Canada's Approach for Assessment of Nanomaterials in Commerce: Prioritization and Tools for Assessing Consumer Exposure

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ABSTRACT

Health Canada and Environment and Climate Change Canada have undertaken an initiative to prioritize and assess manufactured nanomaterials (MNMs) in commerce in Canada for risk to human health and the environment. On the basis of information obtained from a mandatory survey on production/import volume and uses, and literature search on uses, hazard, and physical-chemical properties, over 50 MNMs were identified in Canadian commerce and are being prioritized as low, moderate, high priority for further action, or unable to be prioritized due to a lack of hazard/exposure information. Over 95% of the MNMs were found to be (potentially) used in consumer applications. Due to the lack of measured exposure data, Canada is leading an OECD initiative to identify and assess the applicability of exposure models and databases for use in characterizing consumer exposure to MNMs. This paper will discuss uncertainties/challenges encountered within the context of regulatory risk assessment of nanomaterials.

Keywords: manufactured nanomaterials, prioritization, regulatory risk assessment, consumer exposure models

1 INTRODUCTION

Production volumes and uses of manufactured nanomaterials (MNMs) in consumer products are continuously increasing; however, little is known about their potential risk to human health and the environment. In 2011, Health Canada (HC) published a working definition of MNMs [1]. Following this definition, there is a need to understand the use of MNMs in Canadian commerce and to develop an evidence-based, robust regulatory risk assessment approach for evaluating the risks of MNMs to Canadians.

The Government of Canada proposed an approach for addressing MNMs existing in the Canadian marketplace in 2015 and further detailed the approach in 2016 [2,3]. A mandatory survey pursuant to section 71 (s.71) of the Canadian Environmental Protection Act (CEPA) was launched in 2015 which applied to persons who manufactured or imported MNMs at a quantity greater than 100 kg during the 2014 calendar year. Based on the results, a list of confirmed existing MNMs in Canada was established, and was subsequently prioritized.

Despite the fact that MNMs are broadly used in various consumer products to which the general population is exposed through daily activities, measurement and monitoring data on the release of nanomaterials during the production, formulation, and use of the products are scarce. Currently, exposure assessment approaches are qualitative or semi-qualitative, often considering the particle size and shape and product form. Thus, modelling appears to be an effective way to provide supporting evidence in cases where exposure data may be limited. In 2015, the Steering Group on Exposure Measurement and Mitigation (SG8) within the Organisation for Economic Co-operation and Development's Working Party on Manufactured Nanomaterials (OECD WPMN) was tasked with identifying the available data on consumer and environmental exposure and mitigation measures, with the aim of prioritizing future work and research needs. Following a survey on consumer and environmental exposures to MNMs [4], exposure models for use in characterizing or estimating consumer exposure to MNMs were identified to be of high importance, requiring further investigation.

The objective of this paper is to describe an ongoing regulatory initiative for prioritizing the existing MNMs in the Canadian marketplace, and to introduce an OECD project for compiling available models for consumer exposure to MNMs. The results will inform the development of a nano-specific risk assessment framework for the Canadian regulatory context.

2 DSL NANOMATERIALS PRIORITZATION

Based on the information submitted under s.71 of CEPA, over 50 MNMs on the Domestic Substances List (DSL) were determined to be in-commerce in Canada. Prioritization of these MNMs for further action is being conducted by taking into consideration information from the s.71 survey and in peer-reviewed scientific literature, publically available databases on nanomaterial use and toxicity, as well as outcomes of international activities (e.g., initiatives of the Canada-United States Regulatory Cooperation Council and the OECD WPMN). An overview of the prioritization approach is depicted in Figure 1.

