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Environment and Climate Change Canada  
Substances Management Information Line  
Chemicals Management Plan  
351 St. Joseph Boulevard  
Gatineau, Québec  
K1A 0H3

*Transmission by e-mail: [eccc.substances.eccc@canada.ca](mailto:eccc.substances.eccc@canada.ca)*

**Re: Response to consultation document – Proposed prioritization approach for nanoscale forms of substances on the Domestic Substances List**

Chemical Sensitivities Manitoba (CSM) and Prevent Cancer Now (PCN), are submitting the following comments in response to the consultation document titled, “Proposed prioritization approach for nanoscale forms of substances on the Domestic Substances List”, released in July 2016.<sup>1</sup>

***Present overview***

CSM, PCN and the Canadian Environmental Law Association (CELA) previously submitted substantial comments related to the adequacy of the assessment framework addressing nanomaterials (NMs) in Canada. The present consultation document, a primer for the prioritization of NMs that are on the Domestic Substances List (DSL), requires significant further details including timelines for completion of the work.

Health concerns related to the exposure to NMs have been identified principally on the basis of their very small size such that particles may pass through cellular membranes, and airborne particles are born deep into the lungs. Much of the evidence showing impacts of NMs has focused on the occupational setting, but there are significant data gaps regarding public health and environmental impacts, including degradation, end-of-life and recycling of nano-containing products. This would result with an assessment that would emphasize occupational exposure but fall short on potential impacts to human health and the environment.

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<sup>1</sup> Environment Canada. Proposed prioritization approach for nanoscale forms of substances on the Domestic substances list. July 2016.  
<http://www.ec.gc.ca/lcpe-cepa/default.asp?lang=En&n=FA3C8DBF-1>

For example, one area of burgeoning business is nano food packaging utilizing NMs such as nanosilver and nanoclay, but the degree of migration of these materials into the packaged food product and possible subsequent human health effects from the migrated NMs, are still not defined.<sup>2</sup> Similarly, for NMs that are intentionally added to food and nutritional supplements, there are data gaps for the biological effects of these substances after ingestion. Novel adverse effects must also be considered. For example, nano titanium dioxide (TiO<sub>2</sub>) is a popular sun screen ingredient, but TiO<sub>2</sub> is also a photo-catalyst<sup>3</sup> so it may interact with other chemicals on the skin (including other sun screen ingredients) as well as chemicals in the water. TiO<sub>2</sub> is a possible human carcinogen.<sup>4</sup>

### ***Future context***

While this consultation deals specifically with NMs on the Domestic Substances List (DSL), there is still relevance to new NMs. The present methodology used to assess NMs (existing and new) is inadequate and will be deemed more so, as it attempts to keep pace with these substances and NM-containing products in coming years. While this proposed work is an important component in the assessment of NMs, a more comprehensive hazard based NM-specific policy is required.

### ***Comprehensive, Precautionary Approach to Nanomaterials Needed***

Significant data gaps are expected for the DSL NMs, including data on persistence, bioaccumulation and inherent toxicity. This information is critical as NMs have the potential to embed themselves in tissues – even the mitochondria and nuclei of living cells.

The proposed approach to prioritize, categorize and subsequently assess existing NMs is grounded in a risk-based approach, and is therefore reactive – waiting until harm ensues and has eventually been proven. The government should establish a framework that focuses on a preventive approach that places greater emphasis on avoiding inherently hazardous properties that could be associated with NMs, rather than an approach that relies heavily on estimating exposure risks.

By way of explanation, given the inherently hazardous properties of NMs, establishing a preventive approach that adequately analyzes imported NMs and manufactured products containing NMs before they are allowed to enter the marketplace, will represent substantial strides towards the protection of the environment and human

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<sup>2</sup> Nattinee Bumbudsanpharoke, Seonghyuk Ko. May 2015. Nano-food Packaging: An Overview of Market, Migration Research, and Safety Regulations. *Journal of Food Science*. 80(5): R910-R923.

