BEFORE
ENVIRONMENT CANADA
and
HEALTH CANADA

Comments of the

Industrial Minerals Association - North America
National Industrial Sand Association
International Diatomite Producers Association
and
American Chemistry Council - Crystalline Silica Panel

on the

Substance Profiles
for
Quartz and Cristobalite

Being Considered for Addition to the
List of Toxic Substances
Under
Section 64 of the
Canadian Environmental Protection Act, 1999

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Introduction

In December 2009, Environment Canada and Health Canada released Substance Profiles for Quartz and Cristobalite (two polymorphs of crystalline silica) in connection with the consideration – by the Ministers of Environment and Health – of whether to recommend the addition of quartz and cristobalite to the List of Toxic Substances in Schedule 1 of the Canadian Environmental Protection Act, 1999 ("CEPA 1999"). The two Substance Profiles express the view that crystalline silica – in the form of quartz and cristobalite – should be classified as "toxic" within the meaning of Section 64 of CEPA 1999 – because each of these substances is believed to meet the criterion for "greatest potential for exposure to individuals in Canada," and because each is considered to present a "high hazard to human health" based on the classification for carcinogenicity made by the International Agency for Research on Cancer ("IARC") and the U.S. National Toxicology Program ("NTP").

The IARC and NTP carcinogen classifications of quartz and cristobalite apply to those substances only when they are *inhaled* as *respirable* particles in occupational settings. Thus, the IARC Monograph that is referenced in the Substance Profiles as the basis for the proposed "toxic" chemical listings of quartz and cristobalite limits the Group 1 carcinogen classification to "[c]rystalline silica inhaled in the form of quartz or cristobalite from occupational sources."[1/] Similarly, the listing of crystalline silica in the NTP's 11th Report on Carcinogens applies to "[r]espirable crystalline silica, primarily quartz dusts occurring in industrial settings."[2/] Like IARC and NTP, both Environment Canada and Health Canada appear to recognize that any

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1/ IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 68 (1997) at 211.

2/ NTP, 11th Report on Carcinogens (2004) at III-231.

potential carcinogenic risk associated with exposure to quartz or cristobalite is limited to respirable-size particles "less than or equal to 10 μm in [aerodynamic] diameter and available for inhalation."[3/] Reflecting that understanding, the Notice with respect to Batch 12 Challenge substances states that it does not apply to quartz or cristobalite "if the substance or product, mixture or manufactured item containing the substance, is composed of less than 5% respirable crystalline silica."[4/] In addition, Environment Canada and Health Canada have made clear that their concern about the potential carcinogenic risks of respirable quartz and cristobalite is focused on exposures that may occur as a result of residential uses.[5/]

These Comments provide information and views of the Industrial Minerals Association - North America, the National Industrial Sand Association, the International Diatomite Producers Association, and the American Chemistry Council's Crystalline Silica Panel on the question whether quartz and cristobalite meet the criteria applied by Environment Canada and Health Canada for listing a chemical as a "toxic substance" under CEPA 1999. In brief, we do not believe that the residential use of products or materials containing crystalline silica presents a carcinogenic risk that warrants adding quartz or cristobalite to the List of Toxic Substances in Schedule 1 of CEPA 1999. Our reasons are as follows:

1. Late in 1996, an IARC Working Group recommended that crystalline silica be classified as a Group 1 carcinogen, a classification that was published in Volume 68 of the IARC Monographs in 1997. A few years later, NTP followed suit – based almost entirely on the IARC

3/ *See* Notice with respect to Batch 12 Challenge substances, Schedule 2.

4/ *Id.*

5/ *Id.*

classification.[6/] The IARC classification, however, was (and remains) controversial – because of the conflicting findings in epidemiological studies; the absence of clear exposure-response relationships in many of the studies that otherwise were viewed as positive; difficulties in controlling for the effects of possible confounders; uncertainty as to whether silica exposure in the absence of silicosis, an occupational disease, is associated with increased lung cancer risk; and the failure to find increased lung cancer risks in animal species other than rats (where a particle overload phenomenon may very likely be the causal factor). Thus, despite the recommendation of a majority of the IARC Working Group, questions remained as to whether crystalline silica in any form can properly be viewed as a human carcinogen. The results of studies completed since the IARC evaluation was made in late 1996 have been mixed – but, taken as a whole, they fail to confirm the hypothesis that exposure to respirable silica causes or otherwise increases the risk of contracting lung cancer (particularly in the absence of silicosis).

2. The IARC Working Group itself was conflicted about the carcinogen classification for crystalline silica and limited the finding of *sufficient evidence* in humans to "*inhaled* crystalline silica in the form of quartz or cristobalite *from occupational sources*."[7/] NTP, too, indicated that its listing of *respirable* crystalline silica as a known human carcinogen applies "primarily [to] quartz dusts *occurring in industrial and occupational settings*."[8/] Moreover, IARC noted specifically that "carcinogenicity in humans was not detected in all industrial

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6/ NTP, 9th Report on Carcinogens (2000); *see also* NTP, 11th Report on Carcinogens (2004) at III-231.

7/ IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 68 (1997) at 210 (emphasis added).

8/ *See* NTP, 11th Report on Carcinogens (2004) at III-231 (emphasis added).

circumstances studied."[9/] There was no suggestion that environmental or consumer exposure to crystalline silica increases the risk of lung cancer, or that exposure to crystalline silica other than through the *inhalation* of *respirable* dust presents a cancer risk.

3. Silica-related carcinogenicity, if it exists at all, very likely is a threshold phenomenon. Thus, even if exposure to crystalline silica in respirable form is deemed to present a potential carcinogenic hazard, that hazard (and any associated excess risk) would not be expected to exist unless the carcinogenic exposure threshold is exceeded. And that threshold appears to be well in excess of the consumer exposures that might result from the use of quartz- or cristobalite-containing products or materials in residential settings.

