July 15, 2009

Hon. Leona Aglukkaq, P.C., M.P.
Minister of Health
70 Colombine Driveway, Tunney's Pasture
Ottawa, ON K1A 0K9

Hon. Jim Prentice, P.C., M.P.
Minister of the Environment
10 Wellington Street
Gatineau, QC K1A 0H3

Re: Notice of Objection and Request for Board of Review in relation to the Proposed Order to add Phenol, 4,4' -(1-methylethylidene) bis- (bisphenol A), CAS No. 80-05-7 to Schedule 1 to the Canadian Environmental Protection Act, 1999; Canada Gazette Vol. 143, No. 20, May 16, 2009.

Dear Ministers,

This letter responds to the May 16, 2009, Gazette Notice ("Notice") in which the Governor in Council, on the recommendation of the Minister of Health and the Minister of the Environment ("Ministers"), proposed an Order to add Phenol, 4,4' -(1-methylethylidene) bis- (bisphenol A) to Schedule 1 of the Canadian Environmental Protection Act, 1999 ("CEPA") (hereafter referred to as "Proposed Order").

As provided for by subsection 332(2) of CEPA, the Polycarbonate/BPA Global Group of the American Chemistry Council files this Notice of Objection and requests that a Board of Review be established pursuant to section 333 of CEPA "to inquire into the nature and extent of danger" posed by bisphenol A.

The basis for the Objection and request for a Board of Review follows.

I. The Proposed Order is Inconsistent with Cabinet Directives and Policies Governing Science-based Decision Making by the Ministers

In announcing the Chemicals Management Plan the Prime Minister said it would make Canada a world leader in assessing and regulating chemicals. To achieve this, the management of the CMP is understandably complex and government officials are expected to follow a number of guidelines, policies and legislation as well as directions from Cabinet and Treasury Board when developing regulations[1].

[1] Inter alia:
- Statutory Instruments Act;

A common theme throughout these guidelines, policies and legislation is the important role of science and the weight-of-evidence approach to decision-making. For example, the government of Canada web site says that in *"understanding the CEPA 1999 risk assessment process: Science is the key"*[2]. Canada has a well-earned international reputation due to its history of grounding its decisions in the best scientific processes and evidence.

The Cabinet Directive on Streamlining Regulations specifies that the Government shall make decisions on "the best available knowledge and science in Canada and worldwide."[3] The policy document A Framework for the Application of Precaution in Science-based Decision Making About Risk[4], states one of the guiding principles that the government shall follow is:

> *"Sound scientific information and its evaluation must be the basis for applying precaution; the scientific information base and responsibility for producing it may shift as knowledge evolves."*
>
> *"The emphasis should be on providing a sound and credible case that a risk of serious or irreversible harm exists."*

Environment Canada's own Science Plan[5] provides further guidance:

> *"Environment Canada must produce the highest-quality, leading-edge and unbiased environmental science relevant to support sound policies, effective regulations and informed decision making. …Above all, we must demonstrate transparency and openness in how we conduct our scientific activities, adhering to scientific principles and continuing to use proven quality assurance methods such as international standards, peer review and expert advice."*

However, contrary to the guidelines, policy and legislative directives, the Proposed Order and the screening assessments prepared by the Government of Canada

---

- Financial Administration Act;
- Cabinet Directive on Lawmaking;
- Cabinet Directive on the Environmental Assessment of Policy, Plan and Program Proposals;
- Cabinet Directive on Streamlining Regulation;
- Environment Canada Toxic Chemicals Management Policy;
- Environment Canada's Science Plan
- Assessing, Selecting and Implementing Instruments for Government Action;
- A framework for the Application of Precaution in Science-Based Decision Making about Risk; and,
- A framework for Science and Technology Advice: Principles and Guidelines for the Effective Use of Science and Technology Advice in Government Decision Making.

[2] http://www.chemicalsubstanceschimiques.gc.ca/assess-eval/what-quoi/index_e.html
[3] http://www.regulation.gc.ca/directive/directive01-eng.asp
[4] www.pco-bcp.gc.ca/index.asp?lang=eng&page=information&sub=publications&doc=precaution/precaution-eng.htm (emphasis added)
[5] http://www.ec.gc.ca/scitech/9FA49B9A-2A69-4BE9-AA4C-526C406AE3F7/EC_SciencePlanEn_2006.pdf (emphasis added)

are not based on the best available data and scientific knowledge regarding the potential human health risk properties of bisphenol A.

Risk assessments conducted by the European Union, the European Food Safety Authority (EFSA) and national regulators including those of Australia, Belgium, Denmark, France, Germany, Japan, New Zealand, Norway, Sweden, Switzerland, the United Kingdom and the United States as well as an independent review by NSF International have all determined that the potential exposures to humans do not constitute a danger to human health. Indeed, after reviewing the same data that Canada considered, EFSA determined the Tolerable Daily Intake (TDI) should be increased by a factor of five.

