Comments of the American Chemistry Council (ACC) Crystalline Silica Panel and the California Mining Association.

Comment 1 The Crystalline Silica Panel ("Panel"), housed at the American Chemistry Council, and the California Mining Association ("CMA") are pleased to submit these Comments on the April 2003 Review Draft *Chronic Toxicity Summary, Silica (Crystalline, Respirable)* ("Chronic Toxicity Summary" or "CTS"), which was prepared by the California Office of Environmental Health Hazard Assessment ("OEHHA") in order to derive a chronic inhalation Reference Exposure Level ("REL") for Crystalline Silica. The proposed REL - for which the critical effect is silicosis - is 3 micrograms per cubic meter (3 $\mu g/m^3$). It was derived primarily from a study of South African gold miners, Hnizdo and Sluis-Cremer (1993), the "key study." The proposed REL allegedly is supported by a study of gold miners in South Dakota, Steenland and Brown (1995), and a study of workers in the California diatomaceous earth ("DE") industry, Hughes *et al*. (1998), the two "supportive studies."

The Crystalline Silica Panel consists of trade associations and individual companies that produce or use silica and silica-containing products or that perform operations (such as mining) on natural materials that contain crystalline silica. A list of Panel members is attached to these Comments as Appendix 1. Among its various activities, the Panel sponsors research into potential health effects associated with exposure to crystalline silica and, accordingly, is familiar with the literature on this subject. CMA is a trade association for the mining industry in California - representing companies that produce gold, rare earths, industrial minerals, clays, and aggregates across the state. California is the second largest non-fuel mineral producing state in the nation. Its mining industry accounts for over $3 billion of mineral production annually. California's miners produce and provide the resources needed for the continuing development of the state as well as for the maintenance of its citizens' existing lifestyle.

As discussed below, the Panel and CMA do not believe the proposed REL is justified from a scientific standpoint. Nor do they believe it is practical or responsive to any identified public health concern. In particular, although background concentrations of crystalline silica in the ambient air appear to be about as high as (or, in some cases, higher than) the proposed REL, there is no evidence that silicosis or any other silica-related disease is associated with exposure to crystalline silica outside the occupational setting. Accordingly, from a public health perspective, adoption of a REL for crystalline silica seems unnecessary.

Response. *OEHHA is developing a chronic inhalation REL for crystalline silica because crystalline silica is listed as a chemical subject to the Air Toxics Hot Spots Information and Assessment Act of 1986. The comment suggests that development of a chronic REL for silica is not practical or responsive to any identified public health concern. However, a large literature exists on the adverse effects of silica in human workers. This draft assessment has been developed at the request of the California Air Resources Board to be used in a public health context as part of programs, which aim to prevent any of these adverse effects occurring in the general public.*

Comment 2 A REL based on the key study of Hnizdo and Sluis-Cremer (1993) should fall in the range of 8 $\mu g/m^3$ - 10 $\mu g/m^3$. If OEHHA, nonetheless, recommends a REL, it should be set

at a level no lower than 8 μg/m^3-10 μg/m^3. Our position on these issues is explained in these Comments, as well as in comments that have been prepared at the Panel's request by Drs. Graham W. Gibbs and Geoffrey Berry. The Comments of Drs. Gibbs and Berry are attached as Appendix 2 ("Gibbs Comments") and Appendix 3 ("Berry Comments").

OEHHA has identified the study of South African gold miners by Hnizdo and Sluis-Cremer (1993) as the "key study" for deriving the REL. While we do not quarrel with the choice of Hnizdo and Sluis-Cremer as the "key study" for this purpose, we question the REL that OEHHA has derived on the basis of the study. Two problems, in particular, need to be corrected.

First, as pointed out in the Berry Comments, the number-at-risk denominator OEHHA used to calculate the silicosis incidence rate for the group of workers deemed to be exposed to 0.9 mg/m^3-yr respirable silica (*i.e.*, the group having a midpoint of 3 mg/m^3-yr Cumulative Dust Exposure or "3 CDE") was not correct. There were 9 reported cases of silicosis in that group, so 9 was used as the numerator of the fraction to calculate the incidence rate for the group. A total of 2,014 miners in the South African cohort are estimated to have had cumulative silica exposure of 0.9 mg/m^3-yr *or more*. This includes 474 miners whose exposure never exceeded 0.9 mg/m^3-yr respirable silica and *1,540 who were exposed to 0.9 mg/m^3-yr respirable silica without developing silicosis* and then continued to accumulate additional years of silica exposure at the mines. Thus, a total of 2,014 miners were exposed to *at least* 0.9 mg/m^3-yr respirable silica (*i.e.*, were "at risk" based on that cumulative exposure), and 9 of these developed silicosis based on that exposure. Some of the miners who went on to accumulate *additional* silica exposure also developed silicosis, but they did not become silicotic when their exposures were limited to 0.9 mg/m^3-yr respirable silica. Accordingly, as explained by Dr. Berry, the 9 cases used as the numerator of the silicosis incidence rate in the group of miners exposed to 0.9 mg/m^3-yr respirable silica should be compared to a denominator of 2,014 miners at risk, rather than 474. This produces an incidence rate of 0.4%, rather than the 1.9% assumed by OEHHA for purposes of calculating the REL. At the same time, as Dr. Berry also explains, the 0.4% incidence rate probably should be adjusted upward somewhat to account for the likelihood that some of the 1,540 miners who did not develop silicosis when exposed to 0.9 mg/m^3-yr respirable silica may have developed it later even if their exposures had ceased at that point.

Response. *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 survival. They can be used (1) to ask the question whether silica-exposed workers live as long as unexposed workers and (2) to identify, in conjunction with other tests such as chest radiographs, when 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 health protective levels in groups other than that represented in the population studied. It has also been used as a tool in examining the relationship between risk and the intensity and duration of exposure in cases where there is an expected continuous relationship between population risk and cumulative exposure, such as the examination of increments in relative cancer risk (for tumors with a background incidence in the population) with duration of exposure. 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. The desired objective is the identification of a health protective level at which no cases of the critical end-point (silicosis) would be observed at any time, not the estimation of a time- and dose-related incidence rate. An attempt to develop a benchmark (e.g. 1% incidence) using life-table methodology or a time-dependent incidence model would necessarily be referenced to a projected whole-life exposure of 70 years according to Air Toxics Hot Spots methodology, rather than the much briefer mean exposures of workers in the studies analyzed; the calculated benchmark would therefore probably be significantly lower than that presented by OEHHA. OEHHA does not consider that this is justified either by the extent of the available data, or by the present degree of understanding of the mechanisms and time-courses of silicosis incidence and progression. The OEHHA method does not adjust for the total duration of exposure in the studies, other than to determine whether the mean exposure duration is consistent with criteria defining a "chronic" exposure. Examination of the results (described in the summary) of Park et al (2002), who estimated lifetime risk in diatomite workers with a 45 year exposure, using a linear model, suggests that their results are by no means inconsistent with the 1% incidence benchmark calculated by OEHHA. It should be noted that all members of the study population, whether affected by silicosis or not, are considered by OEHHA's benchmark dose methodology: this is a model fit to the entire population, not a comparison between groups.