4. Finally, even if crystalline silica presents a carcinogenic hazard to humans for which no threshold of exposure exists, it is widely acknowledged that crystalline silica is a very weak carcinogen. Consequently, lifetime annual average and cumulative lifetime exposures to respirable crystalline silica resulting from residential uses of quartz- or cristobalite-containing products or materials will be far below the levels at which anything other than the most negligible increase in lung cancer risk could be expected, assuming that exposure to crystalline silica presents a cancer hazard at all. These negligible potential risks would not justify a finding that residential uses of products or materials containing quartz or cristobalite present a "high hazard to human health," even if the evidence more firmly established that crystalline silica poses a lung cancer hazard to humans.

[9/] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 68 (1997) at 211.

I. The Hypothesis that Crystalline Silica Exposure Increases the Risk of Lung Cancer Was (and Remains) Controversial Even in the Occupational Context.

The IARC Working Group's identification of inhaled crystalline silica in the form of quartz or cristobalite from occupational sources as carcinogenic to humans was controversial when the assessment was made in late 1996 – with a spirited debate ending "in a narrow vote, reflecting the majority view of the experts present at that particular time."[10/] The reasons for the controversy include the conflicting findings in epidemiological studies (a phenomenon that has continued in studies published after the IARC Working Group made its recommendation)[11/]; the absence of clear exposure-response relationships in many of the studies that otherwise were viewed as positive; difficulties in controlling for the effects of possible confounders; uncertainty as to whether silica exposures or only silicosis itself is associated with increased lung cancer risk; and the failure to find increased lung cancer risks in animal species other than rats (where a particle overload phenomenon may very likely be the causal factor). These points were explored at length in a comprehensive review of the literature prepared by Dr. John F. Gamble in 1998,[12/] and in a journal article published in 2000, taking issue with the IARC Working Group Report.[13/]

[10/] McDonald, C. Editorial (2000) Ann. Occup. Hyg. 44:3-14. *See also* Soutar, C.A. *et al*. (2000) Epidemiological Evidence on the Carcinogenicity of Silica: Factors in Scientific Judgement. Ann. Occup. Hyg. 44:3-14.

[11/] *See* Brown, T.P. & L. Rushton (2005) Mortality in the UK industrial silica sand industry: 2. A retrospective cohort study. Occup. Environ. Med. 62: 446-452 (noting that of the nine studies identified as least confounded by IARC, four showed a clear excess cancer risk while five showed a negative or equivocal risk).

[12/] Gamble, J.F., Is Silica a Human Carcinogen? A Weight-of-the-Evidence Review (1998). A copy of Dr. Gamble's Report is submitted herewith as Attachment 1.

[13/] Hessel, P., *et al*. (2000) Silica, Silicosis, and Lung Cancer: A Response to a Recent Working Group Report. JOEM. 42:704-720.

In a report prepared in May 2005, Dr. Patrick A. Hessel reviewed epidemiological studies on silica and lung cancer completed after IARC Monograph 68 was published and concluded that the silica-lung cancer hypothesis remained questionable at that time.[14/] In Dr. Hessel's words:

> Viewed as a whole, and considering the many factors that impact lung cancer risk, the literature published since 2000 (like the literature published earlier) does not suggest that silica exposure is a risk factor for lung cancer or that individuals with radiographic silicosis are at increased risk of lung cancer. Although some of the studies before and after 2000 have found increased rates of lung cancer among working populations exposed to silica and among groups of workers compensated for silicosis, others have not, and exposure-response relationships have rarely been seen. Overall, the data suggest that where increased cancer risks have been seen, they can best be explained by other characteristics of the populations that have been studied (e.g., smoking, lifestyle factors).[15/]

Other investigators also have noted the continuing uncertainty regarding an association between silica exposure and increased risk of lung cancer. Thus, in a Report from an International Workshop on Silica and Lung Cancer, L. Rushton and T. Brown observed that the "epidemiological literature [on silica, silicosis, and lung cancer] is indeed inconsistent."[16/] Based on a meta-analysis of what they characterized as the 30 best studies on silica, silicosis, and lung cancer published between 1966 and 2001, Kurihara and Wada found that while silicosis appears to be a risk factor for lung cancer (particularly among smokers), the studies do not support the view that "'silica itself' increases lung cancer risk in humans."[17/] Similarly, after reviewing 28

[14/] A copy of Dr. Hessel's May 2005 Report is submitted herewith as Attachment 2.

[15/] *Id*. (Attachment 2) at 4-5.

[16/] L. Rushton and T. Brown, Epidemiological Perspectives on Silica and Health - Report from an International Workshop (2005), Electronic letter published in Occup. Environ. Med. 62:430-432.

[17/] Kurihara, N. & Wada, O. (2004) Silicosis and Smoking Strongly Increase Lung Cancer Risk in Silica-Exposed Workers. Industrial Health. 42: 303-314.

cohort, 15 case-control, and two proportionate mortality ratio studies evaluating the association between silica exposure (or silicosis) and lung cancer published between 1996 and 2005, C. Pelucchi *et al.* concluded that an association between silicosis and lung cancer existed but that the "issue as to whether silica *per se* materially increases lung cancer risk in the absence of silicosis" remains open.[18/]

In 2007, Yu *et al*., reported on a study of lung cancer mortality among silicotic workers in Hong Kong. They found no consistent exposure-response relationship between silica dust (measured as duration of exposure, cumulative dust exposure, and mean dust exposure) and lung cancer death, or between severity of silicosis (profusion of small opacities) and lung cancer death. Concluding that their study "did not offer positive support to a link between silica or silicosis and lung cancer," the authors opined that the "classification of silica dust as a human carcinogen might need to be reviewed."[19/]

In a 2007 update and further analysis of the mortality studies of Chinese tungsten miners, tin miners, iron-copper miners, and pottery workers, W. Chen, F. Bochmann and Y. Sun observed no relationship between silica exposure and lung cancer after adjusting for occupational

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[18/] Pelucchi, C. *et al*. (2006) Occupational silica exposure and lung cancer risk: a review of epidemiological studies 1996-2005. Annals of Oncology. 17(7): 1039-1050.