As previously detailed in submissions by the Polycarbonate/ BPA Global Group (attached as Appendix A and Appendix B), the Government of Canada has failed to adhere to the Cabinet Directives and Policies governing science-based decision making.

II. The Assessment Summary and Conclusion of the Proposed Order is Not Supported by the Weight-of-Evidence

A Canadian government Fact Sheet on Bisphenol A states, "*In general, most Canadians are exposed to very low levels of bisphenol A, therefore, it does not pose a health risk* [and with respect to infants under 18 months] s*cience tells us that exposure levels are below those that could cause health effects*."[6] That conclusion, which is consistent with the weight-of-evidence presented in the Screening Assessment, does not justify the further application of the precautionary principle since a "risk of serious or irreversible damage" has not been demonstrated.

Application of the weight-of-the-evidence approach and precautionary principle does not mean that <u>any</u> uncertainty requires action as a precaution. In Canada, the basis for application of the precautionary principle, to the extent that it is applied at all, should be when the weight-of-the-evidence suggests that a potential threat to the environment and human health exists and when that threat is of "serious or irreversible damage." Until both of these conditions are met, application of the precautionary principle to justify actions limiting trade is inappropriate under the plain language of CEPA.

[6] http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/bisphenol-a_fs-fr_e.html

Due to numerous study limitations[7], the data reviewed in the Final Screening Assessment and thus forming the basis of the Proposed Order does not provide a sound and credible case for "a risk of serious or irreversible harm" justifying a precautionary approach. Canada ignored its own acknowledgement in the Final Screening Assessment (page 69) that "Several organizations have recently evaluated the developmental neurotoxicity dataset (ECB 2008; Willhite et al. 2008; NTP 2007; EFSA 2006). Specifically, the EU in the draft Updated Risk Assessment of bisphenol A concluded that 'overall, taking together the low confidence in the reliability of the developmental neurotoxicity studies and the lack of consistency in the results of behavioural testing, no conclusions can be drawn from these studies' (ECB 2008)." Contrary to the assessments of other independent institutions that have evaluated the same scientific data, Canada has here essentially applied the precautionary principle without an articulated scientific basis.

Other national governments have recognized this. For example, in response to a question about bisphenol A and the proposed baby bottle ban in Canada, the French Minister of Health recently stated:

> *"Canadian authorities banned bisphenol A under public pressure and without any serious scientific study. The precautionary principle is a principle of reason, and under no circumstances a principle of emotion."* (Translation)

In Belgium, the Deputy Prime Minister and Minister of Social Affairs and Public Health responded to a similar question by stating:

> *"In the light of new data, including Canadian and American data reported by the media, the EFSA, at the request of the European Commission, did a re-evaluation of bisphenol A. In its last report, dated October 22, 2008, the EFSA took into account the last studies published at the end of 2008, as well as more than 650 other studies on bisphenol A. The conclusions clearly show that the safety criteria used for the European regulation are totally appropriate to ensure the safety of consumers, including the weakest."* (Translation)

Clearly, other national regulators, including countries which themselves have previously applied the precautionary principle, are questioning Canada's scientific risk management approach, and in turn, its credibility.

[7] Note that the suggestion of neurobehavioral effects from the neurodevelopmental and behavioral dataset, which Canada admitted was highly uncertain, formed a basis of Canada's exercise of the precautionary principle. The limitations of the neurobehavioral studies were detailed in our earlier comments as well as the fact that other more robust studies did not identify neurodevelopmental concerns and addressed the concerns raised by the limited studies. See Comments of the Polycarbonate/BPA Global Group on the Draft Screening Assessment and Risk Management Scope for Phenol, 4,4-(1-methylethylidene)bis- (Bisphenol A) (June 18, 2008) at pp. 57- 64. In addition, supplemental information was provided on a guideline neurobehavioral study by Ema *et al.* 2001, which found no effects; this additional information apparently was not considered in Canada's assessment of the scientific evidence, despite the fact that Canada's own draft assessment noted that it would be valuable data. Id. at p. 61-63.

III. Significant New Data Should Be Considered Before Acting on the Proposed Order

It is important to note that no human health effects have been identified for bisphenol A. The Final Screening Assessment devotes only one paragraph to epidemiology studies, primarily to highlight the "*many limitations*" of the few small-scale studies available. Indeed, the Characterization of Risk to Human Health does not mention or rely at all on epidemiology studies or human health effects.

