<u>Comments of Mel J. Mirliss, Executive Director, International Diatomite Producers Association (IDPA)</u>

I am writing this letter on behalf of the International Diatomite Producers Association ("IDPA"), a trade association of producers of diatomaceous earth products that was formed in 1987. IDPA includes in its membership companies both doing business and operating facilities in the state of California. IDPA sponsored one of the principal epidemiology studies relating to crystalline silica exposure and the potential risk of lung disease, and has been a leader in developing safe work practices for the use and handling of diatomaceous earth, which contains crystalline silica.

OEHHA recently released its draft *Chronic Toxicity Summary* for respirable crystalline silica. There has been an ongoing debate regarding this issue for more than a decade. As OEHHA recognizes, crystalline silica is widely present in California. Indeed, its most prevalent polymorph, alpha-quartz, constitutes 12% of the earth's crust.

<u>Comment 1.</u> Prolonged and excessive exposure to respirable crystalline silica dust is a known cause of silicosis. Exposure to crystalline silica dust has also been associated with an increased risk of lung cancer. The scientific community is widely split on the latter issue, but most scientists believe that, if there is a relationship, it is a weak one, and more likely than not carcinogenicity is a threshold phenomenon with silicosis (fibrosis) as a precursor. The disease outcome of exposure to crystalline silica has historically been a workplace issue regulated by California and federal OSHA; we see no substantive information to suggest that it is an environmental issue. The *Chronic Toxicity Summary* for respirable crystalline silica and the associated REL (Reference Exposure Level) have very substantial implications both within and outside of California. The scientific literature on health effects of crystalline silica is very extensive, and interpretation of the studies (including those on which OEHHA principally relies in deriving the REL) is far more complicated and controversial than the draft *Toxicity Summary* suggests.

<u>Response</u>. *OEHHA staff does not agree that the scientific community is now <u>widely</u> split on the association of silica exposure and lung cancer. Meta-analyses, such as Smith, Lopipero, and Barroga (1995) and Steenland and Stayner (1997), indicated that silica exposure was associated with lung cancer and that the risk for lung cancer was higher in silicotics. In 1997 the International Agency for Research on Cancer (IARC) designated crystalline silica (inhaled in the form of quartz or cristobalite from occupational sources) as an agent known to cause cancer in humans. According to Checkoway and Franzblau (2000), "The association between silica and lung cancer is generally, but not uniformly, stronger among silicotics than nonsilicotics. However, the existing literature is ambiguous due to incomplete or biased ascertainment of silicosis, inadequate exposure assessment, and the inherently strong correlation between silica exposure and silicosis which hinders efforts to disentangle unique contributions to lung cancer risk." (Checkoway H, Franzblau A. Is silicosis required for silica-associated lung cancer? Am J Ind Med. 2000 Mar;37(3):252-9; Smith AH, Lopipero PA, Barroga VR. 1995. Meta-analysis of studies of lung cancer among silicotics. Epidemiology. 6(6):617-24; Steenland K, Stayner L. 1997. Silica, asbestos, man-made mineral fibers, and cancer. Cancer Causes Control. 8(3):491-503.)*

Comment 2. OEHHA has proposed an REL of 3 µg/m^3. The recommended chronic REL, which is below even the default level suggested by the USEPA (5 µg/m^3), does not accurately reflect the most recent scientific information available on the subject. For example, Lopipero and Smith in a *Quantitative Risk Assessment for Crystalline Silica Using Human Epidemiological Data*, 1999, concluded that silicosis is not expected to occur at this exposure concentration (5 µg/m^3). Furthermore, OEHHA cites no credible evidence of silicosis occurring in the general population at exposure levels below those found in a workplace environment.