[19/] Yu, I.T.S. *et al*. (2007) Lung cancer mortality among silicotic workers in Hong Kong – no evidence for a link. Annals of Oncology. 18: 1056-1063. The authors explain why other studies (including Pelucchi *et al*.) have been more likely to find a relationship between silicosis and lung cancer than their study – namely, confounding by other occupational exposures, inadequate adjustment for smoking, selection bias, and low socioeconomic status of silicotic workers.

confounders (notably arsenic in tin mines and PAHs in potteries).[20/] In particular, increased lung cancer risk was not found in the tungsten miners, who had the highest silica exposures but no significant confounding exposures to arsenic or PAHs. The authors state that their analysis provides no evidence indicating that exposure to crystalline silica causes lung cancer in the absence of confounding factors, and it does not support the hypothesis that crystalline silica exposure is causally associated with increased risk of lung cancer.[21/]

A recent mortality study of 17,644 medical surveillance participants in the German porcelain industry by T. Birk *et al*. reaches a similar conclusion. The authors found that death from *lung and renal cancers* and from *non-malignant renal disease* was not associated with employment or silica-exposure surrogates in this large cohort (when the analysis used either the German population or the Bavarian population as referents).[22/] Among other things, the SMR for lung cancer was not elevated in the subgroup of men who had work experience in the "preparation area" where silica exposures were highest (averaging in excess of 0.15 mg/m^3). Putting their study in context, the authors noted that research reports and reviews published since the 1997 IARC classification have continued to generate divergent evidence and conclusions as to the human carcinogenicity of crystalline silica in the absence of silicosis and/or at low to moderate levels of exposure.

[20/] Chen, W., F. Bochmann & Y. Sun (2007) Effects of work related confounders on the association between silica exposure and lung cancer: a nested case-control study among Chinese miners and pottery workers. Int. Arch Occup Environ Health. 80:320-326.

[21/] *Id*. In addition, like Yu *et al*. (2007), the authors point to methodological limitations in studies of the relationship between silicosis and lung cancer and an additional possible bias resulting from a positive association between silicosis and smoking.

[22//] Birk, T. *et al*. (2009) Mortality in the German Porcelain Industry 1985-2005: First Results of an Epidemiological Cohort Study. JOEM. 51, No. 3: 373-385.

Recently, T. Erren *et al.* searched the PubMed data base from 1966 through January 2007 for reports of lung cancer in silica-exposed persons with and without silicosis. They then applied meta-analytical techniques to see whether they could determine if silica exposure in the absence of silicosis is associated with an increased risk of lung cancer. While they found a significant link between *silicosis* and lung cancer, their analysis of the studies left open the question whether exposure to silica increases the risk of lung cancer in the absence of silicosis.[23/]

Perhaps of most interest and relevance for present purposes (because many of the workers in the cohort were Canadian and because the cohort has been studied so extensively in the past) is the recently completed mortality study of Vermont granite workers by a group of two American and two Canadian researchers.[24/] While the Vermont granite worker cohort has been studied on a number of previous occasions, this is the most comprehensive mortality study of Vermont granite workers conducted to date. It includes more workers (7,052), has a longer follow-up (average of 38 years), and reflects more complete mortality ascertainment than previous studies. In addition, work histories and exposure estimates were based on multiple sources of information, some of which have not been used in previous studies. The authors performed a nested case-control analysis, using conditional logistic regression to model the relationship between mortality and each of three different exposure variables (cumulative exposure, exposure duration, and average exposure intensity). Cumulative exposure was

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[23/] Erren, *et al*. (2009) Is exposure to silica associated with lung cancer inn the absence of silicosis? A meta-analytical approach to an important public health question. Int. Arch. Occup. Environ. Health. 82(8): 997-1004 (Published online: Dec. 6, 2008 as doi:10.1007/s00420-008-0387-0).

[24/] Vacek, P., Verma, D., Graham, W. & Gibbs, G., A Study of the Relationship between Mortality and Silica Exposure in the Vermont Granite Industry: Final Report (November 16, 2009). A copy of the Final Report is submitted herewith as Attachment 3.

analyzed both as a continuous variable and as a categorical variable. *No significant associations* were observed between respirable silica exposure (measured both by excluding exposures occurring within 10 years of death and, alternatively, by including them) and mortality from *lung cancer*. This was true of all three of the exposure metrics (cumulative exposure, average exposure, and duration of exposure), whether expressed as a continuous variable or a categorical variable divided into quintiles of the distribution.[25/]

In sum, both at the time of the IARC Working Group's narrowly divided vote in late 1996 and in subsequent years, the hypothesis that crystalline silica exposure is causally associated with increased risk of lung cancer was – and has remained – controversial and unsettled. Epidemiological studies have been negative as often as they have been positive; exposure-response trends have generally been absent even in the studies that appeared to be positive; the effects of confounding factors such as smoking or other occupational exposures and/or the necessity of a mediating silicotic response cannot be ruled out where increased risks have been found; and animal studies for lung cancer have been positive only in the rat. Studies performed with mice, guinea pigs, and Syrian hamsters have all been negative, even though some tested animals, such as the A-strain mouse, are notably susceptible to the induction of lung tumors.[26/] The rat, as has been noted by many investigators, is not a good model for evaluating

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[25/] Although the SMR for lung cancer was elevated for the cohort as a whole, the prevalence of smoking among cohort members was higher than in the comparison populations, a factor that the authors noted could account for the elevated SMR observed in their study. In addition, because there were considerable gaps in Vermont granite work among a significant proportion of the cohort, many of the workers may have been exposed occupationally to other lung carcinogens (*e.g.*, asbestos) outside the granite industry.