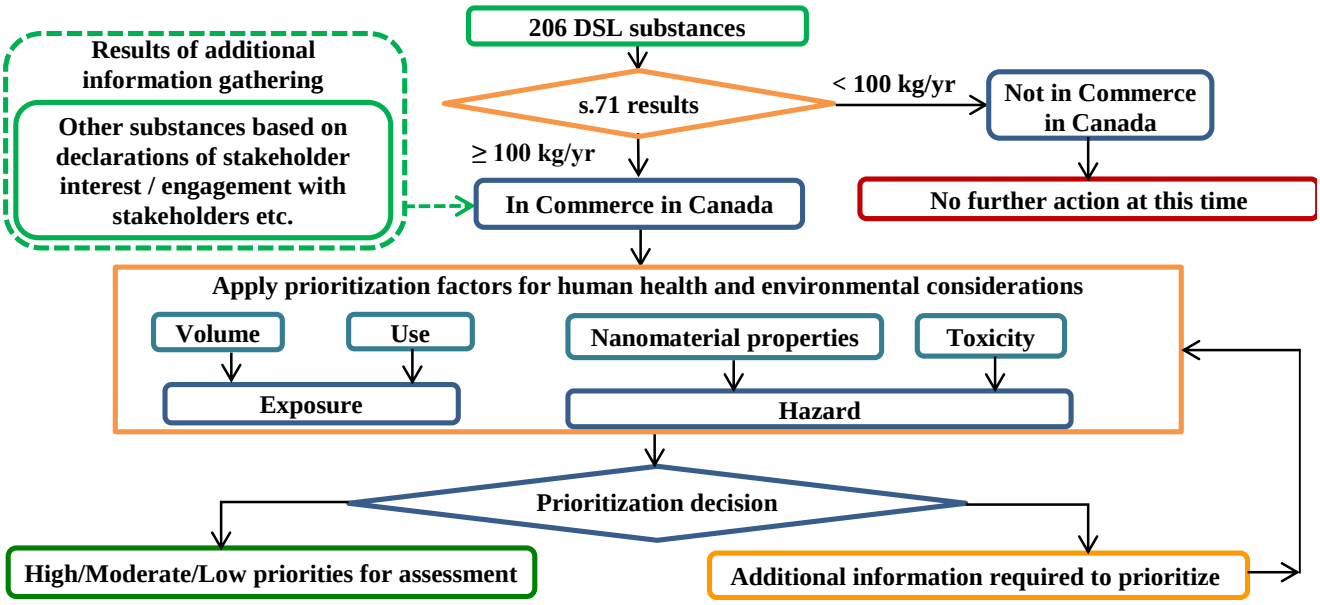

Figure 1: Overall prioritization approach for DSL nanomaterials

Human health approach for prioritizing MNMs for further action involves the use of a risk matrix with both exposure and hazard considerations (Figure 2). Three bins for risk assessment priority are generated as being low, moderate and high. This prioritization exercise is not meant to be a surrogate for a risk assessment and the ranking does not reflect the human health risk assessment conclusion for the MNMs. Instead, it's an effective approach for prioritizing and identifying data gaps. The need for data gathering or generation is identified in this process. The following sections describe the steps required to determine an exposure band (section 2.1) and a hazard band (section 2.2).

		Hazard		
		Low	Moderate	High
Exposure	Low	L	L	M
	Moderate	M	M	H
	High	M	H	H

Figure 2: Human health risk matrix for prioritizing MNMs (L = low priority; M = moderate priority; H = high priority)

2.1 Exposure

The exposure band is meant to denote the potential for exposure of the general population. For a given MNM, both the known quantities in Canadian commerce and its use are considered (Figure 3). On the basis of total import and/or manufacture volume reported under the s.71 survey for the 2014 calendar year, a corresponding volume ranking is assigned as low (100 to 10,000 kg), moderate (10,000 to 100,000 kg) or high (> 100,000 kg). Known and potential uses in Canada were determined based on the uses reported under the s.71 survey, as well as additional information found through various domestic and international sources. MNMs with known use(s) in products available to consumers (e.g., personal care products, cosmetics, and food) or intended to be used for children can be considered to have a high potential for exposure. MNMs found in manufactured items that may leach have a moderate potential for exposure and MNMs with industrial or commercial use only have the lowest relative potential for general population exposure.