Response. *First, OEHHA is not saying that silicosis occurs at ambient exposure levels in California. The definition of a chronic REL is a level at or below which adverse effects are not expected in the general population. Thus we do not anticipate silicosis from background ambient levels. Secondly, although some have concluded that silicosis is not expected to occur at 5 µg/m^3, others have predicted a small incidence of silicosis. As indicated in the chronic REL summary, Park et al. (2002) predicted a risk of 7.8 to 17 cases of silicosis per 1000 diatomite workers exposed to 5 µg/m^3 crystalline silica. Based on their study on Chinese tin miners, Chen et al. expected a risk for silicosis of approximately 1 per 1000 people exposed at work to 5 µg/m^3 crystalline silica.*

Comment 3. OEHHA notes that "silicosis is still being diagnosed in workers exposed at currently allowable occupational levels." We are aware of no evidence to support this statement. While US OSHA's recent SEP (Special Emphasis Program) on crystalline silica reported significant exposures at levels exceeding the current PEL, there was no evidence presented that the diagnosis of new cases of silicosis was or is being reported in facilities in compliance with the current PEL. The SEP results simply show that overexposures continue to occur in inadequately controlled workplaces.

Response. *We have reworded this phrase as "silicosis is still being diagnosed at death in workers who were supposed to be exposed to occupational levels of 50-100 µg/m^3." Since 3439 people died with silicosis in the United States from 1985-1996 (Bang et al., 1999), many facilities may not be in compliance. (Bang KM, Althouse RB, Kim JH, Game SR. 1999. Recent trends of age-specific pneumoconiosis mortality rates in the United States, 1985-1996: coal workers' pneumoconiosis, asbestosis, and silicosis. Int J Occup Environ Health. 5(4):251-5.) Rosenman et al. (2003) believe that deaths from silicosis are low estimates and that there may have been 3600-7200 deaths from silicosis per year from 1985-1996 (Rosenman KD, Reilly MJ, Henneberger PK. 2003. Estimating the total number of newly-recognized silicosis cases in the United States. Am J Ind Med. 44(2):141-7.)*

Comment 4. In its draft document, OEHHA cites a few examples of reported environmental silicosis; however, at the same time the agency acknowledges that the exposure levels "were very high and thus similar to some occupational exposures." Workplace exposure limits for respirable crystalline silica range from 50 to 100 µg/m^3. When converted from the workplace to environmental values by time adjustments for hours per day, days per week, and a continuous 70 year lifetime of exposure, the limits are reduced to 7 to 13 µg/m^3, substantially above the REL proposed by OEHHA. Furthermore while OEHHA has acknowledged a justification for reducing the interspecies uncertainty factor (UF_H) from the default value of 10 to 3, no scientific data is presented to support any factor to protect children, the elderly and females. Such uncertainty factors are more appropriate when animal data is the basis for the establishment of a risk factor and human evidence is lacking. OEHHA even acknowledges that "the workers who developed silicosis at low silica concentrations are by definition the most sensitive workers to silica-induced silicosis."

Response. *In the adopted chronic REL methodology, the default UF_H is 10. Susceptibility to chemical-related health effects may vary over time for the same individual due to changing factors such as age, health status, and activity level. Depending on the chemical in question, sensitive individuals may include children, pregnant women and their fetuses, elderly persons, persons with existing diseases such as lung, heart or liver disease, and persons engaging in physical activity. In the case of silica the UF_H was reduced from 10 to 3, partly because the men affected at low levels were considered to be a sensitive subpopulation among the workers. However, there still are other potentially sensitive populations such as women (Gerhardsson and Ahlmark, 1985; Katsnelson et al., 1986, both cited in the chronic REL summary), children (children have smaller airways than adults and breathe more air on a body weight basis, thus deposition of particles in the airways in children is greater than that in adults exposed to the same concentration), and elderly persons. In addition an argument for a lower UF_H than 10 can be made when the benchmark approach is used with human data, since the use of a benchmark may account for some of the toxicokinetics and toxicodynamic differences among humans. Uncertainty Factors (UFs) for use in extrapolating animal studies to humans have no relationship to the present discussion, which relates to the uncertainty resulting from variation in the human population, as explained in the Technical Support Documents for the Air Toxics Hot Spots program.*

