MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

To: Files for Amorphous Silica Compounds:
Fused Silica (CAS No. 60676-86-0)
Silica Fume (CAS No. 69012-64-2)
Diatomaceous Earth (CAS No. 61790-53-2)
Pyrogenic or Fumed Silica (CAS No. 112945-52-5)
Precipitated Silica and Silica Gel (CAS No. 112926-00-8)

From: Cathy Simon, Air Quality Division

Date: July 3, 2013

Subject: Initial Threshold Screening Level for Amorphous Silica Compounds

The initial threshold screening level (ITSL) for the amorphous silica compounds listed above is 60 µg/m^3 based on an 8-hour averaging time. Background information, supporting data, and the basis for these screening levels are provided below.

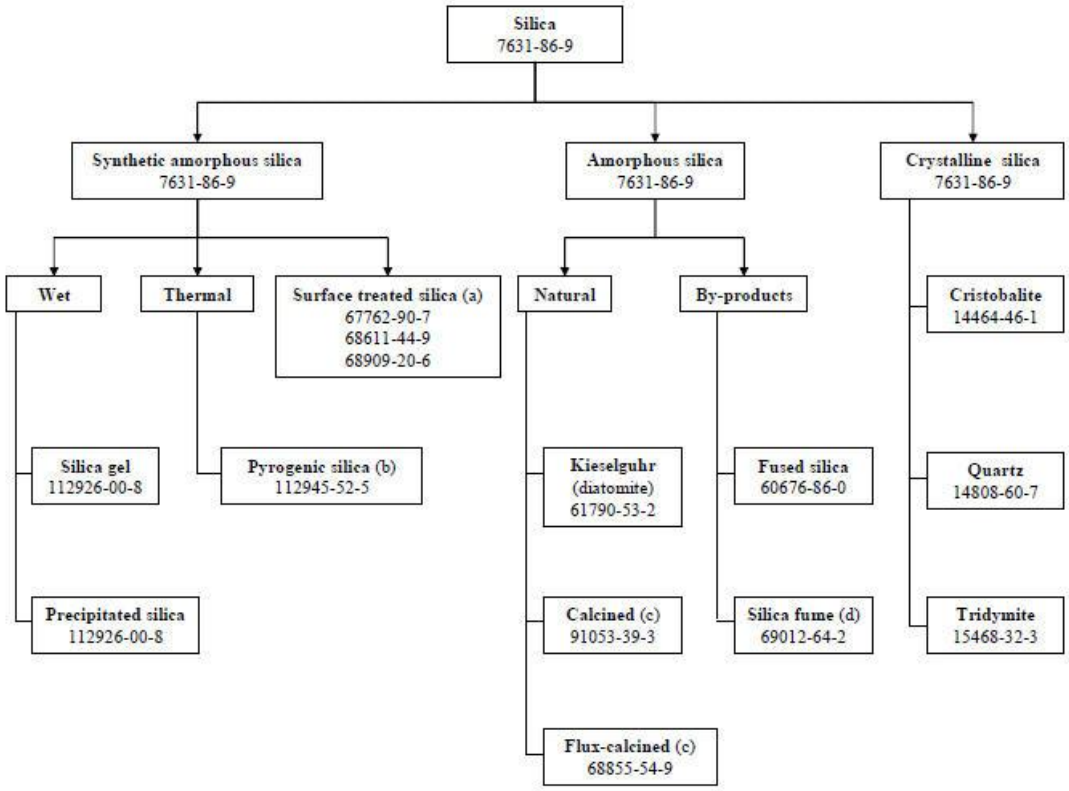
Background Information

The term "silica" refers to the compound silicon dioxide (SiO_2), and can occur naturally in a crystalline or amorphous form. Natural forms of amorphous silica include biogenic forms and silica glass of volcanic origin. One biogenic form is diatomaceous earth which consists of fossilized remains of diatoms, a type of phytoplankton with cell walls made from silica. Diatomaceous earth can also be thermally treated to produce calcined or flux calcined diatomaceous earth. Natural diatomaceous earth typically contains small amounts of crystalline silica, but calcined diatomaceous earth can contain significantly more crystalline silica. Other biogenic forms of amorphous silica are found in various plants such as sugar cane or rice, which produce fibers of amorphous silica.

Synthetic amorphous silica can be divided into two groups, based upon the manufacturing process. Silica gel and precipitated silica are produced from a wet based manufacturing process and pyrogenic silica from a thermal based process. These types of synthetic amorphous silica are generally hydrophilic, but may be surface treated to produce hydrophobic forms of amorphous silica. Synthetic silica is typically free of crystalline silica (ECETOC, 2006).

The Chemical Abstract Services (CAS) number for silica, independent of its form (crystalline or amorphous) is 7631-86-9. Other CAS numbers have been assigned to specific forms of silica as shown in Figure 1 taken from the European Centre for Ecotoxicology and Toxicology of Chemicals document on amorphous silica (ECETOC, 2006).