		Volume		
		Low	Moderate	High
Use	Low	L	L	M
	Moderate	M	M	H
	High	H	H	H

Figure 3: Exposure prioritization matrix (L = low priority; M = moderate priority; H = high priority)

2.2 Hazard

For a given MNM, both physical-chemical properties and its toxicity are considered in prioritizing human health hazard. One key physical-chemical property is whether or not the MNM is a high aspect ratio nanomaterial (HARN), i.e., whether it is fibrous in shape with an aspect ratio > 3:1. It is generally recognized that, similar to asbestos, rigid and biopersistent HARNs may cause a cascade of inflammatory effects that can ultimately lead to cancer [5]. Similarly, if the CAS RN contains a structural alert (e.g., a US EPA Chemical Categories), this signals a higher potential for human health hazard. Toxicity information gathered is fed into the hazard prioritization process. The high hazard band is intended to capture MNMs for which there is sufficient evidence to cause serious health effects (e.g., carcinogenicity, mutagenicity, reproductive/developmental

toxicity, neurotoxicity etc.). MNMs for which the bulk substance is known to be highly hazardous to human health are also included in the high hazard band. The moderate hazard band includes MNMs for which there is evidence of skin sensitization, eye irritation or for which there are mechanistic data suggesting effects such as cardiovascular or inflammatory effects. The low hazard band is intended to capture MNMs that do not show adverse effects in either classical toxicity tests, or alternative test methods, and do not have any of the high or moderate hazard flags identified above.

2.3 Preliminary prioritization results

Preliminary prioritization results indicate that some substances appear to have sufficient information for conducting a risk assessment at this time, whereas the others cannot be prioritized or assessed due to a lack of confirmed exposure or hazard information and require further data gathering activities. Further research needs to fill in hazard data gaps are also identified for conducting risk assessments on DSL MNMs.

3 CONSUMER EXPOSURE TOOLS

There is a need to develop an effective strategy to assess human exposure to MNMs in consumer products when monitoring data are very limited. As such, under the OECD WPMN SG8, Canada is leading a project to compile available tools and models used for the assessment of environmental and consumer exposure to MNMs, and to evaluate their applicability to regulatory exposure assessment of MNMs. In collaboration with OECD project partners (e.g., the United States of America, the Netherlands, France, Germany), an inventory of available models and databases for assessing human exposure to MNMs was created, based on information collected from other OECD projects and international initiatives, consultations and inputs received within the SG8 member countries, and an extensive literature review. Examples of models and databases collected are shown in Figure 4, as categorized into three groups. The current inventory includes 14 nano-specific models (incl. control banding), 12 models designed for exposure to chemicals but could be adjusted for MNMs exposure modelling, and 24 nano-specific databases specifically developed for searching nanomaterials, or products containing nanomaterials. For each model and database, detailed information was recorded as to its version, country of origin, description, input parameters, availability, intended domain of applicability, product type, product form, routes of exposure considered, extent of validation and assumptions for models. The second phase of this project is underway, with a focus on prioritizing the models collected in the first phase for an in-depth evaluation. Model evaluation will include an investigation of the scope and intended