Exposure groups defined on the basis of the dose metric developed by Hnizdo and Sluis-Cremer were used as summary data since individual values were not available. If individual exposure data (or a validated surrogate, such as a biomarker of exposure) were available, OEHHA staff would attempt to calculate a chronic REL for silica using each individual's exposure and whether or not that individual developed silicosis. OEHHA used this approach with each individual's exposure and fluorosis status in developing a chronic inhalation REL for fluoride. Although preferable from a statistical standpoint, the analysis using individual data did not produce a substantially different result from an alternative analysis of grouped data. Similarly, if individual data on the time course of disease incidence and progression were available, this information could be integrated with the exposure data in the selection on appropriate health protective levels. However, as noted above, OEHHA does not consider that the data available from the occupational studies cover a sufficiently wide range of exposure durations and life stages, or provide sufficient detail on individual exposure histories and health outcomes, to allow prediction of the disease time-course in a hypothetically exposed general population. The benchmark dose approach used here is based purely on the disease incidence as measured, as a fraction of the population experiencing a specific range of exposure conditions. This analysis is correctly presented in the draft document.

In fact, the true incidence of silicosis may be underestimated in any given exposure category. Only those workers with an ILO reading of 1/1 or greater are being included as silicotics. In 1993 Hnizdo and coworkers published a paper on the "Correlation between radiological and pathological diagnosis of silicosis: an autopsy population based study" of 557 South African gold miners and used three radiograph readers. An ILO reading of 1/1, based on rounded opacities in the "most recent good quality X-ray" (not the X-ray where silicosis was first seen) detected 64-67% of miners with marked or moderate silicosis, based on silicotic nodules at autopsy, and an ILO reading of 1/1 detected 94-98% when slight silicosis was also included.

	Reader 1 [a]	Reader 2 [a]	Reader 3 [a]

ILO category ≥ 1/1	131 [b]	129 [b]	82 [b]
No silicosis at autopsy	2	5	4
Insignificant	1	3	1
Slight "	41	38	22
Moderate "	53	49	28
Marked "	34	34	27
Marked + moderate	87/131 = 66.4%	83/129 = 64.3%	55/82 = 67.1%
Marked+moderate+slight	128/131 = 98%	121/129 = 94%	77/82 = 94%

[a] Each reader read the same 557 radiographs.
[b] The remaining radiographs (see table below) were classified as < 1/1.

However, as shown in the following table, a number of workers (17-22%) whose radiographs did <u>not ever</u> reach an ILO reading of 1/1 had <u>moderate to marked silicosis</u>, based on a moderate to large number of silicotic nodules as determined by autopsy. If slight silicosis on autopsy is included, the number missed increases to 43-52%.

	Reader 1 [a]	Reader 2 [a]	Reader 3 [a]
ILO category < 1/1	426 [b]	475 [b]	475 [b]
No silicosis at autopsy	153	150	151
Insignificant "	75	73	75
Slight "	123	126	142
Moderate "	63	67	88
Marked "	12	12	19
Marked + moderate	75/426 = 17.6%	79/475 = 16.6%	107/475 = 22.5%
Marked+moderate+slight	198/426 = 46%	205/475 = 43%	249/475 =52%

[a] Each reader read the same 557 radiographs.
[b] The rest of the radiographs were classified as ≥ 1/1.

Since we do not know to which silica level exposure categories the various autopsy-positive silicotics belong (other than realizing that there is some sort of dose-response relationship involved), it is not clear how to adjust the numbers to recalculate the dose-response slope. OEHHA therefore did not incorporate this consideration in the risk assessment.

<u>Comment 3</u> The second problem with OEHHA's use of Hnizdo and Sluis-Cremer (1993) involves the exposure estimates. As pointed out in the Gibbs Comments, recent peer reviewed work shows that the exposure values used by Hnizdo and Sluis-Cremer are most probably underestimated by a factor of about 2. This new evaluation of exposures in the South African cohort is particularly significant, since one of the co-authors of the article, Dr. R.S.J. Du Toit, was a source of the information on which Drs. Hnizdo and Sluis-Cremer relied for the exposure assessment in their study. Since the data from Hnizdo and Sluis-Cremer that OEHHA used to derive the REL have not been adjusted to take this two-fold underestimation of exposure into account, the resulting REL reflects an overestimate of risk.

In his Comments, Dr. Geoffrey Berry recalculated the 1% Benchmark Concentration ("BMC_{01}") based on use of a corrected denominator and an exposure adjustment for the Hnizdo and Sluis-Cremer cohort. And he has made a further adjustment to account for the possibility

that some of the miners who did not develop silicosis when exposed to 0.9 mg/m^3-yr respirable silica might have developed it later even if their exposure to silica had ceased. He found that the lower 95% limit on the BMC_{01} was in the range of 5.6 to 6.9 mg/m^3-yr respirable dust (or CDE). Assuming a 30% silica content of the dust, and making the same intraspecies uncertainty factor adjustment as OEHHA, Dr. Berry concluded that the REL would fall in the range of 8 µg/m^3 - 10 µg/m^3 respirable silica.

Response *In regard to the commentator's concern over exposure estimates, OEHHA staff has reviewed the paper by Gibbs and Du Toit (2002) for possible application to the cREL derivation. Acceptance of the Gibbs and Du Toit analysis would change the percent quartz in the South African gold mine dust from 30% to 54%. However, Gibbs and Du Toit (2002) cite the work of Kielblock and coworkers (1997) indicating that recent measurements of mine dust indicate 15% respirable quartz content. (Kielblock AJ, Franz RM, Unsted AD, van der Linde A, Ashworth SGE. 1997. Quantification of occupational health risks in the South African mining industry and assessment of sources of uncertainty in the estimates. Final project report. Project no. SIMRISK 401. Safety in Mines Research Advisory Committee. Johannesburg: CSIR Division of Mining Technology).*

Kielblock et al. (1997) studied an unspecified number of South African gold mines with a total employment of approximately 300,000 underground and surface workers. For 223,104 mineworkers sampled during 1996, the average respirable dust exposure was 412 µg/m^3 (Table 4.3.1a). Among 137,439 mineworkers sampled for alpha-quartz, the average alpha-quartz exposure was 62.5 µg/m^3 (Table 4.3.1b). The average percent alpha-quartz in the respirable dust was therefore 15.08%. The percent alpha quartz concentration in the dust ranged from 0-5% for approximately 10% of the miners to >40% for approximately only 1% of the miners (Figure 4.3.3j). The data of Kielblock et al. (1997) indicate that few miners have recently been exposed to 54% quartz.

In a personal communication, Dr. Eva Hnizdo, now with the U.S. National Institute of Occupational Safety and Health (NIOSH), provided a summary of various other estimates that have been made. "Past surveys indicate that the amount of airborne respirable dust in SA gold mines in 1980's and in 1970's was on average around 0.4 mg/m^3 with average quartz concentration of 0.08 mg/m^3 (about 20%)." She also mentions a Ph.D. thesis (unpublished) by R.E.G. Rendall, in which the silica percentage averaged 22% during the period from 1956 to 1972, which overlaps the period of the 1960s studied by Beadle (1971). Thus OEHHA staff is somewhat reluctant to accept only the highest value available (54%) for % quartz in the mine dust.