Figure 1: CAS Numbers for different forms of silica (ECETOC, 2006)



(a) All forms of SAS can be surface-treated either physically or chemically; most common treating agents are organosilicon compounds (Appendix B: Table B.2)
(b) Pyrogenic silica is also known as fumed silica in the English speaking countries
(c) Partial transformation into cristobalite
(d) By-product from electrical furnace

The Air Quality Division has previously established ITSLs for several forms of amorphous silica. All of these ITSLs were derived by dividing the Threshold Limit Value (TLV) adopted by the American Conference for Governmental Industrial Hygienists (ACGIH) by a factor of 100. The ITSLs and relevant ACGIH TLVs are listed in Table 1.

Table 1: Previous ITSLs for Amorphous Silica

Name	CAS No.	ITSL ($\mu g/m^3$)	Averaging Time	ACGIH TLV (mg/m^3)	Date ITSL Established
Fused silica	60676-86-0	1	8-hour	0.1	January 2000
Silica fume	69012-64-2	20	8-hour	2	September 1993
Precipitate and Gel	112926-00-8	100	8-hour	10	September 1993
Fumed (pyrogenic)	112945-52-5	20	8-hour	2	September 1993

In 2006, the ACGIH withdrew the TLVs for the above amorphous silica compounds, citing insufficient data as the basis for this change (ACGIH, 2012). As a result of this move by the ACGIH, a review was undertaken to determine if data were available to set an ITSL using an alternative basis to the ACGIH

TLV. This evaluation did not include an independent review of all relevant scientific literature, but relied primarily on reviews done by various organizations such as the US Environmental Protection Agency (EPA), International Agency for Research on Cancer (IARC), Texas Commission on Environmental Quality (TCEQ), and European Centre for Ecotoxicology and Toxicology (ECETOC). Information from these and other sources, as well as the findings of the evaluation are presented below.

While the ACGIH has withdrawn its TLVs for all forms of amorphous silica, the National Institute of Occupational Safety and Health (NIOSH) and the Occupational Safety and Health Administration (OSHA) have maintained existing occupational exposure levels.

The current NIOSH recommended exposure level (REL) of amorphous silica is 6 mg/m^3 (NIOSH, 2013). The NIOSH Pocket Guide to Chemical Hazards uses the CAS number 7631-86-9 for this REL. As previously mentioned, this CAS number is for all silica, independent of the form. The synonyms and trade names listed with the amorphous silica REL include the following: diatomaceous earth, diatomaceous silica, diatomite, precipitated amorphous silica, silica gel, and silicon dioxide (amorphous).

The current OSHA permissible exposure level (PEL) for amorphous silica is based upon an algorithm that takes into account the percent of silica present in the material of concern. The PEL is as follows:

$$\text{OSHA PEL} = \frac{80\ mg/m^3}{\%\ SiO_2}$$

When 100 % amorphous silica is present, the OSHA PEL is 0.8 mg/m^3.

Other than occupational exposure limits, no inhalation health benchmark values were identified from any federal governmental agency. The US EPA has reviewed the available epidemiological and toxicological data for crystalline and amorphous silica (EPA, 1996). While the EPA used the human epidemiology data for crystalline silica to quantify health risks, no such evaluation, using either human or animal data, was done for amorphous silica. The IARC has reviewed the carcinogenicity data for amorphous silica, finding inadequate evidence in humans and experimental animals. Overall, the IARC concluded that amorphous silica is not classifiable as to its carcinogenicity to humans (IARC, 1997).

The Wisconsin Department of Natural Resources (WDNR) recently conducted a survey of states, and found that three states, Michigan, Texas, and Vermont, had established health benchmark levels for amorphous silica (WDNR, 2011). The Vermont Agency of Natural Resources has set health benchmark values with annual averaging times of 24 $\mu g/m^3$ and 0.02 $\mu g/m^3$ for diatomaceous earth (CAS No. 61790-53-2) and fused silica (CAS No. 60676-86-0), respectively (VANR, 2007). Both of these values were derived by dividing the respective ACGIH TLV by an uncertainty factor and time adjustment factor. The Texas Commission on Environmental Quality (TCEQ) has established a short term health benchmark value (acute ReV) of 91 $\mu g/m^3$ (1-hour averaging time) and a long term health benchmark value (chronic ReV) of 6.6 $\mu g/m^3$ (annual averaging time) for several forms of amorphous silica. Both of these values were derived from animal toxicity data (TCEQ, 2011) and are discussed below in more detail.