Comment 5. In its derivation of an REL, OEHHA has relied primarily on Hnizdo and Sluis-Cremer's 1993 study of South African gold miners. It has recently been reported that the exposures to quartz reported in this study were underestimated by a factor of approximately 2 (Gibbs and Du Toit 2002). This alone would have significantly increased OEHHA's derived value. In addition, OEHHA calculated from this study that there was a 1.9% incidence of silicosis (9 cases/474exposed) at exposures to 0.9 mg/m^3-yr silica. The denominator should have also included all of the workers who passed through that level and who received additional exposures, but did not get silicosis, as discussed by G. Berry[1] in his response to the REL to be submitted by the Crystalline Silica Panel. The authors of the study (Hnizdo and Sluis-Cremer) found a 0.4% incidence at 1 mg/m^3-yr.

Response. *OEHHA has reviewed Gibbs and Du Toit (2002) for possible application to the cREL derivation. If the report of Gibbs and Du Toit were compelling, the REL would increase by a factor of 1.8 (54%/30%). However, OEHHA's analysis the exposure data using the earlier report of Page-Shipp and Harris (1972) and concluded that Hnizdo and Sluis-Cremer mainly used correct data for exposure of various types of jobs, despite an incorrect footnote to Table II of Hnizdo and Sluis-Cremer. This point is addressed in more detail in the revised chronic REL*

Summary for respirable crystalline silica, and in OEHHA's response to Comment 1 by the American Chemistry Council.

In regard to the denominator used to calculate incidence, the proposal in this comment and that of Dr. Berry is incorrect. The 1.9% incidence (9 cases/474exposed) is appropriate for the derivation of a benchmark concentration. This point is also addressed in more detail in OEHHA's response to Comment 1 by the American Chemistry Council. The approach to determining the population at risk described in the comment appears to derive from that given in the original publication as part of a life table analysis. Life tables were developed to analyze <u>survival</u>. They can be used (1) to ask the question <u>whether</u> silica-exposed workers live as long as unexposed workers and (2) to identify, in conjunction with other tests such as chest radiographs, <u>when</u> they get silicosis. Although the life-table methodology is validated as a tool for description of the health outcomes within a measured cohort, it is seldom used to predict risk in groups other than that represented in the population studied. OEHHA has chosen to apply an entirely different type of analysis, i.e. the benchmark dose methodology, for estimating a health protective dose level. This makes no attempt to predict future outcomes in the exposed groups; it is not a time-dependent analysis in that sense. It should be noted that all members of the study population, whether affected by silicosis or not, are considered by the benchmark dose methodology: this is a model fit to the entire population, not a comparison between groups.

<u>**Comment 6.**</u> As a supportive study, OEHHA cites Hughes, et al.'s 1998 study of diatomaceous earth workers. The draft implies that quantitative measurements were used to develop exposure data. The quantitative measurements used were, in fact, for total dust, not crystalline silica, and extrapolations were made for years prior to 1948. Further, the development of the crystalline silica (cristobalite) content of the dust was based on estimates rather than measurements. Thus, the assigned exposure assessments made for individual job classifications were at best semi-quantitative. For the years prior to 1948, where the greatest excesses of disease are shown, the silica estimates were based on multipliers from estimated ordinals and thus could not even be considered semi-quantitative. Furthermore, silicosis cases in this study were defined in terms of chest X-ray readings as small opacities of profusion of 1/0 or greater, considering both rounded and irregular opacities. This again results in an overestimation of the cases by comparison to the Hnizdo, Sluis-Cremer study and others who generally use 1/1 as the basis for cut-off.

