November 18, 2008

Executive Director
Existing Substances Division
Environment Canada
Gatineau, Quebec
Canada
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Subject: Notice of Objection and Request for a Board of Review Regarding the Proposed Addition of 1,4-Benzenediol (CAS No. 123-31-9) to the List of Toxic Substances in Schedule 1 of the Canadian Environmental Protection Act; Canada Gazette Vol. 142, No. 38 — September 20, 2008

Dear Sir/Madam:

This letter is in response to the September 20, 2008, Gazette Notice announcing the proposed addition of a number of substances to Schedule 1 of the Canadian Environmental Protection Act (CEPA) and is being sent on behalf of the Hydroquinone Group[1]. As provided for by section 332(2) of CEPA, we are filing a **notice of objection and request that a Board of Review** be constituted pursuant to section 333 of CEPA regarding the proposed addition of 1,4-benzenediol, also known as hydroquinone, to the list of toxic substances in Schedule 1 of CEPA.

As discussed more fully below, we believe a Board of Review is warranted as there are significant deficiencies in the screening level risk assessment (SLRA) which served as the basis for the Ministers' CEPA toxic determination and recommendation for addition of the substance to Schedule 1. Accordingly, the Governor in Council's (GiC) proposed order to add 1,4-benzenediol to Schedule 1 is based on an assessment that fails to appropriately characterize the true nature and extent of danger, if any, posed by the substance.

I. A conclusion that 1,4-benzenediol meets the CEPA section 64 toxic definition is at odds with the fully-elucidated Mode-of-Action provided to the Ministers of Health and Environment.

The SLRA indicates that there has been no *Mode-of-Action* (MoA) determined for 1,4-benzenediol, and that the preparation of one according to accepted guidelines would reduce the uncertainty in the final SLRA. In the summary of public comments and responses to public comments[2], the Ministers indicate that**, "**[a] mode of action for 1,4-benzenediol has not been fully elucidated." However, a peer-reviewed, fully elucidated MoA developed in accordance with a framework accepted by Health

[1] The Hydroquinone Group is comprised of major global manufacturers of hydroquinone.
[2] http://www.ec.gc.ca/substances/ese/eng/challenge/batch1/batch1_123-31-9_pc.cfm

Canada has been published, and it was submitted to the Ministers in response to the Challenge Program.[3]

We are dismayed that the government has elected to ignore the MoA evaluation that was submitted during the original Challenge because, while peer-reviewed, it had not yet been incorporated into the conclusions of any foreign governments, an exceptional requirement that is far beyond the international norm. If all jurisdictions followed this model for assessing clearly relevant information, no new scientific evidence would ever be accepted. By incorporating an extraterritorial requirement for data acceptance after announcement of the Challenge, which included no such requirement in it, the Ministers have created a data acceptance hurdle that is unique among the requirements for data acceptance by Canadian and other international regulatory authorities.

In short, we believe strongly that the MoA study warrants careful review and consideration by the Ministers, especially given that the results of the study are clearly at odds with a CEPA toxic designation for 1,4-benzenediol.[4] It is particularly discouraging that the government refuses to consider this MoA document when its own findings correctly note that over 99.9 percent of human exposure in Canada comes from the consumption of healthy fruits and vegetables – as recommended by the Canada Health Guide.

II. A conclusion that 1,4-benzenediol meets the CEPA section 64 toxic definition is based on an inaccurate portrayal of European and IARC findings.

The SLRA's "Characterization of Risk to Human Health" inaccurately portrays an assessment of 1,4-benzenediol by the European Union as indicating that the substance is a non-threshold or genotoxic carcinogen. The SLRA indicates that the critical effect for characterization of the risk to human health from exposure to 1,4-benzenediol is carcinogenicity and that its characterization is based principally on the assessment of the European Union.[5] During its review of 1,4-benzenediol, the European Union convened a group of specialized experts to consider the classification of 1,4-benzenediol for carcinogenicity on June 4-6, 1997.[6] The specialized experts did not make a conclusion that is consistent with the findings in the SLRA. Instead they placed 1,4-benzenediol in Category 3 for carcinogenicity which is not used for non-threshold carcinogens.

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[3] McGregor, D. (2007). Critical Reviews in Toxicology 37:887-914.

[4] Although the Ministers reference in the final SLRA that a MOA was provided, neither the SLRA the Risk Management Approach reflect that the MOA received serious consideration. Instead, the Ministers cite older literature as indicating that it is possible for 1,4-benzenediol to act through indirect mechanisms. None of the alternative modes-of-action mentioned in the final SLRA support the risk characterized in Section 3.1 as "*carcinogenicity , for which a mode of induction involving direct interaction with genetic material cannot be precluded.*"

[5] http://ecb.jrc.it/classlab/SummaryRecord/3297r1_sr_CMR0797.doc, See also pages 1 and 12 of the final SLRA.

[6] http://ecb.jrc.it/documents/Classification-Labelling/ADOPTED_SUMMARY_RECORDS/2897_sr_SE0697.pdf

Furthermore, IARC has not classified 1,4-benzenediol as a potential human carcinogen – in fact, IARC has classified 1,4-benzenediol as a Group 3 substance: *not classifiable as to its carcinogenicity*.[7]

Neither the EU nor the IARC group considers 1,4-benzenediol a non-threshold or genotoxic carcinogen. To re-interpret their works as concluding that 1,4-benzenediol is a non-threshold or genotoxic carcinogen while ignoring the primary peer-reviewed literature is not precautionary – it is an untenable stretch based on an apparent misunderstanding or misapplication of the database on 1,4-benzenediol and the opinions of the European Union and IARC expert groups.