Gibbs and Du Toit (2003) state that the percent quartz in the South African gold mine dust in the Hnizdo and Sluis-Cremer (1993) study should be increased by a factor of 1.8 (54% rather than 30%). ("In the absence of systematic side-by-side thermal precipitator and modern respirable mass measurements in the South African gold mines, the true relationship between the respirable mass concentrations and the theoretically derived concentrations cannot be known. However, with many uncertainties, we estimate that the quartz exposures of South African miners derived from past theoretically based conversions from particle number to respirable mass underestimate the actual quartz exposures by a factor of about 2." Two was rounded up from 1.8 in the text.) Mine dust samples are heat treated (pyrolysed) to remove organics and

treated with hydrochloric acid to remove acid-soluble materials before the heat resistant, acid insoluble silica particles are quantified. According to Hnizdo (personal communication, 2004), "the issue Gibbs pointed out is that the respirable dust concentration was measured after acid treatment by hydrochloric acid. Hydrochloric acid may dissolve some components of the respirable dust and increases the concentration of silica. The uncertainty is how much did the hydrochloric acid dissolve. I was told that the acid was used to allow them to measure the surface area and count the particles under the microscope." OEHHA staff does not know how much material the hydrochloric acid dissolved and Gibbs and Du Toit admit there is much uncertainty in their estimate. Given the uncertainty in their estimate and the variability in percent quartz given by various samplings of the dust, OEHHA staff does not believe that there is a compelling case to take the highest estimate available. For this reason we are retaining the intermediate value of 30%.

Comment 4. OEHHA cannot properly rely on Steenland and Brown (1995) or Hughes *et al.* (1998) to support the proposed REL of 3 $\mu g/m^3$. The Draft CTS identifies Steenland and Brown (1995) and Hughes *et al*. (1998) as "supportive" studies for the proposed REL of 3 $\mu g/m^3$. In fact, however, neither of these studies supports the proposed REL.

There are several problems with the Steenland and Brown study of Homestake gold miners that limit its usefulness in deriving a REL. For one thing, as OEHHA recognizes, silicosis outcome was determined through a mix of death certificates and radiographic surveys, with most being determined solely on the basis of death certificates. As Dr. Berry points out: "The problems arising out of diagnosing silicosis mainly from death certificates with the possibility of a certification bias because of known occupational history, past worker's compensation claims etc. mean that this study is not strong in terms of defining an exposure-response relationship." Moreover, as the authors themselves note, some deaths due to chronic obstructive pulmonary disease may have been "misdiagnosed as silicosis." And some of the 5 cases of silicosis with a low cumulative exposure, < 0.2 mg/m^3-years, may have been due to silica exposure "before or after working at the gold mine." Yet that is the exposure group OEHHA used as a LOAEL for the study. Furthermore, as Drs. Berry and Gibbs point out, the life-table method of analysis used by Steenland and Brown is not appropriate, because prevalence rates were used as if they were incidence rates - when, in fact, the dates of incidence are unknown for those miners defined as having silicosis through death certificates. This results in overestimates of the actual risk.

The exposure assessment in Steenland and Brown suffers from enormous uncertainty as well. Job-exposure matrices expressed in terms of respirable silica were developed on the basis of particle count measurements to which a particle-to-respirable mass conversion factor was applied. For the years prior to 1937, no exposure measurements were available; instead, based on estimates by industrial hygienists, exposures were assumed to average 25 million particles per cubic foot ("mppcf") prior to 1920, and the estimate was decreased gradually from 1920-1937 as a function of decreased time spent underground. Particle count measurements were taken in each year from 1937 to 1975. However, there apparently were no exposure measurements for the years after 1975, and the authors assigned zero exposure to the post-1975 period, even though 14% of the cohort was still employed at that time. In addition, the authors appear to have assumed no silica exposure for work performed above ground, even though primary crushing of the ore was transferred above ground in the mid-1930s, and an increasing percentage of daily

time was spent above ground after the 1920s. An industrial hygiene survey performed by NIOSH in 1977 indicated that workers engaged in crushing operations at the surface had higher time-weighted average dust exposures than underground workers. As noted by the authors of the NIOSH survey: "Many of the employees in the surface crushing mills are subject to high dust concentrations during various work activities."

The particle count values from 1937 to 1975 were converted to respirable silica mass by use of a conversion factor of 10 mppcf = 0.1 mg/m^3 of respirable silica. This conversion factor was *not* based on side-by-side comparisons at the Homestake mine. Instead, the authors used a conversion factor of 10 mppcf = 0.075 mg/m^3 proposed by Davis *et al*. for Vermont granite workers and increased it by the ratio of 13/9.5 to reflect what they believed was the respirable silica content of the dusts at the Homestake mine and in the Vermont granite industry, respectively. There are substantial questions about use of this conversion factor:

Response: OEHHA has broken this comment into six sub-comments and answered them below.

Comment 4a. First, use of the 10 mppcf = 0.075 mg/m^3 conversion factor proposed by Davis *et al*. as the starting point for a conversion factor at the Homestake mine is problematic. Three different conversion factors have been proposed for the Vermont granite industry. In addition to the factor proposed by Davis, Sutton and Reno proposed a conversion factor of 10 mppcf = 0.1 mg/m^3, and Ayer *et al*. found a conversion factor of 10 mppcf = 0.2 mg/m^3 based on side-by-side comparisons of granite dust generated in operations at a reconstructed 1920s shed. Ayer's results suggest that when particle count levels are high (averaging 92 mppcf in the reconstructed 1920s shed), a higher conversion factor of 10 mppcf = 0.2 mg/m^3 is appropriate. By contrast, the lower conversion factors found by Davis and by Sutton and Reno reflected average particle count levels of 3.4 mppcf and 3.2 mppcf, respectively. It may be that at high dust levels, it becomes difficult to count all the particles, so the particle count is understated as compared to measurements of respirable mass, thereby pushing the conversion factor upward—*i.e*., relatively speaking, the number of particles counted would be associated with a higher measurement of respirable mass when dust levels are high than when they are low. If this is correct, it arguably would have been more appropriate for Steenland and Brown to have used the Ayer conversion factor of 10 mppcf = 0.2 mg/m^3 as the starting point for developing a conversion factor applicable at the Homestake mine - at least for the period before 1937 when estimated particle count levels were near 25 mppcf and when 50% of the exposures of the silicotic miners occurred.

Response. *OEHHA staff agrees that the study of Steenland and Brown (1995) has limitations. The various mppcf to mg/m^3 conversion factors(10 mppcf = 0.075 mg/m^3; 10 mppcf = 0.1 mg/m^3; 10 mppcf = 0.2 mg/m^3) vary by a factor of 2.7 (2/0.75). Thus the silica exposure levels before 1937 might be off by a factor of 2.7.*

By itself an assumption of zero exposure to silica after 1975 will have a small impact on their results since only 14% of the miners were still employed after 1975. The lack of inclusion of surface crushing exposure would further add to the underestimate of exposure.

