Government of Canada Gouvernement du Canada

Chemicals Management Plan Science Committee
First Term Report

Fall 2013- Fall 2016

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1. Background

Ensuring a strong science foundation for decision-making is one of the priorities of the Chemicals Management Plan (CMP). As one of several steps in support of this, Health Canada (HC) and Environment and Climate Change Canada (ECCC) created a Science Committee in 2013 to contribute expertise pertaining to scientific considerations moving forward under the CMP.

The creation of the CMP Science Committee (the Committee) followed the end of the mandate of the Challenge Advisory Panel (2006-2013), which was established in the first phase of the CMP to examine the use of weight-of-evidence and precaution in risk assessments.

2. Purpose

The purpose of the CMP Science Committee First Term Report is to summarize the CMP Science Committee meetings of the first term (2013-2016) and their outcomes for interested stakeholders and the public.

3. Scope

This Report summarizes the 5 meetings of the first term of the Committee. These meetings took place in Ottawa, Ontario (Canada) in February 2014, November 2014, June 2015, November 2015 and November 2016.

This Report represents the status and opinions of the first term Committee members (both core and ad hoc) at the time they were presented and discussed at the various meetings, and since then, progress/advances in science may have been made, such as in the application of new assessment methodologies in risk assessment.

The Report also summaries the Review of the Committee's work and its findings.

4. Message from the Co-chairs

As co-chairs of the first term of the Committee, we would like to express our sincere thanks to the core and ad hoc members of the Committee for their contributions since the first meeting in February 2014. There have been numerous lively and stimulating deliberations and respectful debates during the meetings, and extensive email communications while preparing for the meetings and during the creation of the final

Committee Reports. We believe the Committee worked very well together to provide input to the Government of Canada, particularly in light of the challenging and thought-provoking range of scientific topics that were discussed. We further recognize that the Committee members made a substantial personal commitment in time and energy to review the subject matter and provide the insightful responses that were the norm. This allowed the Committee to provide comprehensive and pertinent input to HC and ECCC as the Departments moved forward in the delivery of the CMP. It was also gratifying to see how the Departments used the Committee input, and that they are sharing this information widely through the publication of this First Term Report. We continue to be impressed with the ongoing attempts by the Departments to ensure effective communication and outreach to the public and other stakeholders. The co-chairs wish to thank Christine Norman, Director of the Existing Substances Risk Assessment Bureau (HC), Robert Chénier, (retired) Director of the Ecological Assessment Division (ECCC) and Nicole Davidson, Director of the Existing Substances Risk Assessment Bureau (ECCC) for their leadership, support, and dedication to the first term of the Committee.

Geoff Granville and Barbara Hales

5. Mandate of the External Committee

The mandate of the first term of the Committee is defined in the Terms of Reference as:

“The committee will contribute expertise to Health Canada and Environment Canada pertaining to scientific considerations moving forward under the CMP. These Departments have the responsibility and sole authority to make decisions informed by input provided by the committee.”

The Terms of Reference also provides information on the roles and responsibilities of the Committee, the Executive Secretary and the Secretariat.

6. External Committee Membership

There were 10 core members on the Committee who collectively had comprehensive expertise in key scientific areas, such as environmental or biological science, chemicals management frameworks, weight of evidence and precaution, and knowledge of the chemicals industry. Core members were appointed for an initial 3-year term and had an opportunity to be re-appointed for a second term.

While the members were selected for their expertise, the Departments also invited ad hoc members to participate at the meetings. Once the topic for a Committee meeting was determined, experts in the field were sought out and invited as ad hoc members to contribute their expertise to the deliberations.

The following section lists the names of the first term Committee members, along with their biographies, and their tenure on the Committee. The majority of members were present for the complete term of the Committee. Dr. Robert James Maguire retired and was replaced by Greg Paoli. To maintain openness and transparency, all members of the Committee disclosed all affiliations and interests, including any direct or indirect financial interests and other affiliations and interests that related to the mandate of the Committee. These may have included investments in companies, employment at the time of tenure, research support, grants, contributions, board memberships, and professional/scientific societies. This information was updated annually and posted online for transparency.

Mr. Geoff Granville (co-chair)

Biography

Following his retirement in 2006 from the position of Toxicology and Product Stewardship Manager at Shell Canada, Mr. Granville has worked as a private consultant with expertise in environmental and population health. At Shell, his responsibilities centered on occupational and environmental health issues relating to chemical substances, including toxicity testing, health risk assessments, and regulatory compliance. He has also been an adjunct professor at the University of Alberta and the University of Toronto. In 1991, he took on the role of Associate Director within HC's Environmental Health Directorate in Ottawa as part of a 2-year executive exchange program. Mr. Granville has participated on many committees; examples include membership of the Science Management Committee of the (Federal) Toxic Substances Research Initiative, and participation as co-chair of the (Alberta) Human and Animal Health Team of the Clean Air Strategic Alliance. Mr. Granville was also a member of the Government of Canada's Challenge Advisory Panel for the first phase of the CMP, from 2007 until 2011. Mr. Geoff Granville has a BSc. in biochemistry and toxicology from the University of Surrey
(United Kingdom).

Time on External Committee

November 2013 – November 2016

Dr. Barbara Hales (co-chair)

Biography

Dr. Barbara Hales is a professor in the Department of Pharmacology and Therapeutics at McGill University. As well as being the associate editor of Toxicological Sciences, Dr. Hales is a member of the Editorial Board for Birth Defects Research Part B, Developmental and Reproductive Toxicology. Dr. Hales has held numerous positions, such as: President of the Teratology Society, Director of the International Union of Toxicology - Executive Committee, and President of the Society of Toxicology of Canada. Dr. Hales has been involved in a number of committees over the course of her career with regard to pharmacology and toxicology, including reproductive toxicology.

Her current research interests focus on the mechanisms of action of drugs and environmental chemicals as developmental and reproductive toxicants. Dr. Hales has a PhD in Pharmacology and Therapeutics from McGill University (Canada).

Time on External Committee

November 2013 – November 2016

Dr. Sylvain Bintein

Biography

Dr. Sylvain Bintein is employed at the European Commission in Brussels (Belgium) as the Team Coordinator of the program for registrations, evaluation, authorisation and restriction of Chemicals (REACH) and the program for classification, labelling and packaging of chemicals (CLP) team in the Directorate General for the Environment. Dr. Bintein leads the development of European legislation with regard to hazard and risk for human health and to the environment from chemicals. He also oversees guidance and monitors the implementation of the REACH regulations and the CLP program. Dr. Bintein is a member of the Scientific Committee to the United Nations Environment Program's Stockholm Convention on Persistent Organic Pollutants, where he was the drafter on risk management and risk profile dossiers for several industrial chemicals and pesticides. Dr. Bintein has a PhD in environmental toxicology from the University of Metz (France) and is an engineer from the National School for Water and Environmental Engineering of Strasbourg (France).

Time on External Committee

November 2013 – November 2016

Dr. Peter Campbell

Biography

Dr. Peter Campbell is a professor at the Université du Québec, Institut national de la recherche scientifique, INRS-Eau Terre et Environnement (Canada). He holds a Canada Research Chair and is a member of the Royal Society of Canada (Academy of Science). Dr. Campbell presently works on a number of international science panels/committees. For example, since 2009, Dr. Campbell has been a member of the International Scientific Council, Centre d'Écotoxicologie et Toxicologie Environnementale de Rovaltain, France, as well as the Ecotoxicity Technical Assessment Panel (metals) since 2000. Dr. Campbell also sits on the Editorial Board for a number of Journals, such as Revue des Sciences de l'Eau (since 1993), Chemical Speciation and Bioavailability (since 1988) and Environmental Chemistry (since 2004). Dr. Campbell acts as an advisor on environmental matters for several Cree communities in northern Québec (since 2002). Dr. Campbell has a PhD from Queen's University (Canada) in Organic/Organometallic Chemistry and is a professor at the

Université du Québec, Institut national de la recherche scientifique, INRS-Eau Terre et Environnement (Canada).