<sup>3</sup> Government of Canada. NanoPortal. Materials. <http://nanoportal.gc.ca/default.asp?lang=En&n=19F677BA-1>

<sup>4</sup> IARC Monograph on the Evaluation of Carcinogenic Risks to Humans. Vol. 93. Carbon Black, Titanium Dioxide, and Talc. <https://monographs.iarc.fr/ENG/Monographs/vol93/mono93.pdf>

health. A risk based approach permits the introduction of NMs (with their inherent hazards), to the point where **excessive** human exposure and/or environmental release has been demonstrated. This will be evident only after considerable harm has ensued. We continue to urge the government to establish an approach for NMs through a regulatory framework that is rigorous and precautionary, and one that promotes prevention at the onset.

There should be a regulatory system that includes requests for nano-specific information including physical/chemical and toxicological that would differentiate the NM from the micronized or macroform of the substance, when applicable. Emphasis should be on the impact of environmentally relevant exposure levels as well as the behavior of the NM in the environment for which it is recommended. Also, the assessment trigger thresholds should be further reduced to adequately capture more NMs, and NMs that are present in manufactured articles.

### ***Prioritization of existing nanomaterials***

The prioritization of existing NMs should be a baseline for the work that will ultimately be done to assess the potential hazards related to NMs. The goal is to identify clearly NMs of higher concern and those that will require further consideration.

In the framework for the prioritization of existing NMs, emphasis should be placed on specific inherent hazardous properties. Persistence, bioaccumulation, migration in tissues and innate properties such as reactivity and geometry should be key elements for prioritization. Coated NMs require special consideration. Similarly, NMs that demonstrate specific toxicity impacts such as carcinogenicity, neurodevelopmental or neurotoxic effects or endocrine disruption, should also be factors for prioritization. In a strict hazard determination, consideration of the risk of exposure is not the focus.

As a result, the government should establish a legal obligation that outlines more nano-specific criteria for categorization beyond persistence, bioaccumulation and inherent toxicity. Specific timeframes within which to undertake this work and to receive data would also have to be defined. Strict penalties should ensue from data gaps.

Subsequent to prioritization, the government should consider a categorization exercise similar to that applied to the DSL in 2000. A categorization approach for NMs with an updated inventory will provide substantial advancement in understanding the toxicity and environmental fate of these materials.

Pursuant to modern precautionary approaches aiming for best practices and least-toxic solutions, the merits and hazards of nano-scale products should be justified in an

environmental assessment type process that includes consideration of the null alternative.

A formal multi-stakeholder technical work group to address the evaluation and management of NMs in Canada should be initiated by the government to establish transparent and accountable dialogue between government, industry, academia, and non-governmental organizations. In addition to being beneficial to the process, this working group would also be better positioned to promote alignment with the regulatory framework. The absence of such a working group adds to the complexity of accurately detecting and verifying the presence of NMs on the DSL, reducing transparency and accountability in the system. This recommended group should be a separate entity from the Technical Expert Group for NMs, established within the Regulatory Cooperation Council and the Nanotechnology Sub-committee of the Industry Coordinating Group for the *Canadian Environmental Protection Act*.

Noticeably absent from the consultation document is the mention of ethical considerations for the use of NMs in consumer products as there is generally inadequate labeling as to their presence. This requires an open dialogue with stakeholders; consumers should be more aware of the ingredients in products they use.

At present, two hundred and six (206) possible NMs been identified from the Domestic Substances List (DSL) - 64% of them were identified through technical data and 27% were assumed to be NMs.<sup>5</sup> Twenty one (21) NM groups are represented by these 206 substances. Manufactured materials incorporating NMs are not subject to being reported, representing a significant gap for end of life considerations if these products release particles with wear, or are recycled unknowingly into new products (e.g. plastics).