Instead, the conclusions of the Final Screening Risk Assessment for human health are based on studies in laboratory animals, in particular studies that are acknowledged to have significant limitations and uncertainties. As stated in the Proposed Order:

> *"Concern for neurobehavioral effects in newborns and infants was identified. Given that available data indicate potential sensitivity to the pregnant woman/fetus and infant, and that animal studies suggest a trend towards heightened susceptibility during stages of development in rodents, it was considered appropriate to apply a precautionary approach when characterizing risk."* (emphasis added)

Significant new research published since completion of the Final Screening Assessment, or soon to become available, will substantially address the two specific areas identified as the basis for applying a precautionary approach. These items are briefly discussed below.

a. New Data Will Address the Potential for BPA to Cause Neurobehavioral Effects

To address uncertainty and concerns regarding the potential for bisphenol A to cause neurobehavioral effects, in particular at low doses, our organization is currently sponsoring a comprehensive developmental neurotoxicity (DNT) study in rats. The study was designed to conform to the requirements of the recently established, internationally accepted OECD 426 guideline and is being conducted according to Good Laboratory Practices (GLP).

Substantially beyond the guideline requirements, the study includes five treatment groups that span a wide range of dose levels from very low (10 µg/kg/day) to very high (150 mg/kg/day) along with a negative control. According to the guideline, the study examines a series of validated behavioural endpoints in offspring, including detailed clinical observations, motor activity, auditory startle, and learning and memory, as well as neuropathological evaluation (including brain morphometry) of each group.

Although it would be premature to draw conclusions until all data has been analyzed and a final report is available, no behavioural or neuropathological effects have been reported at low doses (10 µg/kg/day to 5 mg/kg/day) to date, with the study near completion. The final technical report, with all raw data, is expected to be available in

early October 2009 and will be provided to Health Canada for review as soon as it is available.

In addition, it should also be noted that the US Food and Drug Administration has initiated work on a neurodevelopmental study in rodents. As described by FDA in a December 3, 2008 letter to the FDA Science Board:

> *"FDA is currently developing a protocol for a neurodevelopmental study in rodents… The aims of this study are to evaluate the effects of BPA on standard developmental neurotoxicity endpoints and sexually dimorphic endpoints. In addition, this study will examine directly effects of BPA treatment on the sexually dimorphic nuclei and quantify levels of hormones."*

With the industry-sponsored study very near completion, and the FDA-sponsored study following, action on the Proposed Order should not be taken until this highly relevant data is available to resolve, with high-quality data, uncertainties about the potential for bisphenol A to cause neurobehavioral effects.

b. New Data Will Address the Potential for Heightened Susceptibility

It is well known that adults efficiently convert bisphenol A, after oral exposure, to non-estrogenic metabolites, which are then rapidly excreted with a short half-life in the body. As discussed in the Final Screening Assessment, limited data and information suggests that infants and children may not be able to metabolize and eliminate bisphenol A as efficiently as adults.

A recent study, published in the peer-reviewed scientific literature after completion of the Final Screening Assessment, examined exposure of premature human infants to bisphenol A.[8] Urine collected from the infants was analyzed for both parent bisphenol A (i.e., unmetabolized) and bisphenol A metabolites. As stated by the authors:

> *"Furthermore, that > 90% of the BPA excreted in the urine was in its conjugated (e.g., glucuronide, sulfate) form excludes the possibility that the BPA concentrations measured in these infants' urine resulted primarily from contamination and supports the validity of our analytical data. More important, our findings suggest that even premature infants have some capacity to conjugate BPA, in agreement with previous studies suggesting that critically ill premature infants could, to a certain extent, metabolize DEHP metabolites to their urinary glucuronides (Calafat et al. 2004). Furthermore, the fact that the association between the concentrations of free and total BPA was linear across the range of observed total BPA concentrations suggests that saturation of the enzyme(s) responsible for the conjugation of BPA did not occur even at total BPA concentrations orders of magnitude higher those reported among the general U.S. population."*

[8] Calafat, A. M., Weuve, J., Ye, X., Jia, L. T., Hu, H., Ringer, S., Huttner, K., and Hauser, R. 2009. Exposure to bisphenol A and other phenols in neonatal intensive care unit premature infants. Environmental Health Perspectives. 117(4):639-644.

For reasons cited by the authors (i.e., sampling materials were not pre-screened for the presence of bisphenol A), and other reasons not cited (e.g., source and route of exposure of bisphenol A was not determined, potential for hydrolysis of bisphenol A metabolites back to parent bisphenol A during analysis was not assessed), the presence of low levels of parent bisphenol A in urine from the premature infants must be interpreted with caution.

The results of this study unambiguously indicate that even premature infants have the capability and capacity to metabolize bisphenol A at the levels expected from dietary sources (e.g., polycarbonate baby bottles, infant formula), as well as at the elevated levels from other sources observed in this study. These results make it clear that one of the bases for application of the precautionary principle – heightened susceptibility of infants to bisphenol A – is not supported by the scientific data.