Time on External Committee

November 2013 – November 2016

Dr. Nicola Cherry

Biography

Dr. Nicola Cherry is the Director of the Division of Preventive Medicine, and was previously Chair of the Department of Public Health Sciences in the Faculty of Medicine, at the University of Alberta (Canada). She has acted as a member for the Public, Community and Population Health grants committee of the Canadian Institutes of Health Research and as co-chair of the Canadian Association for Research on Work and Health. Dr. Cherry is a Fellow of the Royal College of Physicians and Surgeons of Canada. Previously she has participated in committees such as the Advisory Committee on Gulf War Veterans' Illnesses for the United States Department of Veterans Affairs, the UK Advisory Committee on Toxic Substances and has acted as a consultant for the World Health Organization's International Program on Chemical Safety. Dr. Cherry was a member of the Government of Canada's Challenge Advisory Panel for the first phase of the CMP, from 2007 until 2011. Dr. Cherry has a PhD in psychology from the University of London (United Kingdom) and received her medical degree from McGill University (Canada).

Time on External Committee

November 2013 – November 2016

Dr. Elaine Cohen Hubal

Biography

Dr. Elaine Cohen Hubal has held a number of positions at the United States Environmental Protection Agency, including her present role as Director of the Computation Exposure Division in the Office of Research and Development. Currently, she also serves as chair of the World Health Organization's International Program on Chemical Safety working group on the identification of early life stages for characterizing chemical exposures. She has served as an expert on a variety of scientific panels and committees, including the Voluntary Children's Chemical Evaluation Program Peer Consultation Panel and the Study Design Working Group for the National Children's Study. Additionally, Dr. Cohen Hubal was a member of the editorial board as an associate editor for reviews of The Journal of Exposure Science and Environmental Epidemiology. Dr. Cohen Hubal has a PhD in Chemical Engineering from North Carolina State University (USA).

Time on External Committee

November 2013 – November 2016

Dr. Miriam Diamond

Biography

Dr. Miriam Diamond is a professor in the Department of Earth Sciences at the University of Toronto and is cross-appointed to the Department of Chemical Engineering and Applied Chemistry, the Dalla Lana Faculty of Public Health, and the School of the Environment and the Department of Physical and Environmental Sciences at Scarborough College. Dr. Diamond was the Co-chair of the Ontario Ministry of the Environment's Toxics Reduction Scientific Expert Panel and the Ontario Ministry of the Environment's Multi-Stakeholder Panel on the "Living List" of the Toxics Reduction Act. Dr. Diamond is an Associate Editor of the journal Environmental Science and Technology and a member of the Board of Directors of the Canadian Environmental Law Association. Additionally, she is a Fellow of the Canadian Geographical Society and was named Canadian Environmental Scientist of the Year in 2007 by that society. Dr. Diamond has a PhD in Chemical Engineering from the University of Toronto (Canada).

Time on External Committee

November 2013 – November 2016

Dr. Robert James Maguire

Biography

Dr. Robert James Maguire is a retired public servant, after 35 years with Environment Canada. He was a Senior Research Scientist and Director of the Aquatic Ecosystem Protection Research Division of the National Water Research Institute in Burlington (Canada). Dr. Maguire has served on many Canadian committees related to chemical substances, and has been an associate editor of The Journal of Great Lakes Research, The Water Quality Research Journal of Canada, and Applied Organometallic Chemistry. In addition to being a Fellow of the Chemical Institute of Canada, and a former adjunct professor at the University of Waterloo, Dr. Maguire was awarded the Environment Canada Citation of Excellence for his research. Dr. Maguire has a PhD in physical chemistry from the University of Alberta (Canada).

Time on External Committee

November 2013 – January 2015

Dr. Jonathan Martin

Biography

Dr. Jonathan Martin is a professor at the University of Alberta (Canada) in the Department of Laboratory Medicine and Pathology. He supervises a dynamic research group which focuses on the fate and effects of organic environmental contaminants. Current projects include aspects of analytical method development for non-targeted discovery of contaminants, elucidating sources of human and environmental exposure, neurodevelopmental toxicity and environmental epidemiology. He was elected to the Royal Society of Canada's College of New Scholars, Artists and Scientists in 2015, and he has been acknowledged by Thomson Reuters as a "Highly Cited Researcher" (2014). For his early career research, he has also received awards from the Society of Environmental Toxicology and Chemistry (SETAC), and the Canadian Society for Chemistry (CSC). Currently he is a member of an international systematic review committee of the Swedish Foundation for Strategic Environmental Research. Dr. Martin has a PhD in Toxicology from the University of Guelph (Canada)

Time on External Committee

November 2013 – November 2016

Mr. Greg Paoli

Biography

Mr. Greg Paoli serves as Principal Risk Scientist at Risk Sciences International, Inc. Previously, he was employed as Research Manager at the Institute for Risk Research at the University of Waterloo (Canada). In these capacities, he has been a consultant specializing in risk assessment methodology in the field of public health and public safety for approximately 22 years. Mr. Paoli specializes in probabilistic risk assessment methods, uncertainty analysis, the development of risk-based decision-support tools and comparative risk assessment. Mr. Paoli was invited to serve on a Peer Review panel for the United States Environmental Protection Agency's Framework for Human Health Risk Assessment to Inform Decision Making. Mr. Paoli recently served on a United States National Academy of Sciences (NAS) Committee on the Design and Evaluation of Safer Chemical Substitutions. He previously served on the NAS Committee on Improving Risk Analysis Approaches Used by the United States Environmental Protection Agency, which issued the 2009 report, Science and Decisions: Advancing Risk Assessment (NRC, 2009). Mr. Paoli has served as Councilor of the Society for Risk Analysis and on the Editorial Board of Risk Analysis, and was awarded the Sigma Xi – Society for Risk Analysis Distinguished Lecturer Award. Mr. Paoli holds a Master of Applied Science Degree in Systems Design Engineering from the University of Waterloo.

Time on External Committee

July 2015 – November 2016

Dr. Don Wilke

Biography

Dr. Don Wilke is a Principal Scientist in the Global Product Stewardship organization at Procter and Gamble. Dr. Wilke has over 30 years of experience with regard to substance and consumer product risk assessment, and the consumer products industry. He has been an active participant in activities and initiatives related to chemicals management under the Canadian Environmental Protection Act, 1999 (CEPA 1999) since its inception. Dr. Wilke has also contributed to chemicals initiatives relevant to HC and Environment Canada, including input into updates of the New Substances Regulations (1999-2002) and the development of Environmental Assessment Regulations for Food and Drugs Act substances (2009-2011). Additionally, he is the chairman of the Technical Committee of the Industry Coordinating Group for CEPA. Dr. Wilke has a PhD in Pharmacology and Toxicology from Michigan State University (USA)

Time on External Committee

November 2013 – November 2016

7. Meetings

7a. Topic: Capturing and Communicating Uncertainty

February 19-20, 2014

7a(i). Attendees

Committee Members

- Sylvain Bintein
- Peter Campbell
- Nicola Cherry
- Elaine Cohen Hubal
- Miriam Diamond
- Geoff Granville
- Barbara Hales
- Robert James Maguire
- Jonathan Martin
- Don Wilke

Government of Canada Officials

- David Morin (Director General, Science and Risk Assessment, Science and Technology Branch, ECCC)
- Virginia Poter (Director General, Chemicals Sector, Environmental Stewardship Branch, ECCC)

- Amanda Jane Preece (Director General, Safe Environments Directorate, Healthy Environments and Consumer Safety Branch, HC)
- Robert Chénier (Director, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Christine Norman (Director, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Eeva Leinala (Senior Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Mark Bonnell (Senior Science Advisor, Ecological Assessment Division, Science and Technology Branch, ECCC)

Secretariat

- Jennifer Walter (Senior Policy Analyst, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

Guest Presenter

- Greg Paoli (Chief Operating Officer, Principal Risk Scientist, Risk Sciences International)

7a(ii). Background Information Provided by the Government of Canada

In conducting regulatory risk assessments for the protection of human health and the environment under CEPA 1999, ECCC and HC use a tiered approach and start with conservative assumptions and refine as necessary. Refinement may be limited by data availability. Approaches used are able to accommodate substances and substance groupings with varying amounts and types of information. This includes those that are data poor (use of information from related chemicals, that is analogues, use of computational models, release and exposure estimation) and those that are data rich (use of information on differences in sensitivity between species, and environmental monitoring data). In addition, the approaches need to be flexible for the consideration of emerging scientific knowledge and novel assessment approaches.