III. The Proposed Order is inappropriately premised on a Hazard-Based analysis as compared to the Risk-Based approached prescribed by CEPA 99.

In their application of the precautionary principle approach, the Ministers appear to have stretched the principle beyond its original intention which is to act as a bridge in the absence of scientific certainty where there is sufficient evidence to allow a conclusion to be "reasonable" as outlined in the Government Paper "Application of Precaution in Science-based Decision Making About Risk."[8]

In this case, we believe the conclusions are unreasonable in the sense that as the final SLRA states they are clearly overestimates of the exposures that consumers are likely to experience. These over-estimates, coupled with the misinterpretation of EU hazard classification for carcinogenicity, have resulted in an assessment that is overly precautionary and fails to consider the complete weight-of-evidence. Actual exposures to consumers through the use of hair dyes and nail polish are negligible, both because the use levels of 1,4-benzenediol are low, and because the quantity of 1,4-benzenediol that can be absorbed is extremely low. However, because the SLRA inappropriately concludes that 1,4-benzenediol is a non-threshold carcinogen, the exposure estimates for hair dyes and nail polish are classed as significant. Consequently, the SLRA has been based not on realistic estimates of risk, but rather on exaggerated exposure estimates and an inappropriate assessment of hazard.

IV. Adding 1,4-benzenediol to Schedule 1 would be in violation of the Cabinet Directive on Streamlining Regulations.

The Cabinet Directive[9] requires that the use of precaution must be balanced (this is similar to the weight-of-evidence approach required by section 76.1 of CEPA). This point is clearly elucidated in the *Framework for the Application of Precaution in Science-based Decision Making About Risk*. In section 4.3, the Framework states that "(s)ound scientific information and its evaluation must be the basis for applying precaution" and further states "(s)cientific data relevant to the risk must be evaluated through a sound, credible, transparent and inclusive mechanism … (a)vailable

[7] International Agency for Research on Cancer (IARC). (1999). Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Volume 71 Part 2 In: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, World Health Organization, Lyon

[8] http://www.pco-bcp.gc.ca/docs/information/publications/precaution/precaution_e.pdf

[9] http://www.regulation.gc.ca/directive/directive01-eng.asp

scientific information must be evaluated with emphasis on securing high quality scientific evidence (not quantity)." The SLRA upon which the toxic declaration is based fails in this regard as it selectively interprets and ignores important studies from the large database of material available on 1,4-benzenediol, as was described in detail by McGregor [3] who concluded "the evidence reviewed is consistent with the MOA being irrelevant in human risk assessment."

V. A conclusion that 1,4-benzenediol meets the CEPA section 64 toxic definition is not supported by the weight-of-evidence and is unduly precautionary.

In recommending that 1,4-benzenediol be added to Schedule 1 of CEPA, we believe that the Ministers failed to appropriately and reasonably implement the weight-of-evidence approach demanded by CEPA section 76.1. In particular, the Ministers failed to consider all available scientific evidence pertaining to 1,4-benzenediol, including a published peer-reviewed MOA evaluation that was conducted according to Canadian and internationally-accepted criteria. Rather, the Ministers appear to have relied exclusively on a misinterpretation of an evaluation completed by the European Union.

As noted in the Government's "*A Framework for the Application of Precaution in Science-based Decision Making About Risk*," precautionary measures are to be proportional to the potential severity of the risk being addressed and to society's chosen level of protection. Regulating negligible potential exposures to 1,4-benzenediol from anthropogenic sources, while encouraging the consumption of healthy foods that contain 1,4-benzenediol in amounts that far exceed the anthropogenic sources, flies in the face of this stated regulatory policy objective. The authors of the SLRA concede that millions of Canadians expose themselves to naturally occurring 1,4-benzenediol at levels far exceeding any realistic exposure from anthropogenic sources found in consumer products. Notably, in its response to public comments received on the Risk Management Scope document for 1,4-benzenediol, the Government states "there is no evidence to indicate that hydroquinone in foods poses a health risk to Canadians or that Canadians should avoid foods containing hydroquinone."[10] Nevertheless, the Government is proposing to add 1,4-benzenediol to Schedule 1, presumably so that it can potentially restrict access to consumer products which provide negligible exposures to 1,4-benzenediol while, at the same time, promoting products that provide more than 99.9% of the exposures. Declaring a substance toxic to tackle uses which do not give rise to a risk, while encouraging greater consumption is non-sensical. In short, the conclusions of the final SLRA, which underpin the proposed order, are not reflective of a proportional, risk-based approach.

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[10] http://www.ec.gc.ca/substances/ese/eng/challenge/batch1/batch1_123-31-9_pc.cfm

For all of the foregoing reasons, the Hydroquinone Group objects to the proposal to add 1,4-benzenediol to Schedule 1 and requests that a Board of Review be established under CEPA Section 333 to consider this issue.

Please feel free to contact us if you have any questions regarding this matter or on 1,4-benzenediol, in general.

Sincerely,

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