Derivation of the ITSL

The human data evaluating the effects of amorphous silica have been reviewed by Merget et al (2002). This review indicates pneumoconiosis occurs among diatomaceous earth workers, but has been attributed to the contamination of diatomaceous earth with crystalline silica. Pneumoconiosis has also been found in workers exposed to silica fume in the ferrosilicon industry, however, silica fume may also contain crystalline silica. Intentionally manufactured amorphous silica is not contaminated with crystalline silica.

Merget et al (2002) generally found no silicosis in the few epidemiological studies with long term exposure to intentionally manufactured synthetic silica known to be free of crystalline silica, except for one study in which 4/28 workers were identified with silicosis. Merget et al (2002) stated that the authors of this study couldn't exclude contamination by small amounts of crystalline silica. Epidemiological data on other pulmonary effects such as chronic bronchitis, COPD, or emphysema were too limited to draw conclusions regarding the effect of exposure to amorphous silica (Merget et al, 2002). The available human data are not adequate to use for derivation of an ITSL for amorphous silica.

Animal toxicity data has been reviewed by Merget et al (2002), the US EPA (1996), the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC, 2006), and the TCEQ (2011). The primary effect found in these studies from exposure to amorphous silica is pulmonary inflammation and cytotoxicity. Typically, the effects tend to resolve when exposure is terminated, unlike exposure to crystalline silica, in which effects can progress even after exposure is stopped.

The TCEQ (2011) has done the most recent review of the toxicological data for amorphous silica, including the derivation of acute and chronic health benchmark values. Because these health benchmark values could be relevant to the derivation of an ITSL for amorphous silica, they are reviewed below in more detail.

As stated above, the TCEQ health benchmark values for amorphous silica were derived from animal studies, as the human data were considered limited and not adequate for this purpose (TCEQ, 2011). With regards to derivation of the acute health benchmark value, the TCEQ found that no relevant toxicity data were available for silica fume, fused silica, or diatomaceous earth. Data on animal studies using synthetic amorphous silica were, however, adequate to derive an acute health benchmark value. As a policy decision, the TCEQ uses the health benchmark values derived from synthetic amorphous silica for silica fume, fused silica and diatomaceous earth.

The TCEQ (2011) identified a study by Warheit et al (1995) as the key study for derivation of the acute health benchmark value. Two additional animal toxicity studies (Arts et al, 2007; Lee and Kelly, 1992) were also identified as supporting studies. In the study by Warheit et al (1995), groups of 24 CD rats were exposed to Zeofree 80 (precipitated silica), cristobalite, or Minusil (crystalline quartz) for 6 hr/day for 3 days. Dose levels were 10 and 100 mg/m^3 for the rats exposed to Zeofree 80 and cristobalite, and 100 mg/m^3 only for the Minusil exposed rats. Pulmonary inflammation and cytotoxicity was evaluated 24 hours, 8 days, 30 days and 3 months post-exposure by analyzing bronchioalveolar lavage (BAL) fluids for cell content and levels of lactate dehydrogenase (LDH), N-acetyl glucosaminidase (NAG), and protein levels. In a separate experiment, rats were exposed to 10, 50, and 150 mg/m^3 Ludox (colloidal silica) for 6 hour/day, 5 days/week, for 2 or 4 weeks. BAL fluids were analyzed immediately following the 2- and 4-week exposure periods, and 3 months after the 4-week exposure period.

At 24 hours post-exposure, pulmonary inflammation, as indicated by the presence of granulocytes (primarily neutrophils) in BAL fluids, was present in all of the 3-day exposure groups for both crystalline and amorphous silica. The percentage of granulocytes, estimated from a figure in the study results, ranged from a low of approximately 35% for the group exposed to 10 mg/m^3 cristobalite, to a high of greater than 50% for the group exposed to 100 mg/m^3. Zeofree, with control levels of zero percent. At 8 days post-exposure, the percentage of granulocytes in both Zeofree exposed dose groups were similar to the control groups, while the crystalline silica groups remained elevated at 3 months post-exposure. In the Ludox exposed rats, a significantly increased number of lavaged granulocytes were observed after 2 and 4 weeks in the two highest dose groups, but not in the lowest dose group; these numbers were significantly decreased following a 3-month recovery period (Warheit, et al, 1995).

LDH and protein levels in the BAL fluids were increased within 24 hours post-exposure for all 3-day exposure groups, and returned to control levels by 8 days post-exposure in the Zeofree groups, but remained elevated 3 months post-exposure in the crystalline silica groups. NAG values for the Zeofree groups appeared to be slightly elevated 24 hours post-exposure based on results provided in a figure, but did not differ from control values by 8 days post-exposure, whereas the crystalline silica groups remained elevated 3 months post-exposure. In the Ludox exposed rats, LDH and protein in the BAL fluids were significantly increased only in the 150 mg/m^3 dose group, immediately following exposure; however, these levels were not significantly increased following a three month recovery period. A lowest observed adverse effects level (LOAEL) of 10 mg/m^3 for Zeofree 80 (3-day exposure), and a no observable adverse effect level (NOAEL) of 10 mg/m^3 for Ludox (4-week exposure), were identified from this study (Warheit, et al, 1995).