ECCC and HC characterize, consider and communicate uncertainty in their assessment reports. During the characterization of risk, the level of uncertainty plays an important role and is accounted for by both departments using standard risk assessment methodology. In following the tiered approach concept, the degree of analysis of the uncertainty is fit for purpose and can vary with decision context. Assessment reports typically contain sections regarding uncertainty in risk characterization as well as database confidence. Ideally, the assessment report will clearly communicate to the users (decision makers, risk managers and external stakeholders) the nature of uncertainty and the confidence in the outcome of the assessment. Depending on the nature of the assessment report, it should also reflect how reducing a particular uncertainty could impact the outcome of the risk assessment or further focus the development of risk management measures.

The Departments sought input from the Committee on how to better communicate uncertainty to decision makers and external stakeholders in the context of their regulatory risk assessment reports.

After discussion, the Committee and the Government of Canada agreed to include how to 'capture' uncertainty, in addition to communicating uncertainty, in the charge question.

7a(iii). Information Provided by the Guest Presenter

The Government of Canada invited Mr. Greg Paoli from Risk Sciences International to present at this Science Committee meeting.

Mr. Paoli delivered a presentation on the sources of uncertainty, the value of information, and coping strategies in the context of decision making.

The presentation opened by highlighting that the field of risk assessment is currently at a crossroads (National Academy of Sciences Report on Science and Decisions - Advancing risk Assessment, 2009). Risk assessment is intended to support decision-making, but is at its most useful and efficient when employed to discriminate among clear decision options. Consideration of stopping criteria and the value of information is key. The presentation emphasized the importance of maintaining a constant focus on decision-making options during the phases of problem formulation, planning and conducting a risk assessment and risk management. Uncertainty is used to describe the fact that there is incomplete knowledge of relationships or of quantities and can be treated formally, quasi-formally or informally. Examples of uncertainty were provided, as well as a simple way to differentiate between uncertainty and variability.

Value of information (VOI) was described as a decision-centric valuation of the benefit of new information that would reduce uncertainty. VOI analysis considers if the information is dynamic (in other words, depends on which information came first) and if it is counter-intuitive. Formal VOI calculates the difference between the expected benefit given new information and that same decision without additional information. The concept of value or information also extends naturally to information systems, as opposed to simply discrete pieces of information.

Challenges in estimating the impact of information occur when it is unknown what options the decision-makers are contemplating, when the manner in which the decision-makers select among options is unknown, when one is unwilling to describe the current state of uncertainty, and when one is unwilling to characterize the predictive quality, and therefore the weight, to ascribe to new knowledge.

The guest presenter provided thoughts and guidance on communicating uncertainty and described both qualitative and quantitative methods. Balanced communication was viewed as important with the separation of uncertainty in science from uncertainty in decision-making.

7a(iv). Committee Input

As outlined in the Committee Report, the Committee made 5 suggestions for consideration to HC and ECCC on how to better capture and communicate uncertainty in risk assessments:

1) **Develop and share standard guidance.** The Departments should update existing internal guidance documents to increase the quality, consistency and transparency of communicating uncertainty in risk assessments to facilitate informed decisions and risk management. The guidance needs to explain where assumptions are incorporated into the assessments and how best to document such assumptions. This guidance should be shared with stakeholders and the Departments should work towards harmonizing the guidance with other agencies.

2) **Summarize key uncertainties and ways to reduce them.** The Departments should summarize the key uncertainties and clearly note their impact on the risk assessment conclusions. This will provide insight into the confidence associated with the risk assessment conclusions. Departments should also identify information that would reduce key uncertainties and increase confidence in the decision.

3) **Standardize the format for communicating uncertainty.** The Departments should develop a standard summary table to communicate sources of uncertainty in every Screening Assessment Report (SAR). The table should include both human health and environmental considerations, and include both exposure and hazard endpoints.

4) **Apply best practices to communicate uncertainty.** Continue to summarize major uncertainties; however, the Departments should determine the importance of each in influencing the final risk assessment decision by quantifying each major uncertainty through the best available tools.

5) **Use case studies to develop standard guidance.** The Departments should review a variety of existing CMP SARs that include both data rich and data poor substances to aid in the development of standardized guidance for risk assessors.

7a(v). Use of Committee Input

The Departments posted the Committee Report online and shared the Committee input with internal governance bodies, internal CMP assessment groups, and the CMP Stakeholder Advisory Council.

The Departments sought input on potential summary tables to capture and communicate uncertainty with key users of the SARs, including risk managers and stakeholders. Updated formats for capturing and communicating uncertainty were

developed and used, as appropriate, for CMP priorities. It is important to note that the methods used to capture and communicate uncertainty will vary depending on the assessment approach attributed to a substance or group of substances.

In addition, stakeholder feedback on the different methods and table formats was used to develop guidance for scientific staff on how to best capture and communicate uncertainty in SARs.

Overall, the Departments consider the level of uncertainty for all available lines of evidence when determining whether or not a substance is declared toxic under CEPA 1999. Input from the Committee helped the Departments improve how uncertainty is captured and communicated to stakeholders. Ultimately, if stakeholders better understand how Departments attribute uncertainty to all available lines of evidence in a SAR, it leads to improved confidence in the assessment conclusions that are made by the Departments.

7b. Topic: Rationale for Use of Read-across in Risk Assessment

November 4-5, 2014

7b(i). Attendees

Committee Members

- Sylvain Bintein
- Peter Campbell
- Nicola Cherry
- Elaine Cohen Hubal
- Miriam Diamond
- Geoff Granville
- Barbara Hales
- Don Wilke

Regrets

- Robert James Maguire
- Jonathan Martin

Ad Hoc Members

- Grace Patlewicz (Tier) (Computational Modeler, DuPont Haskell Global Centers for Health & Environmental Sciences)
- Terry Schultz (Professor Emeritus, Department of Comparative Medicine in the College of Veterinary Medicine, University of Tennessee, Knoxville)

Government of Canada Officials

- Robert Chénier (Director, Ecological Assessment Division, Science and Technology Branch, ECCC)

- Christine Norman (Director, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Tara Barton-Maclaren (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Don Gutzman (Manager, Priority Assessments Section, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Adam Doane (Senior Evaluator, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Matthew Gagné (Senior Evaluator, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Alexander (Sasha) Okonski (Senior Evaluator, Ecological Assessment Division, Science and Technology Branch, ECCC)

Secretariat

- Julie Chouinard (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Vanessa Di Cenzo (A/Senior Policy Analyst, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

7b(ii). Background Information Provided by the Government of Canada

Read-across is the technique where endpoint or test results for one or more chemical(s) are used to predict the same endpoint or test results for another chemical(s), which is considered to be similar based upon scientific justification (OECD 2014a). Read-across can be used to predict physicochemical properties, (eco)toxicity, and persistence and bioaccumulation potential of chemicals. Read-across can be conducted within two similar grouping approaches: the analogue or the chemical category approach. Both grouping approaches require a rationale for chemical similarity.

HC and ECCC's Existing and New Substance programs have experience in using the read-across approach. Examples of the use of this approach in risk assessment include the Challenge Initiative, the Substance Groupings Initiative, and through contributing to the drafting of the Organisation for Economic Co-operation and Development (OECD) Guidance on Grouping of Chemicals (OECD 2014).

In the past, read-across was conducted by HC and ECCC by following guidance developed by the OECD (OECD 2014), and by using internal expertise and judgment. There were efforts to develop internal guidance for evaluators, and elements of this guidance were presented at this Committee meeting.

The Departments sought input from the Committee on best practices for deriving a sufficient rationale for read-across within the context of risk assessments conducted under the CMP. The Departments were also seeking input on known challenges with respect to the approach and considerations on how to best address them.

Information on three cases studies was provided to the Science Committee illustrating the approach taken for DMOB-based Direct Dyes, substituted diphenylamines (SDPAs), and Dechlorane Plus.

The revised Terms of Reference was also approved and endorsed at this meeting.

7b(iii). Ad Hoc Committee Member Perspectives on the Charge Question

The Government of Canada invited 2 ad hoc members to participate at this Committee meeting: Dr. Grace Patlewicz (Tier) and Terry Schultz.