Comment 4b. Second, the adjustment to the Vermont granite conversion factor that Steenland and Brown made based on an assumed 13% silica content of the dust at the Homestake mine is

questionable. The 13% figure is an average of 82 samples (ranging from 1% to 48%) taken in two surveys in the 1970s. The authors do not know whether the percentage of respirable quartz in the dust differed in earlier years, and their sensitivity analysis showed that if they underestimated the percentage of quartz, it would have a bigger impact on their risk estimates than if they overestimated the percentage of quartz by the same amount.

Response. *The 13% silica content figure is based on actual measurements at the gold mine studied by Steenland and Brown. More than 82 data points and a range smaller than 1-48% would be preferable, but it is real data. The sensitivity analysis showing that an underestimate of the percentage of quartz would have a bigger impact on the risk estimates than an overestimate of the percentage of quartz by the same amount is true at higher workplace exposure levels where the incidence of silicosis accelerates. However, the relationship is not as strong at very low levels of ambient crystalline silica where the curve is flatter.*

Comment 4c. Third, it seems doubtful that a conversion factor derived from measurements of granite dust can properly apply (even with a quartz content adjustment) to a gold mining operation where the rock is different, the operations performed are different, the particle size distribution probably is different, etc. As NIOSH stated in its 1974 Criteria Document in explaining the particle count-to-gravimetric conversion factor based on Vermont granite industry studies: "Because of variations in types, size, and density of particles in other industries, it is not clear that the same limit, in terms of number of particles, will properly describe safe exposures in other industries producing airborne free silica."

Response. *OEHHA staff agrees that uncertainties arise when applying a conversion factor derived from measurements of granite dust (even with a quartz content adjustment) to a gold mining operation where the rock is different. This is another area of uncertainty in the Steenland and Brown study. However, such exposure uncertainties are common in risk assessment and should not preclude use of the study in estimating a chronic REL. The study was used only as a supportive study, in part because of these types of uncertainty.*

Comment 4d. Based on the foregoing approach to exposure assessment, Steenland and Brown stated that for the cohort as a whole, the median intensity of exposure to silica was 0.15 mg/m^3 for men hired before 1930, 0.07 mg/m^3 for men hired between 1930 and 1950, and 0.02 mg/m^3 for men hired after 1950. And they assumed zero exposure after 1975. These exposure values seem suspect. Thus, a Health Hazard Evaluation conducted at the Homestake mine in March 1978 by NIOSH found that respirable silica exposures for all six personal samples taken in the assay department exceeded the NIOSH REL, the OSHA PEL, and the TLV for quartz - ranging from 0.15 mg/m^3 to 1.33 mg/m^3. In a follow-up survey conducted in May 1978 (after the company had implemented various of NIOSH's engineering recommendations), two of the four respirable silica samples still exceeded 0.1 mg/m^3, and all four exceeded the 0.05 mg/m^3 - ranging from 0.07 mg/m^3 to 0.24 mg/m^3. While these samples related to assay department workers rather than miners, the fact that they ranged from 0.15 mg/m^3 to 1.33 mg/m^3 on the initial survey in 1978 makes one skeptical of the much lower values that Steenland and Brown used for miners employed during the preceding 50-60 years. Moreover, an industrial hygiene survey conducted by NIOSH in 1977 concluded that "before approximately 1952 there is an additional risk of over exposure to free silica [TWA > 0.1 mg/m^3] because of the elevated dust concentrations caused by underground blasting procedures and the lack of efficient dust

suppressive techniques." Yet, Steenland and Brown assumed an average silica exposure of 0.07 mg/m^3 for men hired between 1930 and 1950.

Response. *Based on the comment, the assumption by Steenland and Brown of an average silica exposure of 0.07 mg/m^3 for men hired between 1930 and 1950 appears low by a factor of at least 2 based on real data. But it is still unclear if the all the uncertainties in the estimates will all bias the cREL in the same direction or cancel one another. Uncertainty in exposure assessment is very common and one of the uncertainties we live with in the risk assessment arena. It does not preclude use of these data in estimating a chronic REL.*

Comment 4e. When these points are considered, it is no wonder the British Health and Safety Executive ("HSE") observed that the diagnosis of silicosis in the Steenland and Brown study "was fraught with interpretational problems and very likely subject to bias" and that the exposure assessment "was weak and was based on a number of unverifiable assumptions." For these reasons, the British HSE concluded, "no confidence can be attached to the predicted risk estimates from this study." Given these weaknesses in the exposure assessment and the problems of silicosis determination in the study, it should be no surprise that "[n]one of the BMDS models [used by OEHHA] gave an acceptable fit [to the Steenland and Brown data] at the $p \geq 0.05$ level." This study cannot be used to derive or support a REL.

Response. *The commentator is not surprised that the BMD models used by OEHHA did not yield an acceptable fit. OEHHA staff reexamined the Steenland and Brown data and found that, after dropping the top two dose levels, acceptable model fits were achieved. This is a reasonable practice since the high dose region is not as formative of the BMD as the low dose region is (USEPA, The Use of the Benchmark Dose Method in Health Risk Assessment, 1995; Filipsson et al., Critical Reviews in Toxicology, 33(5):505-542, 2003). Fitting the probit model to the log dose of the five lowest silica levels yielded a BMC_{01} of 0.34 (mg/m^3)–yr CDE ($\chi^2 = 1.32$; p value for fit = 0.5177). Fitting the quantal quadratic model gave a BMC_{01} of 1.02 (mg/m^3)–yr ($\chi^2 = 3.36$; p value for fit = 0.3395). Use of the BMC value from the probit model resulted in a chronic REL estimate of 4 $\mu g/m^3$, while use of the value from the quantal quadratic model resulted in an estimate of 12 $\mu g/m^3$. Even with its limitations the Steenland and Brown study points to a chronic REL similar to the one based on the Hnizdo and Sluis-Cremer key study and to those based on Hughes et al. and Chen et al.*

Comment 4f. The study by Hughes *et al.* has not properly been used to support the proposed REL either. As noted in the Gibbs and Berry Comments, there are uncertainties both in terms of exposure assessment and identification of radiographic silicotic nodules. The British HSE also noted the "poorly defined opacities" in this study, which create "uncertainty as to whether or not the chest radiographs indicated silicosis as opposed to mixed dust fibrosis." Furthermore, OEHHA incorrectly used 22 years as the denominator in translating 330 $\mu g/m^3$-yr of cumulative exposure into an Average Exposure and Human Equivalent Concentration. As stated in Hughes *et al*., the mean exposure period in their study (*i.e*., the period from date of hire to date of the latest film for those judged negative or the earliest positive film for those judged positive) was 11.5 years. Substituting that value for the 22 years used by OEHHA produces an Average Exposure and Human Equivalent Concentration of 29 $\mu g/m^3$ (330 $\mu g/m^3$-yr/11.5 yr = 29 $\mu g/m^3$). Applying the same uncertainty factor of 3 used by OEHHA to that value yields an inhalation

REL of 10 μg/m^3 - which is consistent with the high end of the range calculated by Dr. Berry on the basis of the adjusted exposure data from Hnizdo and Sluis-Cremer.