NMs are intended to be more potent than the bulk substance, in a variety of applications. On this basis, a cutoff for prioritization below 100 kg could be justified and should be considered.

***The following are our responses to the questions in the consultation document:***

***Question 1. The Program is seeking input from stakeholders on possible approaches for grouping nanomaterials for prioritization.***

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<sup>5</sup> Environment Canada. Proposed prioritization approach for nanoscale forms of substances on the Domestic substances list. July 2016.  
<http://www.ec.gc.ca/lcpe-cepa/default.asp?lang=En&n=FA3C8DBF-1>

The proposed list of possible NM groupings for prioritization is based on the parent substance.<sup>6</sup> While this listing gives an indication of the types of NMs and volume present in any parent grouping, prioritization cannot be based solely on chemical composition.

It is possible to have the same chemical composition but varying crystal formation and surface characteristics could result in different physical-chemical properties. As a result, the proposed NMs grouping would require further details (sub-categorization) so that there is more specificity related to the novel physical-chemical properties of the NMs and their potential for toxicity. This could result in a NM being in more than one category. Coated NMs would require separate consideration.

The following should be taken into consideration as more specificity is required for the proposed NMs groupings for prioritization:

**a) *Physical-chemical properties***

- Particle/material geometry (e.g. similar to asbestos) are critical in NMs as they may exert toxic effects with particles migrating through tissues and even accessing intracellular spaces. There are also toxicities inherent to the substance itself (e.g. toxic metals) that may escape/dissolve from particles once the material has migrated. The transformation of a NM in a specific environment should also be considered. Attempting to group similar substances for prioritization and subsequent assessment can have significant limitations at this stage since health and environmental data on NMs do not appear to be readily available.
- Attention should be given to NMs that in their macroform are known or suspected carcinogens, endocrine disruptors, neurodevelopmental toxicants, neurotoxins or sensitizers. Just as nanotechnology is investigated in drug delivery to achieve therapeutic effects with lower doses, nano-carcinogens may also have heightened potency. Persistence, bioaccumulation, biodistribution and inherent toxicity are also top considerations when prioritizing NMs.
- NMs that are fibers or have a tubular form may have the potential to exert effects similar to those of asbestos, with regards to chronic inflammation and disease, and cancers. These materials must be characterized as to occupational exposures, their incorporation into consumer and industrial products, and potential for nano particle releases both initially (e.g. with a personal care product), and over time with wear.
- It should be noted that 100 nm is not a clear cutoff. There could be 'nanoscale behaviour' for some materials with particle dimensions greater than 100 nm and

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<sup>6</sup> Environment Canada. Proposed prioritization approach for nanoscale forms of substances on the Domestic substances list. July 2016.  
<http://www.ec.gc.ca/lcpe-cepa/default.asp?lang=En&n=FA3C8DBF-1>

chemical structures that would not normally be cause for concern. How these would be detected is not established. Some reliance on data from other jurisdictions is expected in order to make comparisons with the present list of NMs that are on the DSL.

**b) Lifecycle**

- Lifecycle considerations are also important with respect to how a NM will be used in a product, released with wear, handled at end of life and be potentially recycled. Furthermore, identification and evaluation of all breakdown products or metabolites and their impacts on the environment and human health are necessary.

**c) Vulnerable populations**

- In light of potential uses for NMs, there should be inclusion of other vulnerable populations such as pregnant women, the elderly, those with allergies, sensitivities and chronic diseases, low-socio-economic populations, and First Nations and the Inuit. Children are especially vulnerable to NM-containing products that are targeted to a particular population or the hazardous residue from wear.

**d) Data gaps**

- The possible use of read-across and analogs to address data gaps for NMs in the prioritization process raises concerns. This data is inherently less certain, and in such cases, the interpretation protocol should be clearly precautionary, with uncertainty being clearly stated. Uncertainty must weigh towards not permitting or registering a substance for use, manufacturing, import, export or sale.
- Industry associations, industries using NMs, and possibly researchers in the NM field, could provide further information to the government that would help quantify further sources of use, exposure and release.