Dr. Grace Patlewicz (Tier), from DuPont Haskell Global Centers for Health & Environmental Sciences, gave a presentation entitled “Perspectives from Practitioners working in Industry”. Considerations before embarking on a grouping approach were listed and included identifying the number of data gaps and for which endpoints; access to data and reliability of data; having a plausible hypothesis for grouping the substances together; consideration of whether the use of the approach will allow for an accurate and credible assessment of the hazards for the substance in question; and, the consequences and costs of the read-across approach not being accepted. Considerations for determining endpoint justification and key issues with the use of read-across were provided. Examples of endpoint considerations were included.

Dr. Patlewicz (Tier) indicated the importance of documenting all category/analogue work in a reporting format. Key issues in the use of read-across are discussed (such as ‘negative read-across’ reading across the absence of toxicity and where the burden of proof is higher) and a number of suggestions are made to address issues. The use of the SAR uncertainty evaluation questionnaire was recommended. A number of suggestions for addressing uncertainty were provided (such as in vitro studies such as Toxcast-type assays and adverse outcome pathway approaches (with pros and cons provided for each). The presentation ended with the following remarks:

- Read across is a term that is loosely used, which complicates the expectations of its utility and application; and,
- Read across is one data gap-filling approach and is endpoint-specific, hence problem definition is critical.

Terry Schultz, from the University of Tennessee, Knoxville, noted that organizations (such as OECD and governments) should work together to create a range of case studies across the spectrum in order to develop a set of guiding principles for the application of read-across.

The goal of any read-across exercise is to explain the similarity which is the basis for the read-across, and describe the type and degree of uncertainty associated with the read-across prediction. Read-across is firstly a case of establishing similarity which can be considered from different perspectives. In gaining acceptance of any read-across prediction, it is essential to explain the basis for similarity between the target

chemical(s) and potential source chemical(s) in a robust and reliable manner. Assuming the rationale for similarity is accepted, final acceptance of the read-across prediction is contingent on identifying and explaining sources of uncertainty. In order to be consistent and transparent in the manner in which similarity is established and uncertainty is assessed in a read-across prediction, it is advisable to establish and follow an assessment framework or work flow. Establishing a framework aids in garnering buy-in from stakeholders. The framework also:

- Describes the similarity rational of the read-across in a transparent manner;
- Documents the logic leading to the prediction so it can be recreated by the reader;
- Describes the uncertainty and separate data uncertainty from toxicological uncertainty; and,
- Clarifies the roles of endpoint specific and endpoint non-specific factors in the assessment.

The best gauge of certainty is a decrease in uncertainty. Therefore, an essential feature to acceptance of a read-across prediction is addressing the uncertainties inherent to the exercises. In the end, high confidence (or low concerns about 'potential error' in the prediction) is assigned to a read-across exercise when there is strong proof the prediction is valid (that there is low uncertainty).

The presentation included information on category formation, sources of data and toxicological uncertainty, as well as the importance of stating the endpoint. Since there are various over-arching scenarios for category formation and read-across, it is advisable to not only note the missing endpoint value and the type of exercise, but also state the hypothesis and assumptions on which the read-across is based. Apart from the major scientific challenge associated with predicting a substance's hazard based on other substances, "process-oriented" challenges to read-across lie in obtaining agreement on guiding principles for a read-across exercise, obtaining agreement on how to document a read-across, obtaining agreement on a template for assessing similarity and obtaining agreement on a template for assessing uncertainty.

7b(iv). Committee Input

As outlined in the Committee Report, the Committee suggested the development of a framework to apply and justify the use of the read-across approach. The guiding principles of the framework should include documentation on the decision context, the rationale for the chosen approach, the identification of factors impacting the assessment, the logic and supporting data of the prediction, and the uncertainties.

The Committee also stressed the importance of consistently capturing uncertainty and communicating the implications of the uncertainty on the interpretation of results. They noted that it is also important to separate data uncertainty from toxicological uncertainty.

If possible, actions should be taken to promote the generation of missing data or "bridging data".

Decisions should be made based on transparent criteria and there is a need to identify up front the risk context, the type of information, and the level of certainty required to make a decision using the read-across approach.

When building a case for similarity through either the analogue of the chemical category approach, the Departments should explain data gaps, endpoints, and the plausible hypotheses for grouping substances. It is important to evaluate, justify and document the basis for all major considerations, in other words, similarities in chemical structure, in chemical transformation (in both environmental and biological systems), in toxicokinetics and in bioactivity.

In some cases, where there is low exposure or wide margins of exposure, a rapid screening approach may be appropriate to avoid a detailed read-across evaluation. Depending on the scope of the problem and the data gaps, the Departments should consider whether or not a read-across approach is merited or whether a Quantitative Structure-Activity Relationship (or another approach such as the Threshold of Toxicological Concern (TTC)) will provide the required information.

7b(v). Use of Committee Input

The Departments posted the Committee Report online and have shared the Committee input with internal governance bodies, internal CMP assessment groups, the CMP Stakeholder Advisory Council, the OECD Task Force on Hazard Assessment, and the OECD Clearing House for New Chemicals.

The Departments addressed input received by the Committee, including the development of internal process documents and evaluator guidance, as well as training.

For example, sections of the draft evaluator guidance for ecological and human health analogue selection and read-across were revised or developed based on the Committee input, including the decision context for use of read-across, the development and support of similarity rationales.

In addition, the weight of evidence wording in the conclusion of the Dechlorane Plus SAR was improved, and certain aspects of the case studies noted in 7b.(ii) have been improved based on Committee input. Specifically, the read-across endpoint information was refined in the health case study on SDPA to more specifically define the target organ effects considered for read-across. In 2015, the case studies were submitted to the OECD Task Force on Hazard Assessment under the Integrated Approaches to Testing and Assessment (IATA) Case Studies Project in order to advance thinking on read-across in international fora.

Overall, input from the Committee has helped inform the use of read-across in both Departments as it resulted in improved guidance for risk assessors. Read-across has emerged as a critical tool for developing a weight of evidence, forming chemical categories and filling endpoint specific data gaps for data poor substances. The guidance increases consistency in how Departments apply read-across, and this is assisting the Departments in meeting their commitment to address approximately 1,500 chemicals in Phase 3 of the CMP.

7c. Topic: Implementation of a Framework for Risk Assessment

June 2-3, 2015

7c(i). Attendees

Committee Members

- Sylvain Bintein
- Peter Campbell
- Elaine Cohen Hubal
- Miriam Diamond
- Geoff Granville
- Barbara Hales
- Jonathan Martin
- Don Wilke

Regrets

- Nicola Cherry

Ad Hoc Members

- Greg Paoli (Chief Operating Officer, Principal Risk Scientist, Risk Sciences International)
- Louise Stedman (Senior Regulatory Scientist, National Industrial Chemicals Notification and Assessment Scheme, Australian Department of Health)

Government of Canada Officials

- Karen Dodds (Assistant Deputy Minister, Science and Technology Branch, ECCC) (Day 2)
- David Morin (Director General, Science and Risk Assessment, ECCC)
- Amanda Jane Preece (Director General, Safe Environments Directorate, Healthy Environments and Consumer Safety Branch, HC) (Day 2)
- Robert Chénier (Director, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Christine Norman (Director, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

- Angelika Zidek (Senior Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Tara Barton-Maclaren (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Don Gutzman (Manager, Priority Assessments Section, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Kristin Macey (A/Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Heather Patterson (A/Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Mark Bonnell (Senior Science Advisor, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Matthew Gagné (Senior Evaluator, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Sarah Vanden Hoven (Physical Sciences Specialist, Strategic Assessment Section, Ecological Assessment Division, Science and Technology Branch, ECCC)

Secretariat

- Julie Chouinard (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Alain Marchand (Policy Analyst, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

7c(ii). Background Information Provided by the Government of Canada

Canada is on track to meet its commitments under the United Nations Environment Programme's Strategic Approach to International Chemicals Management to address legacy chemicals by 2020. Approximately 2,800 substances were assessed in Phase 1 (December 2006 – March 2011) and Phase 2 (April 2011 – March 2016) of the CMP, and approximately 1,500 substances remain to be assessed in Phase 3.