It is also notable that the US Food and Drug Administration has begun work on studies in rodents and rhesus monkeys that will also substantially help to resolve uncertainties about the capability of neonates to metabolize and eliminate bisphenol A. As stated in their December 3, 2008 letter:

> *"FDA has finalized a study protocol designed to analyze pharmacokinetic properties of BPA. This study will examine the absorption, distribution, metabolism and elimination of BPA in adult, neonatal and fetal rats administered low doses of BPA either directly or through maternal transfer via intravenous (IV), oral, or subcutaneous routes. Pharmacokinetic parameters will also be measured in adult and neonatal rhesus monkeys following BPA administration via IV or oral routes. Data gathered in these studies as well as appropriate data from the literature in multiple species, including humans, will be used in developing a physiologically-based pharmacokinetic model."*

In addition to experimental approaches in humans and laboratory animals, the potential for heightened susceptibility of infants to bisphenol A has also been recently examined with pharmacokinetic models. Of most importance is a just-published paper that applies kinetic principles to calculate steady state plasma concentrations of bisphenol A, and a physiologically based model to simulate the blood concentration time profile in several age groups, including newborns.[9] These analyses reveal that blood concentrations of parent bisphenol A, which is the biologically active form, are extremely low (i.e., in the low part per trillion range) even for the highest bisphenol A exposures expected through dietary sources. These levels are even lower than the lowest levels that have been reported to cause biological changes with *in vitro* cell cultures. As concluded by the authors based on their results: *"Hence, we do not share the concerns of some of our colleagues concerning negative health effects by BPA…"*.

c. Human Exposure

[9] Mielke, H. and Gundert-Remy, U. 2009. Bisphenol A levels in blood depend on age and exposure. Toxicology Letters. In Press.

Within the last week, Health Canada has published several new reports on potential sources of human exposure to bisphenol A, two of which specifically focus on foods for infants and very young children.[10],[11],[12] The data in these reports further support the conclusions of the Final Screening Assessment, in particular that *"the current dietary exposure to BPA through food packaging is not expected to pose a health risk to the general population, including infants and young children."* As further noted by Health Canada, *"the nutritional benefits of baby food products far outweigh any possible risk."*

The lack of urgency to proceed with the Proposed Order is further highlighted by information provided in another, more recent proposed order.[13] As stated in this order:

> *"As of 2009, polycarbonate baby bottles represent practically 0% of the Canadian baby bottle market. Major retailers halted their sales of polycarbonate baby bottles in mid-2008 in response to the Government of Canada's announcement of the intention to propose a prohibition of the importation, sale and advertising of polycarbonate baby bottles made with bisphenol A."*

With exposure of infants to bisphenol A from polycarbonate baby bottles essentially eliminated, exposure from baby food and powdered infant formula shown to be extremely low, and the ongoing voluntary initiative to reduce bisphenol A levels in canned liquid infant formula to the lowest level achievable, the basis for the Proposed Order has been substantially weakened.

These new data on potential human exposure to bisphenol A do not support the need for the Proposed Order and, as a minimum, indicate there is no urgency to proceed with the Proposed Order. The lack of urgency is particularly striking in light of the significant new data available now or in the very new future as outlined above in this section.

IV. Summary and Conclusion

Both the preamble to CEPA and the government's own policies recognize the "integral role of science" in the process of decision making. The *Framework for the Application of Precaution in Science-based Decision Making About Risk's* specifically mandates that a "credible scientific basis" must inform the Government's application of precaution to decision making.

This has not been the case in the assessment of bisphenol A. The marked divergence in findings between the Final Screening Assessment and those of other

[10] Survey of Bisphenol A in Canned Powdered Infant Formula Products. Health Canada. July 2009.
[11] Survey of Bisphenol A in Baby Food Products Prepackaged in Glass Jars with Metal Lids. Health Canada. July 2009.
[12] Survey of Bisphenol A in Bottled Water Products. Health Canada. July 2009.
[13] An Order Amending Schedult I to the Hazardous Products Act (bisphenol A). Canada Gazette Part 1, page 1925. June 27, 2009.

national regulators suggests that there is not a credible scientific basis for this proposed action. Furthermore we have outlined to officials a number of fundamental scientific questions in detailed comments; these same scientific questions remain unanswered and undermine the foundation of underlying the Proposed Order. A Board of Review is warranted to assure that the proposed action has a credible scientific basis.

Absent such a review and validation of the science, the observations of other national health ministers that Canada pandered to the hyperbole of emotional zealots will stand unchallenged.

For the foregoing reasons, the Polycarbonate/BPA Global Group objects to the Proposed Order and requests that a Board of Review be convened. Canada's well earned reputation is at risk should this decision not be reviewed by an independent expert panel.

Regards,

By: Steven Russell,
Managing Director, Plastics Division
American Chemistry Council

On behalf of: Steven G. Hentges, Ph.D.
Executive Director
Polycarbonate/BPA Global Group

Attachments: (3)