MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Arsine (CAS No. 7784-42-1)

FROM: Keisha Williams, Air Quality Division

DATE: February 10, 2017

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for arsine is 0.05 µg/m^3 (annual averaging time) based on the Environmental Protection Agency's (EPA's) reference concentration (RfC) (EPA, 1994). This ITSL value was originally established by the Air Quality Division (AQD) on March 1, 1994.

The RfC is based on a no observable adverse effect level (NOAEL) at 0.025 ppm or 0.08 mg/m^3 obtained from inhalation studies in mice and rats (Blair et al., 1990a; EPA, 1994; Hong et al., 1989). The critical effects were related to hematological abnormalities: increased hemolysis, increased spleen weight and abnormal erythrocyte morphology and erythropoiesis. Although the key studies involved subchronic exposures over 3-4 months (Blair, 1990b; EPA, 1994). As shown in Equations 1 and 2, the NOAEL was adjusted for exposure duration, as well as to obtain a human equivalent concentration (HEC). An uncertainty factor (UF) of 10 was used for itraspecies variability, a UF of 3 was used for interspecies extrapolation, and a composite UF of 10 was used for data base deficiencies and for subchronic to chronic extrapolation (Equation 3).

The database deficiency uncertainty factor was deemed necessary as there is a "lack of a two-generation reproductive study" (EPA, 1994). EPA also identified an occupational exposure study which further gives uncertainty as to whether arsine may have significant developmental/reproductive effects. EPA summarized that:

> "Two processes, the "photolithurgic" process and the "diffusion" process, were investigated as potential sources of general illness and spontaneous abortions (Pastides et al., 1988). The photolithurgic process involves coating wafers with a photosensitive material containing glycol ethers and, often, xylene, toluene, and hexamethyldisilazane. The diffusion process involves heating the wafer at very high temperatures in a chamber containing arsine, phosphine, and diborane (dopants). Three groups of workers were selected for participation in this study: (1) all current workers with more than 1 month of employment in the photolithurgic area, (2) workers employed primarily in the diffusion area (but also workers from other areas exclusive of photolithurgy), and (3) administrative staff not exposed to any of the process chemicals. Spontaneous abortion ratios, defined as the number of fetal losses prior to 29 weeks gestation divided by the number of total pregnancies, were increased in both exposure groups. The spontaneous abortion ratios observed for women in the photolithurgic, diffusion, and nonexposed groups were 31.3% (5/16), 38.9% (7/18), and 17.8% (71/398), respectively. An increased relative risk of 2.18 for the diffusion group vs. the nonexposed group (95% confidence interval = 1.11-3.60) was calculated. This observation persisted even after controlling for a variety of risk factors including age at pregnancy, gravidity, consumption

of caffeine during pregnancy, smoking during pregnancy, and consumption of alcohol during pregnancy. The elevated ratio among women in the photolithurgic group was not statistically significant; however, the risk of spontaneous abortion in the photolithurgic and diffusion groups relative to the nonexposed group remained consistent, regardless of which risk factors were considered. This study was subject to several limitations. First, the authors acknowledge that many semiconductor workers have exposures to chemicals found in both the photolithurgic and diffusion areas, and workers were sometimes involved in work in both areas during their tenure with the company. Second, spontaneous abortion rates were based on a small sample size (34 pregnancies in both manufacturing groups). These limitations, along with the lack of quantifiable exposure data for any individual chemical, preclude making any kind of determination regarding the role of arsine in the observed increased spontaneous abortion rate." (EPA, 1994)

Equation 1.

$$NOAEL_{\,adjusted\ for\ duration} = NOAEL\ x \frac{study\ exposure\ hours\ per\ day}{24\ hours}\ x \frac{study\ exposure\ days\ per\ week}{7\ days}$$

$$NOAEL_{\,adjusted\ for\ duration} = 0.08 \frac{mg}{m^3}\ x \frac{6\ hours}{24\ hours}\ x \frac{5\ days}{7\ days} \approx 0.014\ \frac{mg}{m^3}$$

Equation 2.

$$NOAEL_{HEC} = NOAEL_{adjusted\ for\ duration} x \frac{gas: extrarespiratory\ effect\ in\ study\ species}{gas: extrarespiratory\ effect\ in\ humans}$$

where the ratio of gas: extrarespiratory effect values is set to a default value of 1, because the study species and human values are unknown.

$$NOAEL_{HEC} = 0.014 \frac{mg}{m^3}\ x\ 1 = 0.014 \frac{mg}{m^3}$$

Equation 3.

$$RfC = \frac{HEC}{UFs}$$

$$RfC = \frac{0.014 \frac{mg}{m^3}}{3x\ 10\ x\ 10} x \frac{1000\ \mu g}{mg} = 0.05 \frac{\mu g}{m^3}$$

References

EPA. 1994. Summary for Arsine (CASRN 7784-42-1). Integrated Risk Information System, US Environmental Protection Agency, Accessed on May 29, 2015. http://www.epa.gov/iris/subst/0672.htm

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Blair, P., M.B. Thompson, M. Bechtold, R.E. Wilson, M.P. Moorman, B.A. Fowler. 1990b. Evidence of oxidative damage to red blood cells in mice induced by arsine gas. Toxicology. 63(1): 25-34.

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MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

December 10, 1992

To: Arsine file (CAS# 7784—42—1)

From: Gary Butterfield

The interim ITSL for arsine is based on 1% of the NIOSH REL ceiling of 0.002 mg/m^3. Resulting in an ITSL of 0.02 $\mu g/m^3$ with a one hour averaging time. The ACGIH TLV for arsine is 0.16 mg/m^3 for an 8 hour period. The documentation of the TLV discusses an animal study of a few weeks, and many acute human over exposures. The human data identifies hemolysis followed by renal damage as the major adverse effects from acute over exposures to arsine.