Various approaches may be used to appropriately focus resources in Phase 3 of the CMP, but all approaches will continue to incorporate application of precaution and weight of evidence, strong science, and a tailored approach whereby the assessment will focus on sources of concern and key hazard properties.

A proposed level of complexity-based assessment framework and diagram was presented to the Committee which was based on risk assessment approaches used/developed to date. There are five levels of activity within the framework, and the levels are complexity-based. The lower levels in the framework are less complex, and the associated activities (for example, documentation of previous action under CEPA 1999, or rapid screening) may be well-suited to address multiple substances with a single approach which would result in efficiencies. The higher levels in the framework

are more complex, and these activities (for example, cumulative risk assessment or deriving reference levels) would only be conducted when warranted. The framework is flexible because an assigned level for a substance can change once the activity has begun if a different activity is justified. This type of framework is consistent with chemical assessment/prioritization approaches developed in other countries such as Australia and the United States (Department of Health, United States Environmental Protection Agency).

The Departmental levels of activity attributed to the substances do not need to align. Instead, each Department will only complete the level of activity that is required allowing the Departments to focus their respective resources appropriately. The proposed framework is intended to assist with work planning and triaging of the remaining Phase 3 priorities and to facilitate communication of intended assessment approaches.

The Departments were seeking input from the Committee on the proposed level of complexity-based assessment framework and the following:

- **Potential challenges with the proposed framework and suggestions for addressing these challenges;**
- **Specific assessment approaches illustrating the different levels of complexity, as well as suggestions for additional approaches to consider; and,**
- **How to best operationalize the framework and its potential role post-2020.**

7c(iii). Ad Hoc Committee Member Perspectives on the Charge Question

The Government of Canada invited 2 ad hoc members to participate at this Science Committee meeting: Greg Paoli and Louise Stedman.

Greg Paoli, from Risk Sciences International, indicated that the framework design was flexible. The diversity of tools available to risk assessors was acknowledged. It was suggested that it would be worthwhile to test the validity of the framework and to examine the uncertainty of the tools/tiers. This could be done with case studies for each tool.

Louise Stedman provided an overview on how chemicals are assessed through the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) administered by the Australian Department of Health.

The presentation first described the departmental roles for both the Department of the Environment and Department of Health. Notably, the roles of the Department of Health are to focus on occupational health and safety and public health.

Details were also provided on how NICNAS has a strategy to review existing chemicals on their inventory list (similar to the Domestic Substances List in Canada), and they have integrated Canadian and other countries information/strategies into their framework, entitled: Inventory Multi-tiered Assessment and Prioritisation (IMAP). The IMAP Framework is a tiered approach with all Tier 1 assessments completed first.

Based on NICNAS work to date, the following lessons learned were provided:

- Continuous review and improvement are key;
- Increased efficiency can be gained by grouping chemicals;
- Assessment effort should align with risk outcome;
- There are benefits to maximizing the use of international data and assessment reports;
- Focused stakeholder engagement should be done early and often;
- Public comments play a key role; and,
- Electronic tools and data management systems are important.

7c(iv). Committee Input

Overall, as outlined in the Committee Report, the Committee endorsed the proposed framework and concluded that the approach was “innovative, conceptually sound and relevant.” The Committee highlighted the importance of maintaining flexibility to allow for review, modification, and the update of assessment processes if necessary.

The Committee provided detailed comments on potential challenges and suggestions on the 5 different assessment approaches:

1) **Science-based policy response:** Depending on the quantities of the substance in commercial use and the use patterns, the Departments may not be in similar positions to have another program assess the substance. If another program assesses the substance, they should commit to conclude on its toxicity by 2020.

2) **Broad-based approach:** For this approach to be useful, the Departments should define or provide guidelines for “low potential for exposure” for both human health and environmental health. The Departments should also complete an additional review to ensure that additional exposure through the food chain is accounted for appropriately. If the Departments intend to use the TTC in Phase 3 of the CMP, the Departments should consider consulting experts first. The Departments should also seek out new tools that incorporate both hazard and exposure for human health assessments.

3) **Streamlined hazard and/or exposure analysis:** To confirm which concept to use, the Departments should first conduct a pilot exercise with data-rich substances that have information available from multiple sources. The Committee listed efficiencies and challenges for each concept in this approach; for example, a challenge associated with using hazard assessments from other international organizations is that the assessment will need to be updated to

include key information. This process may be challenging depending on the transparency of judgments applied in the original assessment.

4) **Moderate level complexity assessment:** Departmental decisions will be enhanced by clear communication of assumptions and quantification of uncertainties, and significant effort needs to be spent on problem formulation. Departments should clearly justify the critical factors leading to the conclusion. A review of past decisions should be conducted to allow for improvement and learning.

5) **Complex assessment:** For these unique and complex assessments, problem formulation will be critical because cumulative and probabilistic approaches may be included. Departments should also consider potential substitute substances that have similar chemistry and functional use potential during the problem formulation stage.

The Committee highlighted the need for clear documentation and communication as an important step to operationalize the framework for Phase 3 of the CMP. The Committee provided some examples of elements and their associated key considerations that could be used to operationalize the framework such as problem formulation, risk-based stop criteria, and value of information for action.

The Committee also suggested that the Departments consider “de-connecting their individual assessments in order to focus resources on substances of concern for each Department”. In the past, the Departments have worked on risk assessments at the same time, but the Committee members suggested that this change in Phase 3 of the CMP so that each Department can align staff to focus on their respective priorities.

7c(v). Use of Committee Input

The Departments posted the Committee Report online and have shared the Committee input with internal governance bodies, internal CMP assessment groups, the CMP Stakeholder Advisory Council, and other stakeholders.

In response to the Committee’s suggestion that Departments consider “de-connecting their individual assessments” for Phase 3 of the CMP, this modified approach was implemented which allowed the Departments to work on assessments at different times resulting in an appropriate allocation of resources on the remaining priorities. For example, under section 68 of CEPA 1999, either Department could first publish a Science Approach Document (SciAD) for substances with a non-toxic risk characterization for human health or the environment. The SciAD has a risk characterization section, rather than a formal conclusion. The Department that leads the SAR uses certain information from the other Department’s published SciAD and includes it in the SAR. The SAR continues to have a toxic or non-toxic conclusion (draft and final). This approach result in fewer packages overall which in turn results in gained efficiencies for Phase 3 of the CMP.

Some Committee comments from the Report were related to increasing clarity of the diagram, and the Departments made the following changes based on Committee input:

- The Complexity-based Assessment Framework was renamed to the Risk Assessment Toolbox;
- The “level of complexity” attributed to Type 1 and 2 approaches was removed since Type 1 and 2 approaches could also be highly complex;
- The format and labelling was changed so the Toolbox appeared less hierarchical; and,
- Several criteria were identified to select one approach over another, but flexibility was maintained so that new approaches can fit in existing boxes.

The remaining 1,500 substances that are being addressed in Phase 3 of the CMP have been assigned to the various approaches in the Toolbox. The changes made to the Risk Assessment Toolbox have enabled the Departments to better and more clearly communicate to stakeholders how the chemicals in Phase 3 of the CMP will be addressed, and this will help stakeholders understand the level of engagement that will be required of them. Ultimately, this enabled stakeholders to better provide timely and relevant information to the Departments. The improved communication to stakeholders and the gained efficiencies from “de-connecting individual assessments” assisted the Government of Canada in meeting its international commitments on addressing legacy chemicals by 2020.