The TCEQ (2011) used the LOAEL of 10 mg/m^3 for Zeofree 80 (6 hours/day, 3-day exposure) to derive the acute ReV. This value was first adjusted to a 1-hour exposure time period using Haber's Rule as modified by ten Berge, as follows: $(C_1^n \times T_1 = C_2^n \times T_2)$, with a default value of n = 3, as per guidelines in TCEQ (2012). The TCEQ also "chose to adjust the exposure from 6 h/d to 1 h/d rather than adjusting the total duration of exposure in the study over the 3 days of exposure (i.e., 6 h/d for 3 days = 18 h to 1 h) in consideration of protecting against intermittent exposure and the possibility of delayed inflammation" (TCEQ, 2011). This adjustment resulted in an adjusted point of departure (POD_{ADJ}) value of 18.2 mg/m^3 as follows:

$$C_2 = [(C_1)^3 \times (T_1/T_2)]^{1/3} = POD_{ADJ} = [(10\ mg/m^3)^3 \times (6\ h/1\ h)]^{1/3} = 18.2\ mg/m^3$$

To account for dosimetric differences between the rat and humans, the TCEQ derived a regional deposition dose ratio (RDDR), with the tracheobronchial and pulmonary regions identified as the target regions. Because the mass median aerodynamic diameter (MMAD) was given as a range in the study by Warheit et al (1995), the resulting RDDR ranged from 1.001 – 1.060. The TCEQ selected the lower end of the range to calculate the human equivalent concentration (HEC) for the POD as follows:

$$POD_{HEC} = POD_{ADJ} \times RDDR = 18.17\ mg/m^3 \times 1.001 = 18.19\ mg/m^3$$

The POD_{HEC} was then divided by uncertainty factors (UF) to account for extrapolation from a LOAEL to NOAEL (UF_L), animal to human extrapolation (UF_A), intraspecies variability (UF_H), and data base uncertainties (UF_D) to derive the acute ReV as follows:

$$\text{Acute ReV} = POD_{HEC}/(UF_L \times UF_A \times UF_H \times UF_D)$$

$$\text{Acute ReV} = 18.19\ mg/m^3/(2 \times 3 \times 10 \times 3)$$

$$\text{Acute ReV} = 91\ \mu g/m^3 \text{ (rounded to two significant figures)}$$

While the acute ReV derived by the TCEQ is consistent with their guidelines and policies and could be considered as a possible acute ITSL, other alternative acute health benchmark values could also be derived from the same key study. In particular, the TCEQ adjusted the study duration of 6 hours/day for 3 days to a 1-hour exposure time, considering only 6 hours of total exposure, not 18 hours, and using a default value (n = 3) in the algorithm based on Haber's Rule. Alternatively, the LOAEL could be used as the POD with no adjustment. Additionally, a data base uncertainty factor of 3 was used to account for the lack of acute studies in other species. Alternatively, no database uncertainty factor could be used. Lastly, an alternative value of 3 could be used for the LOAEL to NOAEL uncertainty factor. Using these alternatives to derive a potential acute ITSL would result in the following:

$LOAEL_{HEC}$ = LOAEL x RDDR = 10 mg/m^3 x 1.001 = 10 mg/m^3 (rounded to two significant figures)

$ITSL_{Acute} = LOAEL_{HEC}/(UF_L \times UF_A \times UF_H)$

$ITSL_{Acute}$ = (10 $mg/m^{3)}$/(3 x 3 x 10) = (10 mg/m^3)/(100) = 0.1 mg/m^3 = 100 $\mu g/m^3$

In the above algorithm and others presented in this document, uncertainty factors of 3 represent the rounded value of $10^{1/2}$, so that when two uncertainty factors with a value of 3 are multiplied ($10^{1/2}$ x $10^{1/2}$), the resulting value is 10.

Use of an 8-hour averaging time with the above potential acute ITSL could be used considering the actual exposure was 6 hours/day. The 8-hour averaging time would be consistent with the averaging time used for many ITSLs, and would also provide some adjustment for the consideration of 3 days exposure. The above potential acute ITSLs are considered further in the section below on derivation of the final ITSL.

As with the acute ReV derived by the TCEQ (2011), the human data relating to longer durations of exposure were also considered not adequate to derive a chronic ReV for amorphous silica. Animal studies using synthetic amorphous silica were adequate to derive a chronic ReV, but relevant toxicity data were not available for silica fume, fused silica, or diatomaceous earth. Therefore, as a policy decision, the chronic ReV derived from data for synthetic amorphous silica is used by TCEQ for all forms of amorphous silica (TCEQ, 2011).

