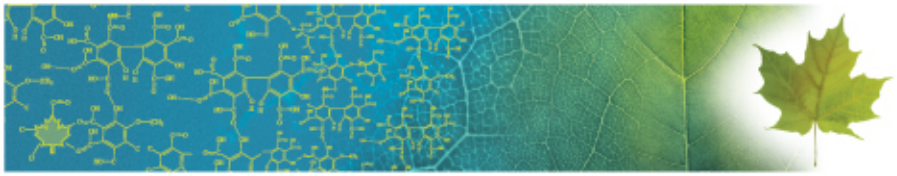
- Biomonitoring data represents exposure from multiple sources.
- First approach based on consideration of prevalence of exposure.
- Second approach based on comparison of biomonitoring data with biomonitoring guidance values to determine risk

Streamlined Assessment Approaches

Ecological Risk Classification Approach

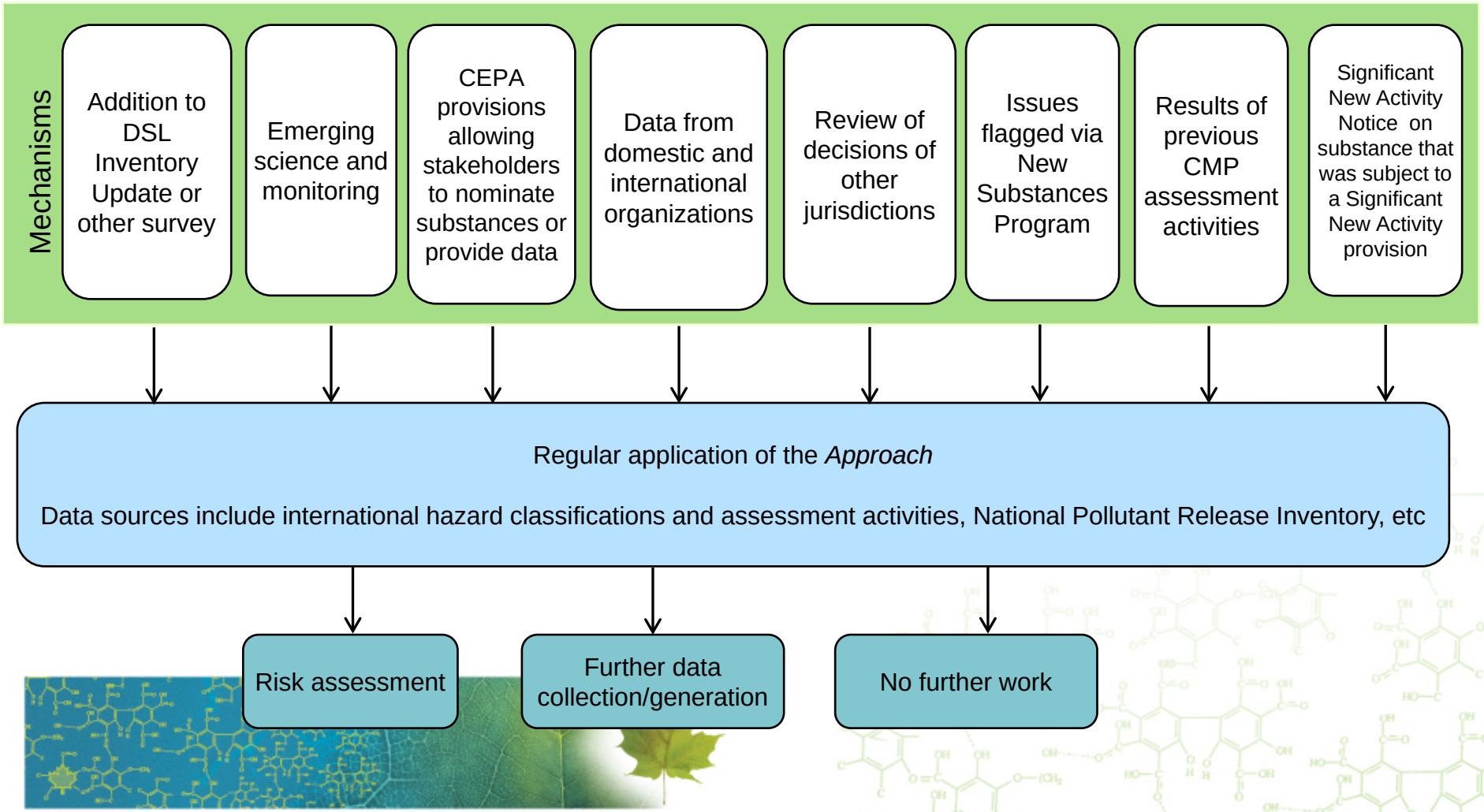
- Establishes chemical profiles to provide a weight of evidence for hazard and exposure with the aim to develop a risk classification matrix for ecological receptors
- Uses several new approach methodologies (mode and mechanism of action, receptor binding, critical emission rate, margin of exposure)
- Substances classified as having higher potential risk concern were generally those characterized as being more potent and having a greater potential for widespread continuous exposure.
- Substances classified as having low potential risk concern generally had short residence times in the environment, do not undergo long-range transport and are expected to only demonstrate baseline toxicity.