7d. Topic: Considerations for Cumulative Risk for Existing Substances under the Chemicals Management Plan

November 18-19, 2015

7d(i). Attendees

Committee Members

- Sylvain Bintein
- Nicola Cherry
- Elaine Cohen Hubal
- Miriam Diamond
- Geoff Granville
- Barbara Hales
- Jonathan Martin
- Don Wilke

Regrets

- Peter Campbell

Ad Hoc Members

- Thomas Backhaus (Professor of Environmental Science, University of Gothenburg, Sweden)

Government of Canada Officials

- David Morin (Director General, Science and Risk Assessment, ECCC)
- Amanda Jane Preece (Director General, Safe Environments Directorate, Healthy Environments and Consumer Safety Branch, HC)
- Robert Chénier (Director, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Angelika Zidek (A/Director, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Ariff Ally (Senior Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Lynn Berndt-Weiss (A/Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Heather Patterson (A/Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Helen El-Koura (Science Advisor, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Don Gutzman (Manager, Priority Assessments Section, Ecological Assessment Division, Science and Technology Branch, ECCC) (Day 1)
- Thomas Kruidenier (A/Manager, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Kelly Potter (Head, Ecological Assessment Division, Science and Technology Branch, ECCC)

Secretariat

- Julie Chouinard (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Christine Allen (Senior Policy Analyst, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

Observers (for the introduction of topic and Charge Question (item #6) and the Government of Canada presentation (item #7))

- Shannon Coombs (President, Canadian Consumer Specialty Products Association)
- Maggie MacDonald (Toxic Program Manager, Environmental Defense)

7d(ii). Background Information Provided by the Government of Canada

There is general recognition that the assessment of chemicals on an individual basis may not reflect conditions in the environment or in humans, where multiple chemicals are typically found together. A more realistic, and possibly more protective, approach would be to consider these combined exposures through a cumulative risk assessment

(CRA). The framework for conducting CRA has been evolving over the last 25 years. It has been used for the assessment of various types of chemical exposures such as pesticides, asbestos fibers, dioxins and evaluation of contaminated sites. Characterization of cumulative risk from multiple chemicals has been undertaken under CEPA 1999 in only a limited number of cases (for example, polybrominated diphenyl ether (PBDE) congeners and nonylphenol and its ethoxylates).

The risk assessment paradigm for a CRA has the same four components as a traditional single-chemical assessment including: hazard identification, dose-response assessment, exposure assessment and risk characterization. However, there are specific considerations that are required when conducting a combined exposure assessment, including the assessment of exposure to multiple chemicals across multiple sources and routes. The hazard identification requires consideration of effects from toxicological interactions, while the exposure assessment will need to account for multiple exposure sources, pathways and routes

Substances that have a common effect can be grouped together for evaluation of potential combined exposures to multiple agents and cumulative risks. With respect to human health, co-occurrence of exposures to chemicals can occur via multiple sources, pathways, and routes of exposures over different exposure durations. For an ecological assessment co-occurrence of exposures to chemicals can occur in various media (for example in water, sediment, soil, and air) through releases from multiple sources to the same geographic area. There are three general concepts for characterizing effects associated with combined exposures to multiple chemicals: Dose (or concentration) addition; Response addition (or independent action); and integrated addition. Further details were provided to the Committee.

The Departments provided definitions of combined exposure, single chemical from all routes/aggregate exposure, combined hazard, risk from combined exposures and cumulative risk assessment. The Committee was given information on international approaches for cumulative risk assessment, as well as what has been done under CEPA to date.

The Departments were seeking input from the Science Committee on the considerations for determining when a cumulative risk assessment is necessary when conducting screening assessments under CEPA 1999, and whether the proposed ecological and health approaches for determining cumulative risk for the phthalates grouping are appropriate.

7d(iii). Ad Hoc Committee Member Perspectives on the Charge Question

The Government of Canada invited 1 ad hoc member to participate at this Science Committee meeting: Thomas Backhaus.

Thomas Backhaus, from the University of Gothenburg (Sweden), provided an overview of two examples of cumulative risk assessment tiering/screening processes. He noted

the importance of problem formulation and specifying the protection goal at the outset. Tiering should proceed from conservative (low resource requirements) to realistic (high resource demands). Proceeding to a higher tier, and investment of more resources, should only occur if there is a case to answer. Scientific correctness is not a paramount parameter at the beginning of the process, as long as one can argue that the results err on the side of caution and are not overprotective. A tiered process should indicate when the outcome would be that no further action is required, or when there is a need for risk management.

Dr. Backhaus indicated that if there is co-exposure, the risk quotients for individual substances should be summed in Tier 0. This should be completed regardless of the critical endpoint. If the results are greater than one, a cumulative risk assessment should be completed. He noted that, from the biological perspective, completely similar and completely dissimilar modes of action do not exist. In his presentation, he also highlighted the difficulty associated with conducting a cost-benefit analysis of a cumulative risk assessment.

7d(iv). Committee Input

Overall, as outlined in the Committee Report, the Committee recognized the motivation to conduct a cumulative risk assessment in recognition of human and ecosystem exposures to multiple chemicals. The Committee noted that conducting a cumulative risk assessment would allow for valuable experience in an area with limited history.

The Report described the possible factors for conducting a cumulative risk assessment, and considerations for the type of assessment required. For the purpose of the CMP, the focus is currently on chemical class assessments and the Committee described that once it is determined that co-exposure of the substances (included in the chemical class) can be reasonably expected, the considerations are whether:

1. the substances are anticipated to share an adverse outcome or endpoint signal that is of concern in either a human or ecological population;
2. an improved understanding of risk(s) associated with co-exposures relative to single chemical exposures is gained; and
3. the added VOI of a cumulative risk assessment in terms of a more efficient decision or an improved risk management decision/action is obtained.

The Report emphasized the importance of an initial and carefully conducted Problem Formulation step and noted other considerations, such as circumstances in which dose addition is not appropriate.

In addressing the specific Charge Question with respect to the phthalates grouping of substances, the Committee suggested that co-exposure, rather than target or action, be the primary determinant in deciding which chemicals constitute an appropriate grouping for a cumulative risk assessment.

7d(v). Use of Committee Input

The Departments posted the Committee Report online and have shared the Committee input with internal governance bodies, internal CMP assessment groups, the CMP Stakeholder Advisory Council, and other stakeholders.

The Committee suggestions were implemented for the ecological assessment of the phthalates grouping and refinements were made to the health assessment.

The Committee Report has helped to inform the Departments' dialogue in other venues on this topic, such as the OECD Combined Exposure to Multiple Chemicals work (for example, HC is co-leading the development of a guidance document focusing on the considerations for assessment of risk from the combined exposure to multiple chemicals).

Additionally, the input provided by the Committee has contributed to discussions on future program considerations in Post-2020 while the Departments work to meet their commitment to address approximately 1,500 chemicals in Phase 3 of the CMP.

7e. Topic: Considerations for Integrating New Approach Methodologies within the Chemicals Management Plan

November 16-17, 2016

7e(i). Attendees

Committee Members

- Sylvain Bintein
- Peter Campbell
- Nicola Cherry
- Elaine Cohen Hubal
- Miriam Diamond
- Geoff Granville
- Barbara Hales
- Greg Paoli
- Don Wilke

Ad Hoc Members

- Niladri Basu (Canada Research Chair in Environmental Health Sciences and Associate Professor, McGill University)
- Russell Thomas (Director of the National Center for Computational Toxicology at the United States Environmental Protection Agency)

- Maurice Whelan (Head of the Chemical Safety and Alternative Methods Unit and Head of the European Union Reference Laboratory for Alternatives to Animal Testing at the European Commission's Joint Research Centre, Italy)

Government of Canada Officials

- David Morin (Director General, Safe Environments Directorate, Healthy Environments and Consumer Safety Branch, HC) (Day 2)
- Nicole Davidson (Director, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Christine Norman (Director, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Tara Barton-Maclaren (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Mark Bonnell (Senior Science Advisor, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Marisol Eggleton (Science Advisor, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Thomas Kruidenier (Manager, Ecological Assessment Division, Science and Technology Branch, ECCC)
- Heather Patterson (Senior Advisor, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 1)
- Matthew Gagné (Senior Evaluator, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Sarah Vanden Hoven (Science Advisor, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC) (Day 2)

Secretariat

- Julie Chouinard (Manager, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)
- Christine Allen (Senior Policy Analyst, Existing Substances Risk Assessment Bureau, Healthy Environments and Consumer Safety Branch, HC)

Guest Presenter

- Michelle Embry (Associate Director, Environmental Science, International Life Sciences Institute (ILSI), Health and Environmental Sciences Institute (HESI))

Government of Canada Observers

- Doug Crump (Biochemical/Molecular Toxicologist, Ecotoxicology and Wildlife Health Division, Science and Technology Branch, ECCC)
- Andy Nong (Computational Toxicologist, Environmental Health Science and Research Bureau, Healthy Environments and Consumer Safety Branch, HC)

External Observers (Present for the introductions, opening remarks, introduction of topic and Charge Questions, and the Government of Canada presentation)

- Shannon Coombs (Canadian Consumer Specialty Products Association)

- Lysane Lavoie (Canadian Paint and Coatings Association)
- Barbara Mackinnon (New Brunswick Lung Association)
- Sandra Madray (Chemical Sensitivities Manitoba)
- Elizabeth Nielsen (Consumers Council of Canada)

7e(ii). Background Information Provided by the Government of Canada

The Departments are developing a roadmap for integrating new approach methodologies (NAMs) with traditional risk assessment. The roadmap is anticipated to cover multiple aspects of chemical risk assessment including priority-setting, hazard characterization, exposure characterization and risk characterization.