The TCEQ identified a study by Groth et al (1981) as the key study for derivation of the chronic ReV, and a study by Reuzel et al (1991) as a supporting study. In the study by Groth et al (1981), groups of male Sprague Dawley rats (80/group), Hartley guinea pigs (20/group), and Cynomolgus monkeys (10/group) were exposed by inhalation to three different forms of amorphous silica (fume, gel, and precipitated) at targeted concentrations of 15 mg/m^3 for 5.5 – 6 hours per day. Rats were sacrificed after 3, 6, and 12 months of exposure, and guinea pigs after 12 months of exposure. The monkeys exposed to the silica fume and gel were sacrificed after 13 months exposure, and the monkeys exposed to precipitated silica after 18 months of exposure. The difference in sacrifice times was because the measured respirable levels (defined as < 4.7 µm in size) of silica was lower in the precipitated silica group (6.9 mg/m^3) vs. the fume (9.9 mg/m^3) and gel (9.4 mg/m^3) groups. The longer exposure duration for the precipitated silica group provided for similar exposure for all three groups when based upon total respirable dust dose (Groth et al, 1981).

Of the three species tested, monkeys were more sensitive to the effects of exposure to amorphous silica than the rats or guinea pigs. Pathological effects were limited to the lungs of all animals. Macrophage and mononuclear cell aggregates in the lung were observed in all three silica exposed groups of monkeys, with more and larger aggregates occurring in the precipated silica group, slightly fewer and smaller in the silica fume group, and much less and smaller ones in the silica gel group. Reticulin fibers were present in the aggregates of all three groups; however, collagen was present in significant amounts only in the silica fume exposed group. Pulmonary function tests were most impacted in the silica fume group of monkeys, with significant differences between exposed and control groups for both ventilatory mechanics and lung volume parameters. In the precipated silica group, some of the lung volume parameters were significantly lower than controls, and in the silica gel group, significant effects were observed on some of the ventilatory mechanic parameters. In the rat and guinea pig silica exposed groups, the only significant effect noted was the presence of macrophage aggregates in the lungs, which were far fewer and smaller compared to those seen in the monkeys (Groth et al, 1981). The exposure concentration of 15 mg/m^3 was considered a free standing LOAEL (TCEQ, 2011).

In the supporting study by Reuzel et al (1991), groups of 70 male and female Wistar rats were exposed to three types of amorphous silica (Aerosil 200 – a hydrophilic fumed silica; Aerosil R 974 – a hydrophobic fumed silica; and Sipernat 22S – a precipitated silica) for 6 hours/day, 5 days/week for 13 weeks. The target concentrations for the Aerosil 200 exposed animals were 1 mg/m^3, 6 mg/m^3, and 30 mg/m^3, whereas the Aerosil R 974 and Sipernat 22S exposed animals consisted of a single exposure group of 30 mg/m^3. Immediately following exposure, 20 rats/sex/group were sacrificed. Additional sacrifices occurred at 13, 26, 39, and 52 weeks post-exposure, consisting of 10, 10, 10, and 20 rats/sex/group, respectively.

Adverse effects in the lung were observed in all amorphous silica exposed groups. In the 30 mg/m^3 dose groups, Aerosil 200 produced the severest effects, followed by Aerosil R 974, and lastly Supernat 22S where effects were much milder. Adverse effects in the lung were dose related in the three Aerosil 200 exposure groups, however, even the lowest dose resulted in some adverse effects. In the 1 mg/m^3 dose group, lung collagen was significantly increased in male rats, and the following effects were significantly increased in both male and female animals: accumulation of alveolar macrophages, intra-alveolar polymorphonuclear leucocytic infiltration, and septal cellularity (seen as an increase in the number of type II pneumocytes and macrophages within the alveolar walls).

The TCEQ (2011) concluded that rats exposed to the targeted concentration of 1 mg/m^3 of Aerosil 200 in the Reuzel et al (1991) study "showed signs of mild and transient inflammatory response and other pulmonary effects", but considered this concentration to be a NOAEL. In contrast, the ECETOC (2006) concluded that the dose level of 1 mg/m^3 for this same study was a LOAEL. It should be noted that while the targeted concentration for the lowest dose group of Aerosil 200 in the Reuzel et al (1991) study was 1 mg/m^3, the measured concentration was actually 1.3 mg/m^3.

To derive the chronic ReV, the TCEQ used the LOAEL of 15 mg/m^3 from the Groth et al (1981) study as a POD, and then adjusted this value as follows to account for discontinuous exposure:

POD_{ADJ} = POD x 6 hours/24hours x 5 days/7days

POD_{ADJ} = 15 mg/m^3 x 6/24 x 5/7 = 2.678 mg/m^3

The POD_{HEC} was then determined as follows:

POD_{HEC} = POD_{ADJ} x RDDR = 2.678 mg/m^3 x 0.739 = 1.98 mg/m^3

The RDDR in the above algorithm was calculated assuming the target regions to be the tracheobronchial and pulmonary regions, and using a MMAD of 3.2 µm for the fume silica.