[26/] *See* Holland, L, Animal Studies of Crystalline Silica: Results and Uncertainties. Appl. Occup. Environ. Hyg. 10(12): 1099-1103 (December 1995); Saffiotti, U, *et al.*, Carcinogenesis by Crystalline Silica: Animal, Cellular, and Molecular Studies. In: V. Castranova, *et al.*, Eds. Silica and Silica-Induced Lung Diseases. CRC Press 1996, pp. 345-381.

potential human lung carcinogenicity – because a particle overload effect is a likely causative factor for lung tumorigenesis in rats.[27/] In effect, the rat epithelium may be "primed" for a tumorigenic response to non-specific particulate exposure, making the rat an inappropriate model for extrapolating lung cancer risk to humans.

In light of the foregoing, we submit that – for purposes of making a "toxic" chemical determination under Section 64 of CEPA 1999 – quartz and cristobalite should not be deemed to present a "high hazard to human health" based on a presumption of human carcinogenicity even when the exposures occur in occupational settings.

II. The Association Between Crystalline Silica Exposure and Lung Cancer Outside the Occupational Context Is Even More Tenuous.

As noted above, both IARC and NTP focused their carcinogenic classifications of crystalline silica primarily on exposures that occur in *occupational settings* – and even there, they acknowledged that the study results were conflicting.[28/] When the exposures of concern are restricted to residential uses of crystalline silica-containing products and materials, as is the case here, a presumption of human carcinogenicity is even less justified.

There has been no finding of an increased lung cancer risk associated with crystalline silica exposures outside the occupational context. This is not surprising – because even if occupational exposures to crystalline silica are presumed to increase the risk of lung cancer (a

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[27/] Results of experimental animal studies indicate that the rat lung is particularly susceptible to tumorigenesis following exposure to nonfibrous durable particles, and the response appears to be non-specific – with a wide variety of nonfibrous particles (including carbon black, coal dust, oil shale dust, talc, titanium dioxide, and volcanic ash) causing intrapulmonary lung tumors in the rat. *See* Mauderly, J. Relevance of Particle-induced Rat Lung Tumors for Assessing Lung Carcinogenic Hazard and Human Lung Cancer Risk. Environ. Health Perspectives. 105 (Supp. 5):1337-1346 (September 1997) at 1338, Table 2.

[28/] *See supra*, pp. 3-4.

presumption that remains controversial), there is widespread agreement that crystalline silica is at most a weak carcinogen, and it very likely operates by a non-linear threshold mechanism under which an increase in relative risk at very low exposures is either absent or negligible.[29/] As a result, environmental exposures to crystalline silica and the short-term intermittent exposures that might occur through the residential use of certain silica-containing products or materials are too limited in nature to cause an increase in lung cancer risk.

III. If Exposures to Crystalline Silica Increase Lung Cancer Risk At All, the Mechanism of Carcinogenicity Very Likely Involves Both a Threshold and Non-Linearity in the Exposure-Response Function.

Silica-related carcinogenicity, if it exists at all, appears to be a threshold phenomenon – most likely mediated through a silicosis pathway. As noted above, crystalline silica has been found to cause lung cancer in only one animal species, the rat (which is the most sensitive species for increased lung cancer risk from inhaled particles), and exposure thresholds for increased lung cancer risk have been described in rats for multiple types of particles, for over a decade.[30/] Crystalline silica is typical in this regard. Mechanistic studies and *in vitro* as well as *in vivo* data exhibit strong concordance in demonstrating that even the earliest changes, such as lung inflammation, exhibit dose-response thresholds for low-toxicity, low-solubility particles.[31/]

Epidemiological studies also suggest the existence of a threshold for any increased risk of silica-related lung cancer. Thus, as noted above, the studies supporting an association between

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[29/] *See* Part III below.

[30/] *See, e.g.*, Oberdorster (1997), Figure 2, http://ehp.niehs.nih.gov/members/1997/Suppl-5/oberdorster-full.html.

[31/] Donaldson, K, Borm, PJ, Oberdorster, G, Pinkerton, KE, Stone, V, Tran, CL. Concordance between in vitro and in vivo dosimetry in the proinflammatory effects of low-toxicity, low-solubility particles: the key role of the proximal alveolar region. Inhal Toxicol. (2008) 20(1): 53-62.

silicosis and increased lung cancer risk (while not conclusive) are much more compelling than the mixed and inconclusive results of studies evaluating the association of *silica exposure* and lung cancer risk in the absence of silicosis. This suggests that the exposure threshold for silicosis may be a threshold for any increased risk of silica-related lung cancer as well. While the epidemiological studies are less clear and powerful than mechanistic studies in this regard, they are most consistent with the existence of a silicosis-mediated pathway in which the production of reactive oxygen species ("ROS") and the release of TNF-ά by alveolar macrophages participate in causing sustained lung injury – although other factors (such as exposure estimation or classification errors) also must be considered to fully explain the conflicting findings from different epidemiological investigations.[32/]

The pooled analysis of 10 studies by Steenland *et al*. (2001)[33/] also suggests the existence of a threshold for any increased risk of silica-related lung cancer. As the authors acknowledge, the best-fitting model considered in their analysis was a spline model (shown in Figure 1 of Steenland *et al*., 2001). This model indicates a flat or declining exposure-response relation at low levels of cumulative silica exposure.[34/] Unfortunately, both the Steenland *et al*. paper and other epidemiological studies have failed to adjust for the effects of uncertainties and errors in exposure estimates in the context of an exposure-response threshold (or threshold-like

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[32/] Cocco, P, Dosemeci, M, Rice, C. Lung cancer among silica-exposed workers: the quest for truth between chance and necessity. Med Lav. (2007) 98(1):3-17.