The planned roadmap is envisioned as a strategy that maps short-term and longer-term program objectives with specific existing and emerging NAM tools/applications. The roadmap would outline available or emerging NAM tools and illustrate their respective scientifically-sound use in the context of priority-setting and risk assessment. The roadmap will guide the Department's efforts to modernize the risk assessment program and facilitate acceptance for the use of emerging technologies in future priority-setting and risk assessment practices, and ultimately strengthen our overall priority-setting and risk assessment regimes.

The Departments were seeking input from the Committee on developing a roadmap for integrating NAMs as part of the risk assessment paradigm and how NAMs can enhance current priority-setting approaches.

7e(iii). Information provided by Guest Presenter and Ad Hoc Committee Member Perspectives on the Charge Question

The Government of Canada invited 1 guest presenter, Dr. Michelle Embry, and 3 ad hoc members: Dr. Niladri Basu, Dr. Russell Thomas and Dr. Maurice Whelan to participate at this Committee meeting.

Dr. Michelle Embry from the ILSI Health and Environmental Sciences Institute (HESI) delivered a presentation on the development of an ecological threshold for toxicological concern (eco-TTC) approach. The project is a multi-stakeholder, multi-sector activity and involves scientists from Europe and North America from government, academia, and industry. The presentation gave an overview of the TTC concept in human safety and provided details on the HESI eco-TTC project. Dr. Embry explained that Eco-TTCs summarize the wealth of ecotoxicological information as Predicted No-Observed Effect Concentrations (PNECs) on diverse chemical substances in the form of statistical (probability) distributions. Eco-TTCs enable the prediction of untested chemicals based on structural attribute (category), mode of action, or functional use.

A database with approximately 110,000 unique ecotoxicological records has been developed based on recent assessments of published data and international chemical management programs.
The dataset and associated tools will be made available via a web-based platform to provide an open, transparent opportunity for stakeholders to evaluate the approach with case examples.

Dr. Niladri Basu, from McGill University focused his presentation on NAMs within the field of ecological risk assessment. The presentation was grounded with the following observations: a) NAMs developed are mainly geared towards human health and thus have limited relevance to ecological species; b) NAMs developed in ecological risk assessment have focused on laboratory models, but extrapolation of results to native species introduces additional uncertainties; and c) although many ecotoxicologists (especially Canadian researchers) have developed NAMs, unfortunately these NAMs struggle to get widely adopted, standardized, scaled-up, or commercialized. A range of ecological risk assessment-related NAMs were described including wildlife monitoring programs to track legacy and emerging chemicals on temporal and spatial scales, cell-free assays and slice cultures from native species to screen and prioritize chemicals, and the development of targeted qPCR arrays (EcoToxChips) for regulatory decision-making. In addition, the presentation covered existing environmental risk assessment-related NAMs including QSAR and PBT models, cell lines and cell cultures for select species, fish early life stage tests, and organismal tests using various species.

Concluding remarks focused on some challenges in the field including:

- Lack of standardized and validated NAMs;
- A reliance on studying select laboratory models when decisions need to be made on many more native species;
- A need to focus efforts on predicting outcomes associated with exposures to complex environmental mixtures;
- Challenges in developing NAMs to cover lifestages and latent outcomes;
- The need to deliver intuitive and accessible bioinformatics;
- The need to better involve end-users (for example, government regulators or industry) in all aspects of NAM development; and,
- Empirical research to determine whether NAMs are really helping move testing to a process that is cheaper, faster, and more predictive.

Dr. Russell Thomas, Director of the National Center for Computational Toxicology at the U.S. Environmental Protection Agency, gave a presentation entitled “Brief State of the Science Overview: NAM in Toxicology and Exposure”. He summarized NAM development based on hazard/bioactivity, toxicokinetics and exposure. Dr. Thomas described the use of bioactivity as a point of departure, the conservation of response based on x-species and ongoing systematic attempts to address key limitations such as biological coverage using high throughput transcriptomics.

With respect to toxicokinetics, Dr. Thomas explained that data generation activities have provided metabolic clearance and plasma protein binding values for approximately 700 chemicals with about an additional 100 per year. Current IVIVE assays and models estimate steady state blood concentrations within 3-10 fold more than 80% of the time.

Currently, exposure estimates for >7,000 chemicals using production volume and chemical use categories are available, with uncertainty. To reduce uncertainty in exposure estimates, the EPA is exploring non-targeted screening of consumer products, human individual and pooled sample biomonitoring. In the next generation of high-throughput exposure modeling, the EPA is combining structural predictions and existing knowledge of consumer/industrial use to define exposure pathways and integrating this information in a mechanistic and empirical modeling framework.

Dr. Thomas ended the presentation on the note that the path for NAMs development and application is one that is convergent between hazard, toxicokinetics, exposure and computer modelling.

Dr. Maurice Whelan, Head of the Chemical Safety and Alternative Methods Unit of the Directorate for Health, Consumers and Reference Materials of the European Commission's Joint Research Centre (JRC), spoke about the need to distinguish between data, information and knowledge when contemplating future strategies to employ new approach methods in chemical risk assessment. A mechanistically-informed paradigm requires knowledge about toxicological processes to be systematically used to define the optimal information requirements for assessing a chemical based on its mechanistic profile, rather than traditional apical-endpoint profiling. Moreover, the same knowledge serves to define what new approach methods can be used to generate the right data to produce the information required.

AOPs are an effective knowledge management tool for developing IATAs. They inform IATA by providing a mechanistic rationale to the selection and integration of data sources and the analysis of uncertainty. Dr. Whelan highlighted that using NAMs leads to unfamiliar uncertainties (for example, the human relevance of an in vitro model as compared with an animal model). Dr. Whelan also presented a framework to establish credibility of computational models intend for regulatory use. The framework illustrates the relationship between testable and untestable models that are based on known or unknown biology and the resulting level of credibility. This analysis helps to inform an appropriate validation approach and indicates what aspects of a model need to be improved to increase credibility and ultimately gain acceptance.

7e(iv). Committee Input

Overall, as outlined in the Committee Report, the Committee is supportive of a shift towards the use of NAMs in prioritization processes. The Report outlines the Committee input in the form of key considerations with developing a roadmap for NAMs and risk assessment modernization in the context of recent developments. The key considerations are:

- Interrogation of the effects at the molecular and cellular levels and increased biological coverage;
- Putting results in a dose/exposure context;
- Customer-driven NAM development;
- Characterization of uncertainty and variability;
- Building scientific confidence and transparency; and
- Collaboration with other international organizations.

The Committee also suggested that consideration be given to a number of systematic approaches within the prioritization process, such as automated data collection. The Committee provided various examples of NAMs available. The use of other NAM tools and outputs, such as the TTC, the ecoTTC, and the Ecological Risk Characterization approach were supported by the Committee.

The Committee members also supported the use of the bioactivity-to-exposure ratio as a cross-cutting approach that should be useful in both ecological and human health applications. The Report indicates that there is an opportunity for the CMP to partner with other international organizations on both the methods and common substances of concern in the application of NAMs.

7e(v). Use of Committee Input

The Departments posted the Committee Report online and have shared the Committee input with internal governance bodies, internal CMP assessment groups, the CMP Stakeholder Advisory Council, and other stakeholders.

The Committee suggestions are being progressively implemented, such as in the development and application of pharmacokinetic approaches to enable risk-based prioritization. Input will help inform an upcoming bioactivity-to-exposure ratio approach document.

The Committee Report supports the ongoing activities of the Departments such as extending the scope of collaborative relationships with international organizations to facilitate information sharing and alignment.