The chronic ReV was then determined as follows:

Chronic ReV = $POD_{HEC}/(UF_L \times UF_A \times UF_H \times UF_D)$

Chronic ReV = (1.98 mg/m^3)/(10 x 3 x 10 x 1) = 0.00660 mg/m^3 = 6.60 $\mu g/m^3$

The TCEQ (2011) also derived an alternative chronic ReV in a similar manner using the supporting study of Reuzel et al (1991). Because no particle size distribution or MMAD was reported in this study, the TCEQ derived a MMAD using data from other animal studies, and used the derived value to calculate the RDDR. A total uncertainty factor of 100 was used to derive the chronic ReV from this study, which consisted of an UF_H of 10, an UF_A of 3, and an UF_{Sub} of 3 for extrapolation from subchronic to chronic exposure. The chronic ReV derived from the Reuzel et al (1991) study was 1.7 $\mu g/m^3$. The TCEQ (2011)

selected the chronic ReV derived from the Groth et al (1981) study because it was of longer duration than the Reuzel et al (1991) study, no particle size distribution or MMAD were provided in Reuzel et al (1991), the chronic ReV of 1.7 µg/m^3 derived from Reuzel et al (1991) was lower than the TCEQ chronic ReV for crystalline silica of 2 µg/m^3, and lastly the TCEQ felt the NOAEL of 1.3 mg/m^3 from Reuzel et al (1991) was not supported by a NOAEL of 10 mg/m^3 from a subchronic exposure study by Lee and Kelly (1992).

While the chronic ReVs derived by the TCEQ could be considered as a possible chronic ITSL, other alternative chronic ITSLs could also be derived from the same key and supporting studies. Groth et al (1981) exposed three species – monkeys, rats and guinea pigs to amorphous silica by inhalation. Although monkeys were found to be the most sensitive species to the effects of amorphous silica, the TCEQ used the results from the rats to derive the chronic ReV. Alternatively, the results from monkeys could be used to derive a chronic ITSL. The preferred methodology for doing this would include derivation of a RDDR based on the data for the monkeys, however, the US EPA software available for this calculation does not include an option for use of monkey data. Because the relevant physiological parameters for monkeys would be expected to be more similar to humans than rats, an alternative would be to assume an RDDR = 1 for the monkeys (RDDR for rats = 0.739) Since the monkeys were exposed for only 1 year, which is only about 3% of their lifetime, compared to 50% of the lifetime for rats (12 out of 24 months), use of an uncertainty factor of 10 for sub-chronic exposure (UF_S) is appropriate. Lastly, the TCEQ used a value of 10 for the UF_L; alternatively, a value of 3 could be used for the UF_L. The resulting potential chronic ITSL using the monkey day would be derived as follows:

$LOAEL_{ADJ}$ = LOAEL x 6 hours/24hours x 5 days/7days

$LOAEL_{ADJ}$ = 15 mg/m^3 x 6 hours/24hours x 5 day/7days = 2.7 mg/m^3

$LOAEL_{HEC}$ = $LOAEL_{ADJ}$ x RDDR = 2.7 mg/m^3 x 1 = 2.7 mg/m^3

ITSL = $LOAEL_{HEC}$ /(UF_L x UF_H x UF_A x UF_S)

ITSL = (2.7 mg/m^3)/(3 x 10 x 3 x 10) = 0.0027 mg/m^3 = 2.7 µg/m^3

With regards to the Reuzel et al (1991) study, while TCEQ (2011) identified the lowest dose of 1.3 mg/m^3 as a NOAEL, alternatively, it could be considered a LOAEL as discussed above. Using this value as a LOAEL and including a UF_L of 3, while maintaining the TCEQ (2011) derived RDDR and other uncertainty factors, would result in a potential chronic ITSL of 0.6 µg/m^3 as derived below:

$LOAEL_{ADJ}$ = LOAEL x 6 hours/24hours x 5 days/7days

$LOAEL_{ADJ}$ = 1.3 mg/m^3 x 6/24 x 5/7 = 0.232 mg/m^3

$LOAEL_{HEC}$ = $LOAEL_{ADJ}$ x RDDR = 0.232 x .715 = 0.166 mg/m^3

ITSL = ($LOAEL_{HEC}$)/(UF_L x UF_A x UF_S x UF_H)

ITSL = (0.166 mg/m^3)/(3 x 3 x 3 x 10) = 0.0006 mg/m^3 = 0.6 µg/m^3

Considering the TCEQ (2011) derived acute and chronic ReVs as potential ITSLs, as well as alternative acute and chronic ITSLs as discussed above, would result in the following ranges for these values:

Acute ITSL = 91 $\mu g/m^3$ (one hour averaging time) – 100 $\mu g/m^3$ (8-hour averaging time).