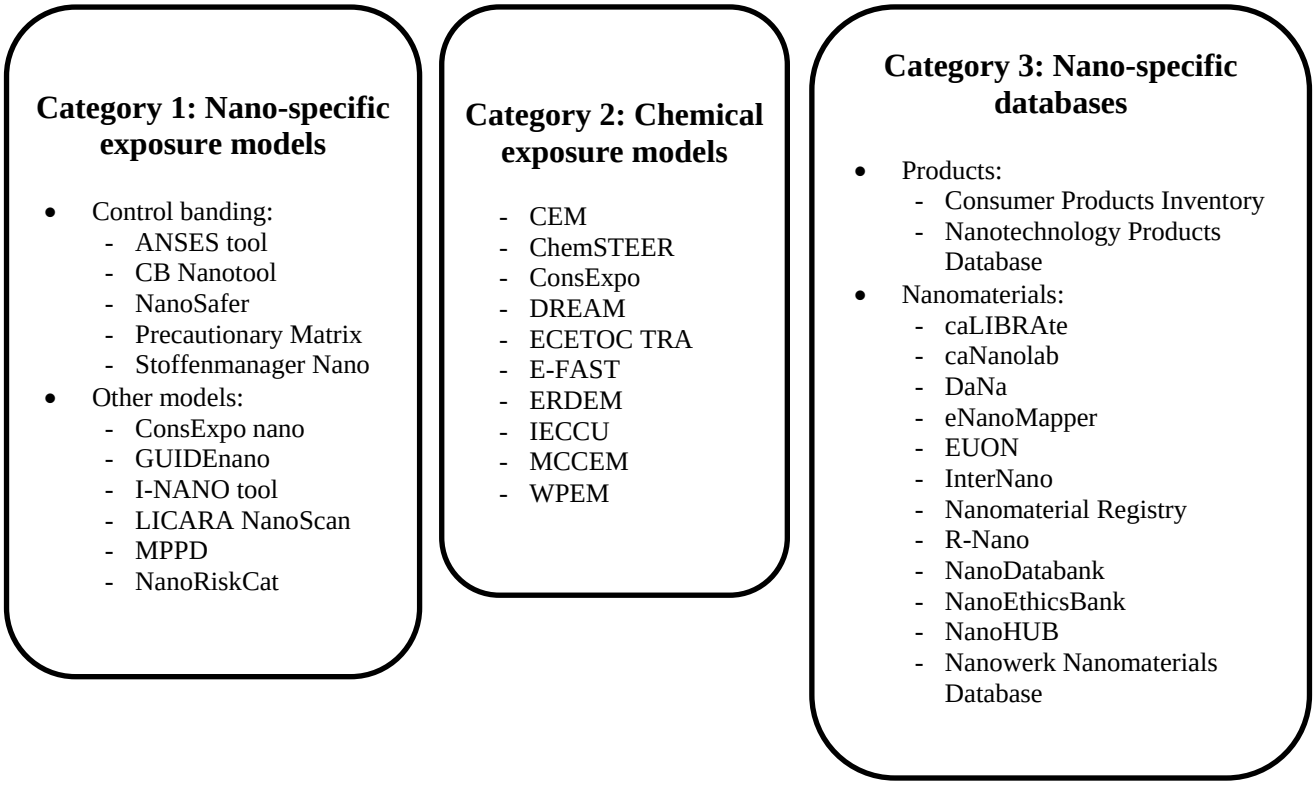

Figure 4. Examples of models and databases identified for consumer exposure

applicability domain, limitations and assumptions, user-friendliness, sensitivity analysis as well as model validation using case studies.

4 NEXT STEPS

Concurrent with the rapid growth of nanotechnology, come challenges and unanswered questions. Some common challenges exist for risk assessment of both chemicals and MNMs, such as lack of monitoring or measurement data and limited model validation. MNMs also pose additional challenges. For example, with a lack of standardized and validated measurement methods for identifying and characterizing a given MNM, it is often difficult to compare different studies on the same MNM. The absence of a nomenclature system for variants of a given MNM (e.g., different sizes, shapes, surface modification) also introduces uncertainty and challenges in grouping, read-across and evaluation of a MNM.

Currently, HC and Environment and Climate Change Canada are finalizing the prioritization of DSL MNMs and are developing a regulatory framework to guide the risk assessment of DSL MNMs by taking into account some of the challenges and uncertainties encountered. Internationally, several attempts have been made to develop frameworks for grouping, prioritizing/ranking and testing MNMs [6, 7]; however there is a lack of evidence-based, robust frameworks for regulatory assessment. Nanomaterial risk assessment presents a unique regulatory challenge, not only because these substances can exhibit different properties compared to their non-nanoscale forms, but because they can exist in many variations of shape, size, and surface modifications. Moreover, a nanomaterial's properties can change throughout its lifecycle, and these changes can affect the potential for exposure and hazard, and thus impact the risk to human health and the environment. It is intended that the regulatory risk assessment framework being developed for DSL MNMs will incorporate uniqueness of MNMs (e.g., intrinsic and extrinsic properties, environmental fate and life cycle, particle toxicokinetics etc.) and will be a science-based approach for protecting the health of Canadians.

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