- **Threshold of Toxicological Concern Approach**
  - Principle of establishing a human exposure threshold value for chemicals below which there is a low probability of risk to human health (Kroes et al. 2004)
  - Assigns a threshold value to a chemical based on structural features and compares this to an estimate of human exposure



Evolution of Priority Setting - Beyond Categorization

- Published in 2014, the **Approach for the Identification of Risk Assessment Priorities (IRAP)** outlines approach to compile and evaluate new information on a cyclical basis to determine if further action may be warranted



Combined Results of the 2015 and 2016 IRAP Reviews

- IRAP looked at a total of ~27 000 substances. For most of these , there was no information identified that indicated further work was required.
  - New data was identified for ~8000, but in most instances did not indicate indicate potential risk
- The combined number of substances identified for further action in 2015 and 2016 are identified below:

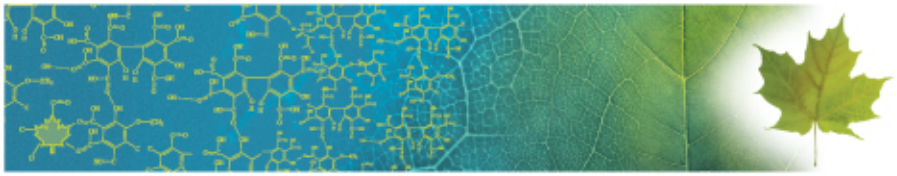
Recommended Action	Number of Substances
Risk Assessment	38
Data Gathering	377
International Outreach	41

Priority-Setting Moving Forward

Enhancements to IRAP are being considered to address some of the lessons learned from the first two cycles and to improve the overall process.

- Development of systematic computational approaches to mitigate the labour intensive nature of manual data collection and processing
    - Automated data mining to screen information
    - Computational algorithms for data processing

- Integration of New Approach Methodologies (NAM) to better address chemicals that lack traditional data sources and to harness emerging science.
    - Hazard – High throughput *in vitro assays*
    - Risk-based Ranking – Bioactivity Exposure Ratio (BER)
    - Exposure – analytical methods, modelling approaches



Priority-Setting Moving Forward

Topic of the CMP Science Committee meeting, November 2016

Integrating New Approach Methodologies within the CMP: Identifying Priorities for Risk Assessment, Existing Substances Risk Assessment Program

High level Committee conclusions:

"At an overview level, the Committee concluded that although these new assessment approaches are still evolving, they are mature enough, in many cases, to begin to have application in priority setting, as supplemental lines of evidence in risk assessment and as high-throughput risk approximation/classification (not assessment) tools. The Committee endorses their use for these purposes…….. The Committee felt that it was reasonable to utilize and integrate new methodologies into the risk assessment program and that further improvements will occur in the future with the increasing development and validation of NAMs."

Further information can be found at:
https://www.canada.ca/en/health-canada/services/chemical-substances/chemicals-management-plan/science-committee/meeting-records-reports.html

Where are we going ?

- Exploration and case studies to date have utilized existing data from international programs where inventory lists overlap. Plan to continue to move forward with new case studies focusing on future priorities.
- Short term
  - Incorporate new approach methodologies (NAM) into future rounds of IRAP;
  - Incorporate *in vitro* high throughput screens as developed (hazard flag) i.e. models built on assays that characterize endocrine activity (EDSP);
  - Science Approach Document - establish utility of Bioactivity Exposure Ratio (BER) in priority setting and assessment under the CMP.
  - Potential risk assessment decisions based on BER approach (late CMP3).
- Medium Term – Post 2020
  - Move away from substance by substance assessment approach toward priority setting on emerging classes of concern; role for NAM and collaborative/coordinated efforts across jurisdictions.
  - Develop a strategy to support advancement of methods development and integration of NAMs at the program level . For this, there is a need for continued and coordinated data generation internationally.

Questions