Response. *In regard to the Hughes et al. (1998) study, OEHHA staff has revised the chronic REL estimate by substituting the mean value of 11.5 years exposure for the mid-point of 22 years, which was incorrectly used in our calculation. With that change the corrected REL is 10 μg/m^3 based on the authors' NOAEL or 3 μg/m^3 based on OEHHA's consideration of the lowest exposure group as a LOAEL. Until it is shown that none of the six workers in the lowest exposure group had rounded opacities, it is prudent to assume that the opacities were due to silica exposure. OEHHA staff read the Hughes et al. (1998) study again and was unable to discern if any of the six workers in the lowest exposure group had small rounded opacities on their chest radiographs. However, the very beginning silicotic nodule may be an irregular opacity. Unfortunately it is not possible to distinguish such irregular small opacities, postulated to be due to silica exposure, from those due to smoking or aging. Even with its limitations the Hughes et al. (1998) study at least points to a chronic REL in the vicinity (a factor of 3) of the one based on the Hnizdo and Sluis-Cremer key study.*

As an additional comparison OEHHA staff has added to the chronic REL summary a comparison REL estimate of 6 μg/m^3 based on Chen et al. (2001) in which 1015 out of 3010 Chinese tin miners developed silicosis at various levels of average silica exposure.

Comment 5. The NOAEL and LOAEL values for crystalline silica are higher than the levels OEHHA has assumed**.** We recognize that OEHHA did not use estimated NOAEL or LOAEL values to derive the proposed REL. However, OEHHA may believe that the NOAEL and LOAEL values for crystalline silica support the results of its Benchmark Concentration calculations. Accordingly, we feel obliged to address this issue, because we believe the NOAEL and LOAEL values cited by OEHHA are incorrect.

Referencing Rice and Stayner (1995), OEHHA identifies a NOAEL for silicosis of 7 μg/m^3 based on Hnizdo and Sluis-Cremer (1993) and a LOAEL of 8 μg/m^3 based on McDonald and Oakes (1984). In addition, OEHHA indicates that it considers the ≤ 1 mg/m^3-yr cumulative exposure category in Hughes *et al*. (1998) to be a LOAEL. These NOAEL and LOAEL values are not justified.

Response: OEHHA has broken this comment into three sub-comments and answered them below.

Comment 5a. As explained in the Gibbs Comments, Rice and Stayner's estimate of the NOAEL for the South African gold miners is not correct, because it ignores the fact that 2,014 miners passed through the cumulative dust exposure range of 0 – 2 mg/m^3-yr without showing evidence of silicosis. Since there were no cases of silicosis below 2 mg/m^3-years of cumulative dust exposure, the NOAEL for the South African gold miners cohort (based on uncorrected exposure data) was 13 μg/m^3 of respirable silica dust—*i.e*., 2,000 (μg/m^3-yr respirable dust)/45 years x 0.3 (silica content) = 13.33 μg/m^3 respirable silica. If the exposures are adjusted by a factor of 2 to reflect the recent work by Gibbs and Du Toit, the NOAEL based on Hnizdo and Sluis-Cremer increases to 26 μg/m^3 respirable silica.

Response. *The comment about some individual "passing through" lower dust concentration ranges is based on a misunderstanding by the commenter of the procedures for deriving NOAELs and benchmark concentrations, as discussed in OEHHA staff's response to Comment 2. Similarly, the questions raised by Gibbs and Du Toit about the silica concentrations reported by Hnizdo and Sluis-Cremer were considered in the response to Comment 3.*

Based on this comment and others, staff has reconsidered referring to 1 mg/m^3-yr as a NOAEL for the South African gold miners. The data indicate that there were no cases of silicosis up to 2 mg/m^3-yr. Thus 2 mg/m^3-yr can be considered the NOAEL from the study, and our document reflects this change from the public review draft. It should be noted that the NOAEL does not enter into the derivation of the REL because the REL is based on the benchmark dose calculation. Thus the change in our document of designating 2 rather than 1 mg/m^3-yr as a NOAEL study does not change the chronic REL. However, staff does not agree with the commentator's calculation above that the human NOAEL would be 13 µg/m^3 [2,000 (µg/m^3-yr respirable dust)/45 years x 0.3 = 13.33], because the commentator used 45 years (maximum work-life) rather than the study's average of 24 years dust exposure. Use of 24 years would result in a value of 25 µg/m^3. After correcting by 1.8 (54%/30% based on the estimation by Gibbs and Du Toit that the silica content is 54%), a NOAEL of 45 µg/m^3 for white male workers is obtained. If one were to utilize the NOAEL/UF approach to estimate the REL, use of time extrapolation (45 µg/m^3 x 10 m^3/20 m^3 x 5 d/ 7d x 48 wk/52 wk) with this NOAEL leads to a value of 15 µg/m^3 under the assumption of 54% silica in the mine dust. Application of a UF_H of 3 to protect other sensitive humans would result in a chronic REL estimate of 5 µg/m^3. This value is quite close to the chronic REL of 3 µg/m^3 derived by OEHHA using the benchmark dose approach. With the use of 30% silica the value would be the same as the proposed REL.

Comment 5b. As far as the paper by McDonald and Oakes (1984) is concerned, the exposure estimates in the underlying study of Homestake gold miners were too approximate to be used as the basis for identifying a NOAEL or LOAEL. As explained by Dr. Gibbs (who was the co-author responsible for developing the exposure assessment in the Homestake gold mine study), the workers were classified into "very low," "low," "moderate," "high," and "very high" exposure categories based on approximate estimates of exposure for the various jobs. The approximate nature of these estimates is recognized in the McDonald and Oakes paper, where the column describing the exposures is labeled as an "assumed level." Furthermore, the exposure estimates were based on midget impinger measurements; no mass equivalent values were reported. McDonald and Oakes provide gravimetric equivalent values in their paper, but they describe them as being only approximate ("approx"). Moreover, they do not explain how they converted the midget impinger values to gravimetric measurements. If they used a conversion factor based on the Vermont granite industry, the resulting gravimetric values likely would be understated—because, as they note, the airborne dust at the Homestake mine was reported to have a free silica content of 39%, while the Vermont granite dust had a silica content of only 10%.

McDonald and Oakes conclude with the observation that "the main uncertainty in [their] analyses of exposure-response stems from unreliable estimates of the former, rather than the latter." They believe their results suggest "that the relativities in the exposure estimates were probably valid, despite questions as to levels in absolute terms." Dr. Gibbs, who was responsible for exposure assignments in the Homestake study, agrees with that assessment. Given the

approximate nature of the exposure values assigned to workers in the Homestake study, the derivation of a precise LOAEL on the basis of that study is not warranted.