***Question 2. The program is seeking input from stakeholders on the proposed approach for ranking ecological and human exposure. The program is also seeking any additional information that would further quantify potential sources of release/exposure.***

The following are the responses for question 2:

**a) Vulnerable populations & population in general**

- For NM-containing consumer products, it is important to note any possible exposures for children; however, it is just as important to identify clearly the general population for human exposure.
- Apart from children, there are other vulnerable populations depending on the type of consumer product. These are outlined in a response to Question 1.

**b) Clarity required**

- Figure 2 - The proposed scheme to determine the priority ranking for human exposure lacks definition in many areas. For example, the difference between “direct use in consumer products” and “contained in manufactured items” should be better defined as “contained in manufactured items” could also entail use by the general public. Examples would better define the schematic and qualify the rankings for human exposure. Uses or applications may be helpful to identify a variety of potential routes of exposure (e.g. abrasion of surface coatings or parts containing embedded particles)

**c) Other considerations for ranking human exposure**

- In attempting to distinguish the differences in ranking for human exposure, it is also imperative to consider these elements more explicitly - how the NM or a hybrid of NMs is incorporated into a product and the impact of this information on human exposure in relation to the lifecycle of the product, exposure scenarios for products that would be subject to abrasion, and disposal of products containing a NM.
- Figure 2 also lacks mention of indoor air that may have NMs attached to dust particles. This is a route of inhalation for the general public, and is of particular importance for young children.
- Possible human exposure should include the possible impacts of nanotechnology-based health and food products. Although there are no regulations specific to nanotechnology-based health and food products, there is an overlap between *CEPA 1999* and the *Food and Drug Act*.

**d) Environmental releases - routes of exposure**

- There is incomplete accounting of industrial/commercial uses and subsequent environmental releases in Figure 2 of the consultation document. There can be releases during manufacturing of a NM, working with a NM or working with a NM containing material (e.g. fabricating). These human exposures should be mentioned despite the gap that occupational health is not mandated under *CEPA 1999*. NMs may also be released to the air from an industrial site, which could result in exposure to residents in the vicinity. As well, NMs will not necessarily be captured in water treatment, or may be carried in runoff, with direct offsite impacts and potential impacts on drinking water. It cannot be assumed that human and environmental exposure would be low simply because there is no release into waste water; these considerations should be included in Figure 2. Given the extensive evidence of groundwater impacts and uncertainties with the

processes, materials used in fracking fluids must be considered to pose high potential for human and ecological exposures.

**e) Ranking of human exposure**

- Taking into account these additional potential routes of exposure, the proposed ranking of direct human exposure (low, medium, high) to NMs may not be as simple as outlined in the consultation document. Many data gaps will have to be filled prior to accurate ranking of low, medium and high human exposures.

***Question 3. The program is seeking input from stakeholders on the proposed approach for ranking human health and ecological hazard.***

The DF4 nanogrouping approach identifies substances with hazards arising from dissolution of particles (potentially after migration into vulnerable tissues such as lung, pleura or tissues along the GI tract); surface activity (that is very common with nanomaterials); or being fibrous, as is asbestos. **Thus, all NM toxicities are potentially exhibited at very low doses.** The “Passive” grouping should be the last option, once all others are actually disproved with data.

Significant toxicological data gaps for human health and the environment are expected for NMs on the DSL. The test procedures can be at times questionable as there can be inconsistencies associated with these procedures. This raises concerns with respect to the filling of data gaps with credible toxicological data.

The following are the responses for question 3:

**a) Data gaps for human health and ecological risks**

Table 2 footnotes are ambiguous. We expect that “effective concentration” is meant to be the concentration at which effects are observed. It is not stated whether all effects will be considered, or restricted to “adverse” effects.