[33/] Steenland *et al*., Pooled exposure-response analyses and risk assessment for lung cancer in 10 cohorts of silica-exposed workers: an IARC multicentre study. Cancer Causes and Control (2001) 12: 773-784.

[34/] Although the authors mistakenly describe this model as showing "a reasonably monotonic increase in risk with increasing cumulative exposure," even a cursory inspection of Figure 1 in Steenland *et al*., 2001 shows that it exhibits a clear threshold (at a cumulative exposure level of about 4-5 mg/m^3-years) below which risk is not increased.

nonlinearity, such as the one shown in Figure 1 of Steenland *et al*., 2001). If the true exposure-response relation has a threshold but the estimated exposure-response relation is fit to data in which some above-threshold exposures are misclassified or misestimated as below-threshold values (with larger errors being less likely than smaller ones), then the net effect will be to smear out the true (threshold) relation, giving an estimated exposure-response relation that incorrectly appears to be monotonically increasing even below the true threshold. This effect has not been corrected for in previous studies (including the log cumulative exposure model of Steenland *et al*., 2001) that claim to find a positive increase in risk even at low exposure levels. We therefore believe that the epidemiological literature to date is consistent with a true threshold relation that has been obscured by the effects of unmodeled exposure misclassification and estimation error.

IV. If Crystalline Silica Presents a Cancer Hazard At All, It Is So Weakly Carcinogenic that Any Increased Lung Cancer Risk Associated with the Residential Use of Silica-Containing Products or Materials Would Be Negligible.

It is widely acknowledged that if crystalline silica does in fact present a carcinogenic hazard, it is a weak carcinogen. Given the extremely low yearly average (or lifetime cumulative) exposure to crystalline silica that might be associated with residential use of silica-containing products or materials, any increased lung cancer risk associated with such activities, as shown below, would be minuscule.

Crystalline silica, a compound consisting of the first and second most abundant elements in the Earth's crust (oxygen and silicon), is the second most abundant mineral in the Earth's crust, making up about 12% by weight of the crustal mass of the Earth. It has been described as one of the building blocks of our planet and is considered to be to the mineral world what carbon is to the organic world. Consequently, it is to be expected that we all come in contact with crystalline silica on a daily basis.

Crystalline silica either uncombined ("free silica") or as an accessory mineral in a silicate[35/] finds wide usage in industrial and construction applications. In many uses the crystalline silica is consumed in the process (*e.g.*, flux agent in steel making), altered to an amorphous phase (glassmaking), left behind after the manufacturing step (sand being ground from a foundry casting), or encapsulated in a finished product and not respirable (ceramic whiteware). Consumer uses of encapsulated silica-containing products do not result in any inhalational exposure unless the product is used in such a way (*e.g.*, crushed, ground, or cut) as to release the silica from its matrix. Many consumer products can contain some small percentage of crystalline silica (though not in respirable form), most often resulting as an accessory component of an industrial mineral.

Most household exposures to crystalline silica are to the polymorph quartz with limited potential cristobalite exposures from calcined diatomaceous earth used as a swimming pool filtering aid or as a filler in paints. In addition to sand containing quartz and calcined diatomaceous earth, other silica-containing industrial minerals that might be found in consumer products include bentonite, kaolin, talc, ball clay, shale, and mica. Consumer products that might include industrial minerals containing crystalline silica include home maintenance products, automotive products, landscape and yard materials, pet care products, pesticides, and arts and crafts materials. The largest use of silica in home maintenance products is in paints,

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35/ When elements such as sodium, potassium, calcium, magnesium, iron, and aluminum are substituted into the crystalline silica matrix (silicon-oxygen tetrahedron), the compound is called a silicate. Some examples of silicates are kaolin, talc, vermiculite, micas, bentonite, and feldspar. *See* Industrial Minerals & Rocks, Seventh Edition (2006) at 13. This reference may be consulted for information as to the many and varied uses of silicate minerals. A copy of Industrial Minerals & Rocks, Seventh Edition (2006) is submitted herewith (in electronic CD format) as Attachment 4.

primers and stains. Other silica-containing home maintenance products include grout, adhesives, cements, mortar mix, joint compound, caulk, spackle, putty, glazes, stucco, concrete patch, sealers and sand mix. Automotive silica-containing products include waxes, polishes, cleaners and cooling system cleaners. Landscape and yard products include limestone, concrete mixes, shotcrete, fibercrete, plant foods and masonry grouts. Pet care products include pet litter, and flea and tick dusts. Pesticides that might contain crystalline silica include fertilizer, turf herbicides and fire ant killer. Clays, sand mixes and glazes may contain crystalline silica in arts and crafts supplies. As one can imagine, in the vast majority of these products, the crystalline silica is not present in the form of respirable dust.

A search of the National Library of Medicine ("NLM") PubMed database of the published medical literature did not identify any studies that measured crystalline silica exposures from uses of silica-containing household consumer products. The most likely reason for this is that the literature does not report any cases or other documentation of silica-related diseases being associated with exposure to silica from consumer products used in residential settings.[36/] A search of the NLM TOXNET database also failed to turn up any useful data regarding household consumer reports of silica exposure. In the absence of such data, estimates of consumer exposures associated with the use of silica-containing products and materials in residential settings can be arrived at in other ways.