7. Review of the Chemicals Management Plan Science Committee

The Health Canada Policy of External Advisory Bodies (2011) recommends that the purpose and functioning of an advisory committee should periodically be reviewed to ensure that the body is operating effectively and efficiently, to confirm that the work is still required and to identify opportunities for administrative and management

improvements. The policy also provides suggestions for the scope of the review, the review approach and timing.

Following this recommendation, a review of the Committee was undertaken in 2016. As the review included an evaluation of the Secretariat's functioning, it was contracted out to an Ottawa consulting firm.

The approach to the review was undertaken in a three step process. First, a draft survey was developed consisting of a series of statements to be rated by respondents. Committee members, government representatives and external stakeholder representatives were invited to participate in the survey. The second step involved interviews with respondents to solicit further qualitative input once the written input had been compiled, focusing primarily on those statements that produced lower average scores. For the third step, findings from each line of enquiry were compiled, analysed and synthesized leading to the preparation of a report. Suggestions for improvement were developed based primarily on input received from respondents.

The review covered the following areas:

- The operations of the Committee;
- The conduct of Committee business;
- Openness and transparency; and
- The contributions of the Committee.

7a Review Findings

Operations of the Committee

Overall the operations of the Committee received high ratings from all respondent groups. For the most part, there had been an appropriate and wide range of expertise, diversity of backgrounds, experiences and affiliations present on the Committee with strategic use of ad hoc members to address topic specific gaps in expertise. As well, the introduction of webinars in advance of Committee meetings helped members to prepare for discussions on what were often very complex issues and topics. The co-chair model was endorsed by the majority of respondents; however, some suggestions were made with regard to the selection process and the term of co-chairs. The Secretariat received high ratings for the support it provided to the Committee, specifically with regard to the development and distribution of pre-meeting materials and objectives papers, as well as for the design and delivery of pre-meeting webinars.

Conduct of Committee Business

Conduct of Committee business received high ratings for the working relationships between Committee members and government officials; attendance of appropriate experts/government officials at meetings; the use of presentations and responsiveness of presenters; and the use of charge questions to focus discussions. Several respondents suggested that the process to clarify and confirm the charge questions in advance of Committee meetings needed to be improved. Respondents also commented

that Committee reports need to be able to stand on their own and suggested an introductory context setting piece derived from the corresponding objectives paper be added to the report.

Openness and transparency

Only one external stakeholder who observed the open portion of a Committee meeting responded to the survey and took part in an interview; however, the level of discussion, challenge and debate that occurred at the Committee meeting clearly contributed to improving her confidence in the CMP. In her words, “this is a good news story that should be told”. This respondent also echoed other comments related to the need for more comprehensive reporting of the context, objectives and results of each meeting.

Contributions of the Committee

Over 80% of respondents agreed or strongly agreed that the Committee contributed expertise to the Departments pertaining to scientific considerations moving forward under the CMP. The vast majority of Committee members and government respondents agreed or strongly agreed that the Committee remained relevant and provided useful information to HC and ECCC. There were also several suggestions that Committee members be more involved in the identification of discussion topics.

7b Suggestions for Improvement

Review core member expertise as new members are recruited

Over the course of time, the Executive Secretary for the Committee had to replace members as they resigned or as their terms came to an end. Prior to the establishment of the Committee, HC and ECCC undertook a thorough analysis process to identify the expertise and perspectives they wished to have represented on the Committee. The grid populated with current member qualifications prepared by HC and ECCC had not been shared with Committee members. Since the Committee was created, one resigning member who brought ecological science expertise to the Committee was replaced. While the newly recruited member brought different expertise that is beneficial to the work of the Committee, there was the impression that the Committee had lost ecological science expertise. To ensure that appropriate skills and expertise are maintained or improved on the Committee, the report suggested that:

- The analysis grid of required expertise and perspectives be shared with Committee members and that they be invited to complete the grid by self-identifying the expertise and perspectives they bring to the Committee. This will provide HC and ECCC with a more comprehensive picture of the expertise and perspectives represented on the Committee.
- With the resignation of each member, HC and ECCC should review the grid, paying particular attention to the gaps in expertise resulting from the resignation in order to avoid a decrease in necessary expertise and to identify the most critical gaps in expertise to be filled.

- As members resign and need to be replaced, and once the required expertise and perspectives has been identified, the report suggested that all members of the Committee be engaged in the process of identifying a suitable replacement. In addition to reviewing the original submissions, current members are able to tap into their often vast networks to help identify suitable replacements (without making any commitments to potential candidates). Members' understanding of the work, the norms and the functioning of the Committee would also be helpful in the identification of candidates who may best fit the established culture of the Committee.

The Departments agreed with this suggestion and asked members to complete their own areas of expertise. For the renewed Committee, the Departments reviewed and revised the original areas of expertise.

Establish and communicate Co-chair selection process and term of office

Most members and government officials were unaware of the co-chair selection process. Those respondents who commented did not object to the selection process and pointed to the terms of reference that stipulated "the committee co-chairs will be selected amongst the assigned core members and appointed by the Executive Secretary". To improve transparency, it was suggested that in future the co-chair selection criteria be shared with Committee members.

Setting term limits for chairs or co-chairs is normal practice on boards and committees as new chairs can bring a freshness of insight. The report suggested that term limits be set for the co-chairs. The suggestion of staggering the appointments of co-chairs was also made and may be of value to ensure continuity.

The Departments agreed with these suggestions and for the Term 2 application process provided details on the ranking for the co-chair selection process. The Terms of Reference were also modified to include more details on co-chairs and to allow for staggering of chairs.

Improve clarity of charge question(s) and seek ways to establish a common understanding of the question(s) prior to the meeting

Members and government officials were very supportive of the use of charge questions to help focus Committee discussion and debate. The challenge associated with the use of charge questions was often the difficulty associated with achieving clarity and a common understanding of the intent of the question. The report suggested that the co-chairs actively engage with members in the time period between the webinar and the face-to-face meeting to ensure a common understanding of the charge questions, and when necessary, bring suggested refinements to the Secretariat for consideration prior to the Committee meeting. The intent was not to eliminate debate related to the charge questions, only to minimize it so that the Committee can dedicate more time to discussion of the issues.

The Departments agreed with this suggestion and have made several changes to address the issue. First, charge questions are now broken down to narrow the focus and interspersed throughout the objectives paper. Second, a portion of the pre-meeting

webinar focuses on the charge questions and spends time ensuring that all members understand what is being asked.

Add a contextual piece to the Committee reports to increase comprehension by interested stakeholders

According to many respondents, the reports as written were most meaningful to those who were present at the meetings. To increase transparency and the value of these reports as stand-alone products, the report suggested that a short context piece derived from the objectives paper be added to the Committee reports as well as some characterization of the issues raised during the discussions and the nature of the debate.

The Departments agreed with this suggestion and have been actively exploring solutions, such as posting the objectives paper with the Committee report and producing executive summaries.

Communicate the Committee's work more actively

As was mentioned by the external stakeholder respondent, the work of the Committee is a good news story which, if told, should contribute to public confidence in the CMP. In addition to improving the publicly available reports, the report suggested that the Secretariat play a more active role in pushing information out to interested stakeholders via the channels available to them.

The Departments agreed with this recommendation and actively seek opportunities to present on the Committee, such as external science meetings.

Engage the Committee members in identification of future topics

The Committee understood that a limited amount of time was dedicated to the identification of possible discussion topics. Several respondents suggested that HC and ECCC were missing an opportunity to leverage the broad range of expertise, diverse backgrounds, experiences and affiliations of Committee members when identifying issues and topics of importance. The report suggested that Committee members be engaged more formally in helping to identify discussion topics.

The Departments agreed with this suggestion and allot time on the agenda for the identification of future topics.

8. Renewal of the CMP Science Committee

The core members of the Science Committee were appointed for an initial term of 3 years. The initial 3-year term began in February 2014, which was when the inaugural face to face Committee meeting took place. The first term ended in the fall of 2016. The Committee has made significant contributions to the delivery of the CMP. The Departments revised the areas of expertise required for membership in order to better address emerging priorities and the needs of the program. As such, a call for representation for the second three year term was completed in the summer of 2017. The core members of the second term of the Science Committee are appointed for a 3-year term.

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