Chronic ITSL = 0.6 $\mu g/m^3$ – 6.6 $\mu g/m^3$ (annual averaging time).

While the above potential ITSLs for amorphous silica are all derived from animal toxicity studies, alternatively, Rule 232(1)(c) of the Michigan Air Pollution Control Rules specifies that the ITSL may be determined by diving the NIOSH REL or ACGIH TLV by a factor of 100. Using the current NIOSH REL of 6 mg/m^3 for amorphous silica would result in an ITSL of 60 $\mu g/m^3$, with an 8-hour averaging time as specified in Rule 232(2)(a) of the Michigan Air Pollution Control Rules.

In an effort to compare all of the above potential ITSLs it is useful to standardize them to a single averaging time. One way to do this would be to use the scaling factors from the US EPA Screen 3 dispersion model for converting a modeled one hour concentration to longer averaging times. The scaling factors from Screen 3 include a factor of 0.7 for a 1-hour to 8-hour averaging time conversion and a factor of 0.08 for a 1-hour to annual averaging time conversion. This exercise assumes a modeled impact equivalent to the potential acute based ITSLs, and then using the above scaling factors to determine the annual average concentrations. Table 2 provides the scaled concentrations for the potential ITSLs. Information from Table 2 suggests that if an emission source had a modeled impact equivalent to the potential acute based ITSLs (1-hour or 8-hour averaging times), the annual average concentration would be in the range of 7 – 11 $\mu g/m^3$.

Table 2: Potential ITSLs Scaled to Annual Averaging Time

Basis for Potential ITSL	Potential ITSL ($\mu g/m^3$)	Averaging Time	Potential ITSL ($\mu g/m^3$) Scaled to an Annual Averaging Time
TCEQ Acute ReV	91	1-hour	7
Alternate Acute from Warheit et al (1995)	100	8-hour	11
NIOSH REL	60	8-hour	7
TCEQ Chronic ReV	6.6	Annual	6.6
Alternate Chronic from Groth et al (1981)	2.7	Annual	2.7
Alternate Chronic from Reuzel et al (1991)	0.6	Annual	0.6

In determining the ITSL for amorphous silica, it is informative to compare the range of potential ITSLs for this compound to available health benchmark values for crystalline silica. Two states, California and Texas, have established health benchmark values for crystalline silica that also include a review of the scientific literature and documentation for the basis of the health benchmark value. The California Office of Environmental Health Hazard Assessment (OEHHA) has established a chronic reference exposure level of 3 $\mu g/m^3$ (annual averaging time) for crystalline silica. The TCEQ has established an acute ReV of 41 $\mu g/m^3$ (1-hour averaging time) and a chronic ReV of 2 $\mu g/m^3$ (annual averaging time) for crystalline silica. The US EPA does not have an inhalation reference concentration for crystalline silica, but has concluded the following:

> Thus, current data suggest that, for healthy individuals not compromised by other respiratory ailments and for ambient environments expected to contain 10% or less crystalline silica fraction in PM_{10}, maintenance of the 50 $\mu g/m^3$ annual NAAQS for PM_{10} should be adequate to protect against silicotic effects from ambient crystalline silica exposures (EPA, 1996).

Based on the above finding by the US EPA, a chronic health benchmark value of 5 µg/m^3 can be inferred for crystalline silica. It should also be noted that the US EPA, California OEHHA, and TCEQ chronic health benchmark values for crystalline silica were all derived from human data. Considering that: 1) the effects from exposure to amorphous silica are expected to be less severe than from exposure to crystalline silica; 2) the data do not indicate that effects from amorphous silica occur at significantly lower exposure levels than crystalline silica; and 3) the crystalline silica chronic health benchmark values are derived from human data compared to animal data for amorphous silica health benchmark values, would suggest that the health benchmark value for amorphous silica should not be lower than that for crystalline silica.

One issue of concern when establishing an ITSL for amorphous silica is that adequate data are not available for all forms of amorphous silica to establish individual ITSLs for each of these forms. Only some of the synthetic forms of amorphous silica have adequate data to derive an ITSL. While this data indicates that similar types of effects are seen with exposure to the different forms of amorphous silica, the severity of effects seen at similar doses can vary. The basis for the differences in these toxicities is not known, but may be due to various things such as differing particle sizes and shapes, differences in the chemical and physical properties of the surface of the particles, or differences in trace element concentrations. As a policy decision, the TCEQ (2011) has established a single acute and chronic ReV for all forms of amorphous silica. Likewise, NIOSH has only a single REL for amorphous silica.