There have been two requests for a Safe Use Determination ("SUD") for silica-containing products under the California Safe Drinking Water and Toxic Enforcement Act of 1986

[36/] There are a few case reports of silica-related diseases resulting from the intentional inhalation of scouring products, but that is hardly a recommended or reasonably expected use. Moreover, most scouring cleansers today do not contain crystalline silica.

(commonly known as "Proposition 65").[37/] The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment ("OEHHA") is the lead agency for making Safe Use Determinations under Proposition 65. A SUD will be made only if use of the product in question can be shown to present an increased cancer risk of no more than 1/100,000 assuming the calculated exposure occurs over the course of a lifetime. The two SUD requests that have been made and granted for crystalline silica are for the use of pet litter and the use of flat latex paint – two activities that are likely to involve some of the highest annual average (and cumulative) exposures to crystalline silica of any activities in a residential setting.

In 1998, the Sorptive Minerals Institute ("SMI") requested a SUD for pet litter and provided testing data on 12 conventional pet litters and nine scoopable pet litters originating from clay deposits from different parts of the country (termed East and West Coast litters by SMI). The data consisted of laboratory measurements of respirable dust concentrations (<10 μm aerodynamic diameter) generated from activities related to the use of pet litter including initial pouring, clump removal (in the case of scoopable pet litter) and replenishment. Respirable dust collected from the different activities was further evaluated by SMI for quartz content. Quartz was assumed to be the only form of crystalline silica in pet litter. Data provided by the SMI also included parameters on normal use in terms of time and amount used by the average consumer.

The OEHHA found the data submitted by SMI to be adequate and appropriate for performing an SUD evaluation. The primary sources of exposure to dust containing crystalline silica from the use of conventional pet litter are from the filling of the litter pan and subsequent disposal following use. Using the data generated during tests in which 10 pounds of litter was poured into a pan and the respirable dust generated was measured over time (up to three

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[37/] *See* http://www.oehha.ca.gov/prop65.html.

minutes), the quartz content of the respirable dust, and the annual use and frequency of activities related to the use of conventional pet litters, average yearly exposure levels were estimated for each of the conventional litter products for which testing data were submitted. OEHHA calculated that the lifetime average exposure concentration to respirable crystalline silica from the use of conventional pet litter ranges from 0.0007 to 0.01 micrograms per cubic meter ($\mu g/m^3$) of air.

For scoopable pet litter, the primary sources of exposure to silica-containing dust are the activities involved in filling the litter pan, removing clumps, replenishing the litter following clump removal, and subsequent disposal following use. Data provided by SMI for scoopable pet litters included measurements over time (up to ~2½ minutes) of respirable dust generated from 10-pound pour tests, clump removal tests and tests of clump removal with replenishment of litter. Parameters on the annual use and frequency of activities related to the use of scoopable pet litters also were provided. Using this information, average yearly exposure levels were estimated for each of the nine products for which testing data were submitted. OEHHA calculated that the lifetime average exposure to respirable crystalline silica from the use of scoopable litter ranges from 0.0018 to 0.06 $\mu g/m^3$.

Using the calculated lifetime average exposure values for the use of both conventional and scoopable pet litter, OEHHA conducted a risk assessment and determined that an excess cancer risk of less than one in 100,000 would result, even using the most conservative cancer slope factor – a slope factor which, as discussed at pages 22-25 below, lacks credibility. Based on that Safe Use Determination, Proposition 65 warnings were not required for the use of these products. A copy of OEHHA's Safe Use Determination for pet litter along with the Supporting Materials is submitted herewith as Attachment 5.

The second SUD request was from the National Paint and Coatings Association ("NPCA") for flat latex paints that are used by homeowners, professional painters, and other consumers. The NPCA request thus differs from the SMI request in that both professional and homeowner painting applications were included. In support of its SUD request, the NPCA submitted technical data and other information, which included the results of testing designed to assess the level of exposure to respirable crystalline silica during normal use of interior flat latex paint. This testing involved sanding activity in preparation for painting as well as painting activity using airless spray guns, considered to be the method most likely to produce respirable aerosols. Three other common methods of paint application – brushing, rolling, and sponging – are far less likely to produce respirable aerosols, and were not included in testing by the NPCA. The NPCA provided estimates of workload factors (*i.e.*, estimates of duration and frequency of painting and sanding activities) for professional painters engaged in painting activity. For those professionals, the average time spent spraying interior paints was five hours per task, 81 days per year – for an annual average of 405 hours.

Homeowners doing their own painting are far less likely to use spray guns; instead, they generally use either brushes or rollers to apply paint, methods unlikely to generate significant amounts of respirable paint aerosol. Consequently, estimates of respirable silica exposure to homeowners from paint spraying (as well as rolling and brushing) were considered negligible by the NPCA, a judgment with which OEHHA concurred. NPCA did, however, provide data for homeowners *sanding* latex paints with silica ingredient concentrations of 0.1%, 0.5% and 6.0%. NPCA estimated that for homeowners, the average time spent sanding interior paints was 2.4 hours per task, 4.2 days per year, for an annual average of 10 hours in the year in which the painting job was performed. Homeowner sanding levels were below the detection limit for

crystalline silica for 3 samples of the 0.1% and 0.5% paint formulations, and were 0.06, 0.08 and 0.05 mg/m^3 for the 6% paint formulation. Using the NPCA homeowner sanding data, OEHHA calculated that the annual average respirable crystalline silica exposures for the 0.1%, 0.5% and 6% paint formulations would be 0.000008, 0.000046 and 0.0046 mg/m^3, respectively. Those levels are orders of magnitude below the concentrations that OEHHA conservatively assumed might be associated with an increased lung cancer risk of 1/100,000 over the course of a lifetime. Indeed, even the respirable silica exposures of professional painters using spray guns in their work were found to be at or below the level conservatively estimated to present an increased lung cancer risk of 1/100,000. Consequently, a Safe Use Determination was issued for these latex paint products even when used by professional painters. Obviously, the exposures of homeowners sanding and applying silica-containing flat latex paints do not even approach the levels that could give rise to concern about potential lung cancer risk. A copy of OEHHA's Safe Use Determination for flat latex paint along with the Supporting Materials is submitted herewith as Attachment 6.