Response. *OEHHA staff reproduced the data from Table 2 of Rice and Stayner (1995) in Table 14 of the report and did not directly use the data in the development of the REL. Staff appreciate the critique of the data and have made a note in Table 14 that McDonald and Oakes (1983) considered their values to be approximations.*

Comment 5c. Finally, as explained in the Gibbs and Berry Comments, the ≤ 1 mg/m^3-yr cumulative exposure category in Hughes *et al*. (1998) should not be considered a LOAEL. Hughes *et al*. included irregular as well as rounded opacities in their radiograph readings. But idiopathic small irregular opacities in non-exposed populations have been reported in the literature—with a pooled prevalence of 1.3% being reported in North American men. This background rate for idiopathic small irregular opacities is similar to the prevalence rate (1%) of small opacities 1/0 or more that Hughes *et al*. found in diatomaceous earth workers having 2.0 mg/m^3-yr cumulative exposure in the later years of the study. Thus, it seems likely that the 1/0 readings by Hughes *et al*. at the less than 1 mg/m^3-yr level were irregular opacities, which would *not* be silica-related. Indeed, as Dr. Gibbs observes, the same is likely to be true of the opacities Hughes *et al*. observed in workers at the 2.0 mg/m^3-yr level.

In sum, the "less than 1 mg/m^3-yr" exposure category in Hughes *et al*. should not be considered a LOAEL. In fact, since the prevalence rate for small opacities in the "2.0 mg/m^3-yrs" exposure category closely matched the idiopathic rate in North American men, it could be argued that even the "2.0 mg/m^3-yr" exposure category represented a NOAEL, rather than a LOAEL—at least for workers whose employment began after 1950 and whose average exposures were ≤ 0.5 mg/m^3.

Response. *In regard to Hughes et al. (1998), the commentator states that it seems likely that the 1/0 ILO readings in that report at the less than 1 mg/m^3-yr level were irregular opacities and thus not silica-related. However, it is prudent to assume that the opacities were due to silica exposure, particularly since the very beginning silicotic nodule may be an irregular opacity. There is not enough information given in the Hughes et al. paper to conclude which individuals had which type of opacity.*

Comment 6. The silicosis incidence rates estimated by Greaves (2000) as the basis for his proposal of a 10 µg/m^3 occupational exposure limit are unreliable. On page 16 of the Chronic Toxicity Summary, OEHHA refers to a recommendation by Greaves (2000) that the occupational TLV for quartz be lowered to 10 µg/m^3. Greaves' recommendation was based on exposure-response data from a community study of former miners in Leadville, Colorado by Kreiss and Zhen (1996). That study cannot serve as the basis for assessing exposure-response relationships for silicosis or establishing occupational or environmental exposure limits.

For one thing, as OEHHA observes, the Kreiss and Zhen study is limited by the small number of subjects (100) in the study group. Moreover, as the British Health and Safety Executive ("HSE") notes, some of the miners invited to take part in the study "already had a physician's diagnosis of silicosis, so there may well have been some selection bias involved."

And, because it "was a population-based survey, ... the design of the study does not permit exposure-response relationships to be identified."

In addition, as the British HSE observes, "there are major weaknesses in the exposure assessments for this study which strongly undermine the quantitative risk estimates for silicosis." The cumulative and average respirable silica exposure estimates were developed on the basis of job title-specific exposure values derived from gravimetric dust and gravimetric silica measurements made from 1974-1982 at the major molybdenum mine in the area. Even for the 1974-1982 period, however, there apparently were few, if any, gravimetric measurements available for many of the jobs at the molybdenum mine. Exposure values for those jobs had to be extrapolated from measurements made at other jobs believed - on the basis of subjective retrospective estimates - to be of the same relative dustiness.

The uncertainties regarding exposures during the 1974-1982 period are compounded for earlier years when gravimetric dust and silica measurements were not available for any job titles at the mine. Instead, Kreiss and Zhen assumed that historical job-specific exposures dating back to the 1920s and 1930s were the same as those that were measured at the mine in 1974-1982. This seems implausible, and other information from the study underscores its implausibility.

No dust measurements were available for the period before 1941. Midget impinger particle count measurements were available for the years 1941 through 1976, and the particle count measurements in the 1940s were about 3½ times higher than those in the 1970s. In addition, the authors note that: "The opening of new mining levels in 1954, 1965, and 1972, which were worked concurrently, was likely accompanied by improvement in mine ventilation in comparison to the older level worked from the 1930s until 1974." Thus, the authors' failure to account for secular trends in exposures clearly must have led them to underestimate the cumulative and average exposures of miners in the survey. Indeed, they virtually concede as much, stating that their "estimates of cumulative dust and silica exposure are subject to error, since pre-1974 exposure estimates were based on job-specific gravimetric data collected since 1974, a period which accounted for 30.4% of the person-years worked by study participants. . . . We suspect that historical exposures may have been higher than those used in our calculation of the cumulative dust and silica exposure indices, particularly in the 1940s. "

In short, as the authors acknowledge, there are "large uncertainties in historical dose reconstruction" in this study. And the historical exposure uncertainties could have had a major impact on risk estimates, because pre-1974 exposures accounted for 70% of the person-years worked by study participants.

An additional source of uncertainty regarding exposures involves the conversion of gravimetric dust measurements to respirable silica concentrations. Kreiss and Zhen made the conversion by assuming that 12.3% of the respirable dust was silica. This value was the mean silica content of 483 paired silica and respirable dust measurements which ranged from 0.2% - 100% silica. But the mine ore had a silica concentration of approximately 35%, and the average silica content of 80 dosimeter samples taken from the crusher area was 19%. So the estimation of silica exposures based on respirable dust sampling and an assumed 12.3% silica content may have understated the actual silica exposures.

Finally, Kreiss and Zhen provided no exposure data for the smaller lead, zinc, and gold mines, which accounted for 17.1% of the person-years worked in mining by survey participants. Exposures for jobs at the larger molybdenum mine were assumed to apply to these other mines as well. As the British HSE notes, however, this assumption is "questionable, and it would also seem a remarkable coincidence if the silica content in all of these different mines was the same."

In sum, as the British HSE concluded, "the risk estimates from . . . [the Kreiss and Zhen] study are of very doubtful reliability, primarily because of uncertainties in the exposure estimates, but also because it was a small-scale study, with possible problems in terms of selection bias of the study population." The use of this study to develop occupational or environmental exposure limits is unwarranted. Accordingly, Greaves' proposal of a 10 $\mu g/m^3$ occupational TLV on the basis of the Kreiss and Zhen study is unjustified and does not support a REL of 3 $\mu g/m^3$.

Response. *OEHHA staff did not calculate a chronic REL from Kreiss and Zhen (1996), but agrees that they studied a small number of subjects (n = 100) on which Greaves based the recommendation of 10 $\mu g/m^3$. However Kreiss and Zhen also had a longer follow-up of silica-exposed workers than any other group. This could result in detection of cases of silicosis with longer latency periods.*

In addition to Kreiss and Zhen (1996), Greaves (2000) also reviewed Steenland and Brown (1995) and Hnizdo and Sluis-Cremer (1993). Based on Figure 1 of Greaves (2000), both these studies would indicate a somewhat higher workplace recommendation of approximately 20 $\mu g/m^3$.