<u>**Response**</u>. *Admittedly the Hughes et al. study (1998) has deficiencies in estimating exposure, like many epidemiological studies. However, the data do not predict a chronic REL very different from other estimates. The authors of the study did not discuss specifically in their paper the shape of the opacities seen on the radiographs of the six workers at the less than 1 mg/m^3-yr level. In the absence of a definitive statement it is prudent from the viewpoint of public health to assume that the opacities were due to silica exposure. In addition, the very beginnings of some silicotic nodules may be irregular opacities. In fact Dick et al. (1992) state: "The development of irregular opacities is also related to exposure to various mineral and other dusts, and although their prevalence increases with cumulative dust exposure, in general the type of dust, whether fibrogenic or relatively inert, seems to be of little moment." Presumably quartz might be one type of dust involved.*

Comment 7. We are further concerned that at any given time, background ambient levels can be essentially equal to or greater than the proposed REL of 3 $\mu g/m^3$. As an example, a recent study conducted in Santa Barbara County for the LIWG (Lompoc Interagency Working Group) reported background ambient levels ranging from a low of 0.2 $\mu g/m^3$ in Buellton to a high of 2.6 $\mu g/m^3$ in Santa Maria, and nationally a range of from 3-8 $\mu g/m^3$ has been reported by the USEPA, hardly insignificant in relation to a proposed REL of 3 $\mu g/m^3$. OEHHA's treatment of this important issue is minimal at best. OEHHA should examine the subject more thoroughly to provide the appropriate guidance to the California Air Resources Board (CARB) and subsequently to the local Air Districts on how ambient levels might be dealt with in terms of regulatory compliance to provide some uniformity in how it is handled state-wide at the air district level.

Response. *OEHHA staff realizes that the proposed REL is close to some background levels. California has had to deal for many years with the fact that the standards for several pollutants (including ozone and other criteria pollutants) are within an order of magnitude of background levels. OEHHA emphasizes that the Reference Exposure Levels are levels at or below which it can be reasonably predicted that no adverse effects will be experienced in the general population. Where these levels are exceeded there may be (but not necessarily will be) such effects. CARB and the Air Districts have regulatory approaches designed to provide the best feasible protection for public health, taking into account the specific features of each individual situation.*

Comment 8. The measurement of low levels of respirable crystalline dust has significant limitations and here again OEHHA should provide some guidance to CARB and the local Air Districts in their enforcement policies. For example:

The PM_{10} particle size method used in EPA Method 501 can have errors up to 15% (page 93).

USEPA's ambient air test method for PM (40 CFR 50 Appendix J, Section 4) indicates precision is 5 $\mu g/m^3$ for ambient concentrations of 80 and below.

Federal Register, Tuesday April 15, 2003, pg 18467 discusses modeling errors of +/- 10 to 40%.

The AIHA PAT (Proficiency Analytical Testing) program reports a standard deviation for crystalline silica analyses of ± approximately 20%.

Lastly, there are significant differences in the collection characteristics of the equipment used to measure ambient levels, determine stack emissions levels, and the personal exposure monitoring levels on which the REL was based.
The above issues should be addressed to provide guidance to CARB as they raise questions regarding the ability to reasonably and accurately compare and measure respirable crystalline dust at the recommended REL of 3 $\mu g/m^3$.

Response. *Measurement error is a universal phenomenon and does not preclude development of a Reference Exposure Level.*

In proposing a chronic REL for crystalline silica, OEHHA agrees that the silica particles should be ‘respirable’. California EPA usually defines respirable particles as those of 10 µm or less in MMAD. However, there are differences in the size range distribution between a typical PM_{10} measuring device and that used by the investigators in the epidemiological studies. Clearly the level of confidence in the use of the Reference Exposure Level is greatest for materials where the particle size (and reactivity) are similar to those seen in the occupational studies. This size range includes particles with the ability to penetrate to the alveolar region of the lung, where it is generally considered that the pathological events leading to silicosis are initiated. Following various public comments, and discussion with the Scientific Review Panel, OEHHA has concluded that the REL should be specified as applicable to concentrations of crystalline silica particles having a size range similar to those measured in the occupational studies [respirable as defined by the occupational sampling method, most recently described in NIOSH (2003) and applied by ACGIH (2004)/ISO (1995)].