Determination of adversity of effects can introduce inappropriate decisions (e.g. one pesticide key study was interpreted such that low post-partum maternal body weights (half the controls) were not “adverse,” with the “adverse” designation being reserved for death). Thus all effects, including those at lower concentrations should also be published in assessment documents.

**b) Human health implications**

- There are many scientific studies focusing on the inhalation route because it is viewed as the most important route of exposure, but other systemic effects are not often investigated. Some animal studies have indicated that NMs under

investigation affected the lymph nodes, haematological system, the pleura and the liver.<sup>7</sup> Therefore, it is essential that there is emphasis also on systematic toxicity.

- In Table 1 of the consultation document, dictating the proposed guidance on the ranking human health hazard using toxicological studies, neurotoxicity, should be included as a criterion for the high hazard flag listing.
- Repeat-dose toxicity should consider very low concentrations or relevant environmental exposures because of the enhanced reactivity of NMs as compared to the macroform or the micronized form of the same substance. This is particularly relevant for the detection of endocrine disruption and other health impacts that occur at very low concentration levels or with non-monotonic dose responses.

**c) Ecological considerations**

- As previously mentioned, the lack of toxicological studies related to the environment will make it challenging to rank ecological hazards. The possible use of read-across and analogs to address these data gaps raises concerns with regards to decision-making in the face of uncertainty associated with the data. With read-across or other interpolation and extrapolation methods, validation of some endpoints is necessary in order to have confidence in the conclusions. Doubt should work in favour of NOT permitting the substance in commerce.

***Question 4. The program is seeking input from stakeholders on mechanisms that could be used to fill data gaps for nanomaterials that require additional information to prioritize.***

For existing NMs, significant data gaps are expected as these substances have been in commerce for many years without industry always acknowledging their use.

The following mechanisms are recommended:

**a) Mandatory survey**

- To obtain information to fill the additional data gaps, as is essential in the process of a meaningful and accurate prioritization process, another mandatory survey, not voluntary, should be initiated. The questions should be specific, to attempt to fill the current data gaps.

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<sup>7</sup> Katrin Schroeder, et al. July 2014. Carcinogenicity and Mutagenicity of Nanoparticles – Assessment of Current Knowledge as a Basis for Regulation. Fraunhofer Institute for Toxicology and Environmental Medicine, Hannover. (On behalf of the Federal Environment Agency, Germany)  
[http://www.umweltbundesamt.de/sites/default/files/medien/378/publikationen/texte\\_50\\_2014\\_carcinogenicity\\_and\\_mutagenicity\\_of\\_nanoparticles\\_1.pdf](http://www.umweltbundesamt.de/sites/default/files/medien/378/publikationen/texte_50_2014_carcinogenicity_and_mutagenicity_of_nanoparticles_1.pdf)

**b) Data-sharing – changes in policy**

- Claims were made at the consultation that industry has the information but would require more specific requests as to the type of information required by the government. That said, more effective ways to share existing data including more open access to industry data (non-CBI) and government data, could be incentives for improved information gathering.

**c) Researchers & international resources – further consultation**

- Further consultation with academic researchers in the field of NMs – industrial applications, food and drug applications and international contacts, can be all useful in filling additional data gaps.
- The inclusion of real-world exposure data should be sought in an attempt to fill data gaps.

**d) Canada-wide inventory of manufactured NMs**

- The development of a comprehensive, accessible, Canada-wide inventory of NMs that are in commerce in Canada, together with their applications, could eventually help the government obtain more relevant information on NMs.

**e) When is additional information required?**

- At the end of the flowchart in Figure 1, additional information for prioritization comes after the decision for prioritization. The need for additional information required for prioritization could be realized during the prioritization process provided that a guidance document is used for the process. To complete the prioritization process, there should be loop between the additional information stage and the prioritization decision stage.

Respectfully submitted by:

Sandra Madray  
Chemical Sensitivities Manitoba

Meg Sears, PhD  
Prevent Cancer Now