OEHHA also describes the study of 1015 silicotics among 3010 Chinese tin miners by Chen et al. (2001). These authors obtained silicosis estimates comparable to Kreiss and Zhen (Table 13 of OEHHA's chronic REL toxicity summary and Table 6 of Chen et al.) and suggested an even lower occupational exposure limit of 5 $\mu g/m^3$ based on their cohort of silicotics. Although Chen et al. (2001) reported a very low percent (3.6%) of silica in tin mine dust, the curve of cumulative silica exposure versus cumulative risk of silicosis from Chen et al. was similar to those of Hnizdo and Sluis-Cremer (1993) and Steenland and Brown (1995)(Figure 2 of Chen et al.) As stated above, OEHHA staff added a comparison chronic REL of 6 $\mu g/m^3$ based on Chen et al. (2001) to the chronic REL summary.

Comment 7. Although background levels of crystalline silica in ambient air are about the same as the proposed REL, there is no evidence that non-occupational ambient air exposures are causing silicosis or any other silica-related disease**.** Data regarding background levels of crystalline silica in the ambient air derive from a miscellany of sources and are still relatively limited. Based on a review of various published research papers available in 1993, R.P. Ruble and D.F. Goldsmith concluded that the best estimate of ambient air levels of crystalline silica was 6.0 $\mu g/m^3$ (95% CI: 1.04 – 34.75 $\mu g/m^3$). In November 1996, U.S. EPA reviewed additional studies and concluded that although the data were limited, "there is enough indirect evidence to indicate that average ambient levels [of crystalline silica] …. in U.S. metropolitan areas generally have ranged between 1 and 3 $\mu g/m^3$ and, in most circumstances, are not likely to exceed an 8-$\mu g/m^3$ annual average" - with the particle size of most airborne crystalline silica falling "in the range of 2.5 to 10 µm aerodynamic diameter."

These estimated background levels of crystalline silica are comparable to the REL of 3 $\mu g/m^3$ proposed in the Chronic Toxicity Summary. Yet there is no evidence that ambient air concentrations of crystalline silica are causing silicosis or any other silica-related disease. From this, we conclude that exposures to crystalline silica in the ambient air outside the occupational setting are not - and should not be - a matter of public health concern. The absence of silica-related disease outside the occupational context - despite exposure to ambient air concentrations that approximate the proposed REL - also indicates that a REL of 3 $\mu g/m^3$ is below the level at which any potential adverse health effects might be expected. Indeed, it calls into question the need to adopt any REL whatsoever.

Response. *The Reference Exposure Level (REL) is defined as a level at or below which adverse health effects are not anticipated. There should be a level of silica below the occupational limit and above the background level that poses minimal risk of respiratory disease to humans including sensitive subpopulations. This level would be the chronic REL. OEHHA staff agrees that there is no evidence that average ambient levels of crystalline silica in California have been associated with silicosis. However, current medical practice is unlikely to detect silicosis due to background levels of silica, since:*

(1) the rounded nodules would be few in someone with silicosis due to background silica levels,

(2) small irregular opacities, if due to silica exposure, could not be distinguished from those due to smoking or aging,

(3) most people, except those in dusty occupations, only get chest X-rays when they are ill (even then, if a patient had serious pneumonia, the average radiologist would likely have difficulty seeing a few small rounded opacities in the presence of pneumonia, even if the radiologist were looking for them),

(4) the likelihood appears low that in a routine autopsy a pathologist would detect a few silicotic nodules in the lung unless he was looking for them, and

(5) autopsy rates in the general population are very low so that such putative silicosis would not likely be detected because of the rarity of an autopsy. (Hospital autopsy rates have decreased from 41 percent in 1960 to 5 percent in 1997 due partly to the cost. Coroners, however, do a goodly number of autopsies.)

Silicosis is also under-recognized and undercounted among silica-exposed workers. Goodwin et al. (2003) studied a group of 177 silica-exposed New Jersey decedents whose cause of death was chronic obstructive pulmonary disease, tuberculosis, or cor pulmonale. Two expert readers re-evaluated the chest X-rays to determine the presence or absence of silicosis. The decedents had presumably had exposure to silica dust based on their industrial employment listed on the death certificate (e.g., construction, foundries). Radiographic evidence of silicosis (ILO ≥ 1/0) was found in 8.5% of this population (15 decedents). (Evidence of asbestosis was found in another 10.7% (n = 19).) (Goodwin SS, Stanbury M, Wang ML, Silbergeld E, Parker JE. 2003. Previously undetected silicosis in New Jersey decedents. Am J Ind Med 44(3):304-11.)

Comment 8. Whatever REL value is derived from occupational studies will have to be adjusted upward to account for the difference in collection efficiency between size-selective occupational

samplers and the higher collection efficiency of the sampling methodology used to predict ambient air concentrations under the air toxics hot spots program. The proposed REL is based on exposure-response data developed from studies of silicosis incidence in working populations exposed to respirable crystalline silica. The exposure values used in those studies were defined by conventional occupational health particle size-selective sampling characteristics (or converted to such gravimetric values from particle-count data). Size-selective sampling refers to the collection of particles below or within a specified aerodynamic diameter size range, usually defined by the upper 50% cut-point size (*i.e.*, 50% of particulates less than the specified aerodynamic diameter will pass through the inlet of the sampler). Size-selective sampling was developed in an effort to measure particle size fractions with some special significance (*e.g.*, health, regional deposition in the lung, visibility, source apportionment, etc.). The significance of size-selective sampling for present purposes is illustrated by Figure 2-6 below, which is taken from Volume I of U.S. EPA's Third External Review Draft of Air Quality Criteria for Particulate Matter (April 2002).

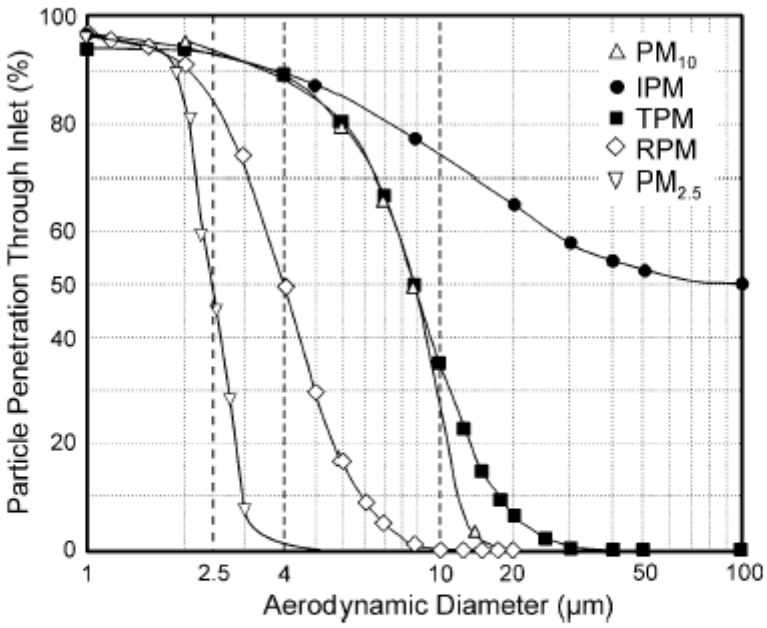

Figure 2-6. Specified particle penetration (size-cut curves) through an ideal (no-particle-loss) inlet for five different size-selective sampling criteria. Regulatory size cuts are defined in the Code of Federal Regulations; $PM_{2.5}$ (2001c), PM_{10} (2001a). $PM_{2.5}$ is also defined in the Federal Register (1997). Size-cut curves for inhalable particulate matter (IPM), thoracic particulate matter (TPM) and respirable particulate matter (RPM) size cuts are computed from definitions given by American Conference of Governmental and Industrial Hygienists (1994).