Considering all of the above information, the NIOSH REL based ITSL of 60 µg/m^3 (8-hour averaging time) is selected as the final ITSL for the following forms of amorphous silica: fused silica (CAS No. 60676-86-0); silica fume (CAS No. 69012-64-2); diatomaceous earth (CAS No. 61790-53-2); pyrogenic or fumed silica (CAS No. 112945-52-5); precipated silica and silica gel (CAS No. 112926-00-8). The basis for this selection includes the following: derivation of the ITSL is consistent with Rule 232(1)(c) and Rule 232(2)(a) of the Michigan Air Pollution Control Rules; the potential ITSLs based on animal toxicity data are of similar magnitude and supportive of the NIOSH REL based ITSL; and the NIOSH REL applies to various forms of amorphous silica, supporting the use of the ITSL for all of the above forms of amorphous silica. Additionally, based on the information on Table 2, compliance with this short term averaging time ITSL would result in an ambient concentration of amorphous silica in the upper end of the range for potential long term ITSLs. The upper end of this range should provide adequate protection from long term exposure to amorphous silica considering the information discussed above on health benchmark values for crystalline silica and comparative toxicity with amorphous silica.

While the ITSL of 60 µg/m^3 (8-hour averaging time) applies to all of the above listed forms of amorphous silica, alternative ITSLs for specific forms of amorphous silica may be determined on a case-by-case basis as warranted and supported by the data. Additionally, in the situation where more than one form of amorphous silica is present, the combined impact of all forms of amorphous silica with the above listed CAS numbers should meet the ITSL of 60 µg/m^3 (8-hour averaging time).

References

ACGIH. 2012. 2012 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Arts, J.H., H. Muijser, E. Duistermaat, K. Junker, and C.F. Kuper. 2007. Five-day inhalation toxicity study of three types of synthetic amorphous silica in Wistar rats and post-exposure evaluations for up to 3 months. Food Chem. Toxicol. 45:1856-1867 (Not reviewed – as cited in TCEQ, 2011).

ECETOC. 2006. Synthetic Amorphous Silica (CAS No. 7631-86-9). European Centre for Ecotoxicology and Toxicology of Chemicals. Joint Assessment of Commodity Chemicals (JACC) programme. JACC No. 51. Brussels, Belgium.

EPA. 1996. Ambient Levels and Noncancer Health Effects of Inhaled Crystalline and Amorphous Silica: Health Issue Assessment. Office of Research and Development, US Environmental Protection Agency, Washington DC. EPA/600/R-95/115. November 1996.

Groth, D.H., W.J. Moorman, D.W. Lynch, L.E. Stettler, W.D. Wagner, and R.W. Hornung. 1981. Chronic effects of inhaled amorphous silica in animals. In: Dunnom, D.D., ed., *Health Effects of Synthetic Silica Particulates*. American Society for Testing and Materials Special Technical Publication 732, pp. 118-143.

IARC. 1997. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Silica, some silicate, coal dust, and para-aramid fibrils. Vol 68. Pages 41-242.

Lee, K. P. and D. P. Kelly. 1992. The pulmonary response and clearance of Ludox colloidal silica after a 4-week inhalation exposure in rats. Fundamental and Applied Toxicology 19:399-410.

Merget, R., T. Bauer, H.U. Kupper, S. Philippou, H.D. Bauer, R. Breitstadt, T. Bruening. 2002. Health hazards due to the inhalation of amorphous silica. Arch. Toxicol. 75:625-634.

NIOSH. 2013. Pocket Guide to Chemical Hazards (Web version). Amorphous Silica. Accessed on 5/29/13. http://www.cdc.gov/niosh/npg/npgd0552.html

Reuzel, P.G.J., J.P. Bruijntjes, V.J. Feron, and R.A. Woutersen. 1991. Subchronic inhalation toxicity of amorphous silicas and quartz dust in rats. Fd. Chem. Toxic. 29:341-354.

TCEQ. 2012. TCEQ Guidelines to Develop Toxicity Factors. Texas Commission on Environmental Quality. Revised RG-442. October 2012.

TCEQ. 2011. Silica, Amorphous and Other Non-Crystalline Forms. Development Support Document. Texas Commission on Environmental Quality. July 29, 2011.

VANR. 2007. Air Pollution Control Regulations, Including Amendments to the Regulations Adopted Through: April 27, 2007. State of Vermont, Agency of Natural Resources. http://www.anr.state.vt.us/air/AirToxics/docs/apcregs.pdf

Warheit, David B., Tim A. McHugh, Mark A Hartsky. 1995. Differential pulmonary responses in rats inhaling crystalline, colloidal or amorphous silica. Scand J Work Environ Health 21 Supplement 2:19-21.

WDNR. 2011. Report to the Natural Resources Board: Silica Study. AM-407 2011. August 2011. Wisconsin Department of Natural Resources. http://dnr.wi.gov/files/PDF/pubs/am/AM407.pdf

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