While direct measurements of household exposures to crystalline silica have not been made, or at least published, it is reasonable to believe that the highest exposures to respirable crystalline silica from residential uses of silica-containing products and materials involve household maintenance and remodeling activities in which silica-containing materials are cut, ground, or otherwise manipulated in ways that may release respirable silica dust into the air. Then resulting exposures – though severely time-limited – might be expected to be comparable to occupational exposures in construction trades where similar activities are performed. Accordingly, exposure data for such construction activities can serve as the basis for estimating

exposures to crystalline silica by homeowners performing "do-it-yourself" remodeling and repair work in residential settings.

There is a substantial database of crystalline silica exposures in occupational settings. A 2005 paper by Yassin *et al*. used silica exposure data from OSHA inspections for the period 1998-2003 to assess crystalline silica exposures of workers in a variety of jobs, some of which were in the construction industry.[38/] Three of the construction jobs examined by Yassin *et al*. are good surrogates for exposures of homeowners performing home improvement projects related to plastering and drywall finishing, tile setting, and masonry and stonework. For these three construction jobs, the OSHA inspection data for 1998-2003 showed that plastering and drywall work had an arithmetic mean exposure concentration of 0.045 mg/m^3 (SD ± 0.046) and a geometric mean concentration of 0.031 mg/m^3 (SD ± 0.920); tile setting had an arithmetic mean exposure concentration of 0.036 mg/m^3 (SD ± 0.027) and a geometric mean of 0.025 mg/m^3 (SD ± 0.958); and stonework masonry had an arithmetic mean exposure concentration of 0.088 mg/m^3 (SD ± 0.093) and a geometric mean of 0.065 mg/m^3 (SD ± 1.140). If we take the higher arithmetic mean values to represent average exposure concentrations of "do-it-yourself" homeowners performing these tasks and focus on the job having the highest exposure values of the three (stonework masonry), we can calculate the lifetime annual average residential use exposure as follows:

- Assume very conservatively that the homeowner spends 5 hours per day, 5 days per week, for 6 weeks performing these tasks during a remodeling project – and that he performs three such large-scale remodeling projects during his lifetime. That would amount to 450 hours of such exposure during a lifetime.

[38/] Yassin, A. *et al*. Occupational Exposure to Crystalline Silica Dust in the United States, 1988-2003. Environ. Health Perspectives (2005) 113(3): 255-260.

- The homeowner's total cumulative lifetime exposure to respirable crystalline silica would be 450 hours x 0.088 mg/m^3 = 39.6 mg/m^3-hours or **0.00452 mg/m^3-years** (39.6 mg/m^3-hours ÷ 8,760 hours/year = 0.00452 mg/m^3-years).[39/]

- Assuming an average lifetime of 75 years, the **lifetime annual average exposure** would be **0.00006 mg/m^3** (0.00452 mg/m^3-years ÷ 75 years = 0.00006 mg/m^3).

This lifetime annual average exposure value of 0.00006 mg/m^3 is orders of magnitude lower than the lifetime annual average exposure concentrations for which OEHHA made Safe Use Determinations for pet litter and flat latex paint. Based on OEHHA's most conservative estimated inhalation cancer potency slope for crystalline silica (1.85 x 10^{-5} for continuous 24-hour lifetime exposure to 1 μg/m^3 respirable silica), the increased lung cancer risk associated with a lifetime annual average exposure of 0.00006 mg/m^3 respirable crystalline silica would be 1 in 1 million.[40/] Using the alternative inhalation cancer slope factor employed by OEHHA (6.8 x 10^{-7} for continuous 24-hour lifetime exposure to 1 μg/m^3 respirable silica), the increased lung cancer risk associated with a lifetime annual average exposure of 0.00006 mg/m^3 respirable crystalline silica would be 4 in 100 million.[41/] Greater weight should be placed on this latter risk value than on the 1 in 1 million value – because the study from which the higher cancer potency slope of 1.85 x 10^{-5} was derived is subject to manifold uncertainties.

[39/] The expression "0.00452 mg/m^3-years" of cumulative exposure can also be expressed more precisely as "0.00452 (mg/m^3) (years)." However, since the accepted convention is to express cumulative exposure as "mg/m^3-years," we have adopted that format here.

[40/] The increased risk value of 1 in 1 million is derived by solving for x in the following equation:

$$\frac{1.85 \times 10^{-5}}{1\ \mu g/m^3} = \frac{x}{0.06\ \mu g/m^3}$$

[41/] The increased risk value of 4 in 100 million is derived by solving for x in the following equation:

$$\frac{6.8 \times 10^{-7}}{1\ \mu g/m^3} = \frac{x}{0.06\ \mu g/m^3}$$

That study is Hnizdo, E. & Sluis-Cremer, G., Silica exposures, silicosis, and lung cancer: a mortality study of South African gold miners. Br. J. Ind. Med. (1991) 48:53-60. The exposure-response coefficient for lung cancer estimated on the basis of this study is far higher than the exposure-response coefficients derived from all other studies that have been considered for use in silica-related lung cancer risk assessments. *See* Steenland *et al*. (2001), Table 3. That alone raises questions about its reliability as a predictor of silica-related lung cancer risk. And there are multiple reasons to question its reliability. For one thing, the exposure assessment used in the study relies on estimates of respirable surface area and conversions to gravimetric values, and it assumes that silica exposures in South African gold mines remained largely unchanged from the 1930s through the 1980s, thus making its exposure assessment questionable. In addition, only particles in the size range of 0.5 – 5.0 μm were counted, thus ignoring a portion of exposures in the respirable size range. Furthermore, as IARC observed, the presence of radon in the mines was a potential confounding factor, a consideration which led IARC to exclude this study from its evaluation of whether exposure to quartz presents a lung cancer hazard for humans.[42/] Moreover, the apparently positive association between silica exposure and lung cancer risk found in this study conflicts with the failure to find an association between silica