The two curves of interest in Figure 2-6 are the curve identified by upward-pointing triangles, representing the particle penetration through an ideal inlet of a PM_{10} sampler, and the curve identified by diamonds, representing the particle penetration through an ideal inlet of a respirable particulate sampler such as a cyclone pre-selector. The reason for the difference in the two curves is that the penetration of interest in PM_{10} sampling involves all particulates that might be inhaled, regardless of whether they are likely to be deposited in the extra-thoracic region, in the trachea-bronchial region or in the pulmonary region. By contrast, in studies of silicosis, only the pulmonary region of the respiratory system (alveolar space) is of interest, because it is in this region where deposited silica may initiate the silicosis disease process.

As can be seen in Figure 2-6, the 50% cut-point for an ideal PM_{10} sampler is around 10.0 micrometers aerodynamic diameter, whereas the 50% cut-point for a cyclone device would be 4.0 micrometers. For a given particulate size distribution and density, the mass contribution of these larger particles in a PM_{10} sample will overwhelm the mass collected by a cyclone sample, because the mass varies as the cube of the particle diameter. This effect may be especially pronounced when ambient air measurements are involved, because most respirable silica in ambient air falls in the range of 2.5 to 10.0 micrometers aerodynamic diameter.

In sum, ambient air measurements of respirable silica made with a PM_{10} sampler would be expected to show significantly higher concentrations of silica than measurements made in the same exact location using an occupational cyclone sampler. Because the REL is based on studies that used occupational cyclone samplers (or particle count equivalents) to derive exposure-response relationships, the REL would have to be adjusted upward to reflect the expected difference between cyclone and high volume sampler measurements if a high volume sampler (or equivalent measurement method) is used to determine whether the REL is exceeded under the Air Toxics Hot Spots program.

Our understanding is that the stack sampling and AP-42 emissions factor methodologies used to estimate ambient air concentrations under the Air Toxics Hot Spots program do not reflect the size-selective characteristics of an occupational sampler designed to measure respirable particulate. Accordingly, the Air Quality Control Districts will have to be advised of the need to adjust the REL upward so that an "apples-to-apples" comparison can be made with ambient air concentrations estimated under the Hot Spots program.

Response. *OEHHA staff is proposing a chronic inhalation REL for respirable, crystalline silica. The graph provided by the commentator shows that RPM (respirable particulate matter) as defined by the NIOSH sampler has a 50% cut point at 4 µm based on an ACGIH document (1994), while PM_{10} has a 50% cut point of 9 µm based on the Code of Federal Regulations. Hnizdo and Sluis-Cremer (1993) based their study on silica particle measurements similar to that of the NIOSH sampler. The implication for the cREL is that using the silica content of PM_{10} as the measurement of near-source ambient concentration resulting from Hot Spot facility emissions includes many larger silica particles that probably do not get into the deep lung and thus do not purportedly contribute to silicosis, but they inflate the Hazard Index.*

OEHHA staff agrees that the silica particles should be 'respirable'. California EPA defines 'respirable' as particles 10 µm or less in MMAD. The selection of the 10 µm or less MMAD criterion is consistent with this intention, and also reflects the fact that this type of

sampler (for "PM_{10}") is the one used for ambient air sampling in the general environment. Colleagues in the California Air Resources Board advise us that the NIOSH-specified personal samplers used in many occupational studies have not been validated for the combination of sensitivity, sampling duration, and operating conditions required for environmental measurements.

We agree that 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. The NIOSH samplers used in the epidemiological studies captured particles in a size range where the median of the distribution was 4 µm; thus half the particles were larger than 4 µm. These samplers are meant to mimic the size range of particles that reach into the bronchiolar and alveolar spaces (what the occupational community calls respirable). PM_{10} samplers are meant to capture particles that deposit along the entire respiratory tree including those that deposit in the tracheobronchial, and alveolar regions. Deposition by particle size is complex, and is dependent on the aerodynamic diameter, hygroscopicity, and electrostatic charge of the particles, and on a number of host factors including airway structure and geometry, as well as depth, rate, and mode of breathing (nasal vs. oronasal). The fractional deposition in the various regions of the respiratory tract is not linear with respect to size. Generally, though, larger particles impact higher in the respiratory tree (the extrathoracic and tracheobronchial regions), while smaller particles show greater deposition in the lower tracheobronchial and alveolar regions.

There are a number of models of regional deposition in the respiratory tract as well as some measurements. Chan and Lippman (1980) showed peak alveolar deposition for particles about 3 µm MMAD with deposition dropping above and below that. Their data and model indicate tracheobronchial deposition rises rapidly above about 3 µm MMAD. Data also indicate significant interindividual variability in fractional deposition. The ICRP (1994) model used in evaluating risk from radioactive particles indicates that total deposition in the respiratory tract for particles 3 µm in activity median thermodynamic diameter (AMTD) is about 0.78 with a regional deposition fraction of 0.077 for the alveolar region for a reference male worker during nasal breathing. The same model predicts a total deposition in the respiratory tract of 0.77 for 10 µm AMTD particles and a deposition fraction of 0.024 in the alveolar region. Clearly 10 µm particles get into the alveolar space. A smaller difference in regional deposition is predicted for mouth breathers. Therefore, if only the size range measured by the samplers used in the studies were considered, the measurement might underestimate the amount of silica that is deposited in the gas exchange regions of the lung, depending on the actual particle size distributions in the occupational studies and in the environments in which the REL is to be applied. Unfortunately, neither the occupational nor the environmental silica particle size distributions are known; measurements have been reported only in terms of PM_4 or PM_{10} cutoff values. Although it is frequently assumed that the silicosis is induced by that fraction of the silica that reaches the alveolus, we do not have data clearly indicating that there is no concern for the coarser fraction of particles captured by PM_{10} measurements.

Another complication in determining what particle size range to which the REL should apply is the fact that we do not have data on the particle size distribution from all the epidemiological studies or from sources of crystalline silica in the ambient air from facilities in

the Hot Spots program. It is unfortunate that we do not have better data on the particle size distribution of various sources of crystalline silica particles. That would allow a more certain comparison between typical ambient source exposures that the Hot Spots program would evaluate (e.g., diatomaceous earth processing plants, quarries, mines) with occupational sources such as the mines evaluated in the studies. It seems likely that the industrial sources of concern produce smaller crystalline silica particles than blowing crustal material.

All things considered, although the fractional deposition of coarser particles is less in the lower airway, such particles clearly can enter the bronchioles and alveoli. OEHHA staff does not believe that applying the chronic REL to silica captured in a PM_{10} sampler (or to modeled concentrations of PM_{10} crystalline silica) will result in a gross overestimation of the hazard index from industrial sources of silica.