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[42/] *See* IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 68 (1997) at 92-93, 206-207.

exposure and increased lung cancer risk in other studies of South African gold miners.[43/] The gold miner studies that IARC considered to provide the least confounded examination of the association between silica exposure and lung cancer risk were those of U.S. gold miners in South Dakota.[44/] And those studies did not find an association between silica exposure and increased risk of lung cancer.[45/]

[43/] *See* Reid, P. & Sluis-Cremer, G., Mortality of white South African gold miners. Occupational & Environmental Medicine (1996) 53: 11-16 (Authors find no significant risk of lung cancer associated with exposure to dust.); Hnizdo, E. *et al*., Lung Cancer in Relation to Exposure to Silica Dust, Silicosis and Uranium Production in South African Gold Miners. Thorax (1997) 52:271-275 (In this nested case-control study of South African gold miners, the authors found that when silicosis was included in the model, neither cumulative dust exposure nor duration of underground mining contributed significantly to predicting the risk of lung cancer, and there was no trend for increasing lung cancer with increasing cumulative dust exposure.); Hessel, P. *et al*., Case-Control Study of Silicosis, Silica Exposure, and Lung Cancer in White South African Gold Miners. American J Industrial Medicine (1986) 10: 57-62 (In this case-control study based on lung cancer cases identified in records of the South African Gold Miners Provident Fund, no association was found between lung cancer and various measures of silica dust exposure); Hessel, P. *et al*., Silica exposure, silicosis, and lung cancer: a necropsy study. British J Industrial Medicine (1990) 47: 4-9 (Case-control study of S. African occupational necropsy records found no case-control differences in lung cancer risk noted for any indicator of silica dust exposure.).

[44/] *See* IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 68 (1997) at 207.

[45/] *See* McDonald, J. *et al*., Mortality after Long Exposure to Cummingtonite-Grunerite. Am. Rev. of Resp. Disease (1978) 118: 271-277 (no excess of respiratory cancer in South Dakota gold miner cohort); Brown, D. *et al*., Retrospective cohort mortality study of underground gold mine workers. in D. Goldsmith, *et al*. Eds., Silica, Silicosis & Cancer, Controversy in Occupational Medicine (1986) 335-350 (overall risk for lung cancer not elevated and no trend for lung cancer with latency, length of underground employment, or cumulative dust exposure days — even though total dust exposure was significantly associated with increased mortality from nonmalignant respiratory disease and respiratory TB); Steenland, K. & Brown, D., Mortality Study of Gold Miners Exposed to Silica and Nonasbestiform Amphibole Minerals: An Update With 14 More Years of Follow-Up. American Journal of Industrial Medicine (1995) 27: 217-229 (lung cancer only marginally elevated – without statistical significance – and no exposure-response trend found with increasing cumulative exposure to silica, even though there was a clear dose-response trend for silicosis and TB; indeed, in a case-control analysis, there was a *negative*, though nonsignificant, trend with increasing exposure).

In short, the cancer potency slope factor derived from the South African gold miner study by Hnizdo & Sluis-Cremer (1991) lacks credibility and should not be used to estimate potential increased lung cancer risks associated with exposure to crystalline silica. But – whether one uses the cancer potency slope derived from Hnizdo & Sluis-Cremer (1991) or the alternative cancer potency slope of 6.8×10^{-7} that OEHHA used in calculating a range of risks in its Safe Use Determinations – the resulting risks associated with uses of silica-containing products or materials for residential maintenance or remodeling projects are vanishingly small (ranging from 1 in 1 million to 4 in 100 million) and certainly would not justify a finding that crystalline silica presents a "high hazard to human health."

This is particularly true, since the foregoing risks are derived on the basis of very conservative exposure assumptions as well as a very conservative exposure-response model that presumes a no-threshold mechanism of action and low-dose linearity. In fact, based on the best-fitting (spline) model derived in the Pooled Analysis of Steenland, *et al*. (2001), the excess lung cancer risk associated with a lifetime annual average exposure of 0.00006 mg/m^3 respirable crystalline silica is *zero*.[46/] The only way to avoid that conclusion is to force-fit a no-threshold linear dose-response relation to the data in order to derive a hypothetical slope factor. That exercise, however, ignores the best-fitting model and obscures the fact that the best estimate of excess risk is zero for low-level exposures of the sort that may be associated with residential use of silica-containing products.

[46/] *See supra*, pp. 12-14. According to the spline model shown in Figure 1 of Steenland *et al*. (2001), there is no evidence of excess risk (in fact, the dose-response relation appears to be slightly negative) at low exposures of the magnitude at issue here.

Conclusion

For the reasons discussed above, Environment Canada and Health Canada should not add quartz and cristobalite to the List of Toxic Substances in Schedule 1 of CEPA 1999. Exposures to respirable crystalline silica associated with the residential use of quartz- or cristobalite-containing products and materials are unlikely to present any increased risk of lung cancer at all. And, if they do present any such risk, the risk would be vanishingly small – most likely in the neighborhood of 1 in 100 million over the course of a lifetime. In these circumstances, it cannot credibly be maintained that quartz or cristobalite presents a "high hazard to human health" within the meaning of CEPA 1999.