MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

September 6, 1995

TO: File for Tungsten Carbide (CAS # 12070-12-1)

FROM: Dan O'Brien

SUBJECT: Initial Threshold Screening Level for Tungsten Carbide (WC)

The initial threshold screening level (ITSL) for pure tungsten carbide is 50 $\mu g/m^3$ based on an 8 hour averaging time. The initial threshold screening level for cemented tungsten carbide having a Co content >2%, based on the ITSL for cobalt, is 0.2 $\mu g/m^3$ based on an 8 hour averaging time. The initial risk screening level (IRSL) for cemented tungsten carbide having a Co content < 2% and a Ni content > 0.3%, based on the IRSL for nickel, is 0.0042 $\mu g/m^3$, based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: AQD chemical files, IRIS, HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP Management Status Report, EPB Library, IARC Monographs, CAS On-line and NLM/Toxline (1967 - February 3, 1995), CESARS, Handbook of Environmental Data on Organic Chemicals, Patty's Industrial Hygiene and Toxicology, Merck Index and Condensed Chemical Dictionary.

Tungsten (W) is a grey, hard, brittle, metal (ACGIH, 1992). Its commercially important compounds are divided by the American College of Governmental Industrial Hygienists (ACGIH) into water-insoluble compounds (of which tungsten carbide is one, along with the sulfide, carbonyl, silicide and oxide, and tungstic acid) and the soluble compounds (including tungsten chloride, fluoride and oxychloride). The major uses of tungsten are in cutting and wear-resistant materials (65%), mill products (12%), specialty steels, tools, stainless, and alloys (9%), hard-facing rods (8%), super alloys (3%), and chemicals (2%) (Beliles, 1994). Tungsten carbide specifically is employed as an abrasive and in cemented carbide tools, dies, and wear-resistant parts.

Most of the research on the physiological effects of tungsten followed the commercialization of cobalt-cemented WC, and consequently, most of the human toxicological literature deals with exposure to cemented WC, rather than tungsten and its compounds themselves (NIOSH,1977), all of which has blurred the true toxicity of tungsten (Beliles, 1994). The few determinations of toxicity of tungsten and its compounds not associated with hard metal clearly showed a difference between soluble and insoluble compounds, the soluble compounds being distinctly more toxic. These investigations were conducted almost exclusively in animals, and the occupational effects from the soluble compounds of tungsten are virtually unkown (ACGIH, 1992; NIOSH, 1977).

Pure tungsten carbide is the major component of the metal mixture known as "cemented" tungsten carbide, also known as "hard metal". Hard metal is produced by powder metallurgy from tungsten and carbon, with cobalt (Co) used as a binding (or "cementing") agent. Other metals such as tantalum, titanium, vanadium, molybdenum, nickel, niobium and chromium may also be added (Beliles, 1994; NIOSH, 1977). Typically, cemented WC contains 80-90% WC, 8-18% Titanium carbide (TiC), and 5-25% Co (Beliles, 1994). The distinction between pure WC and cemented WC is critical from a toxicological standpoint, since the vast weight of evidence from human occupational studies suggests that pure WC is probably responsible for little of the toxicity attributable to cemented WC (Morgan, 1984); the evidence supports Co as being the predominant causal agent. The clinical manifestations of cemented WC exposure, also known as "hard metal disease", consist of a variety of adverse respiratory effects ranging from simple upper respiratory irritation to chronic obstructive pulmonary disease due to interstitial fibrosis. The most sensitive endpoint in the hard metal disease syndrome is the occurrence of bronchial hypersensitivity reactions due to cobalt exposure in sensitized individuals, or "cobalt asthma". The ITSL derivation for cobalt (7440-48-4) contains an extensive discussion of hard metal disease, with emphasis on the immunological aspects underlying cobalt asthma and the evidence of causal associations between hard metal disease and cobalt. The interested reader is referred to that document for more information, as well as to the extensive discussion on occupational hard metal exposures summarized in the National Institute For Occupational Safety and Health (NIOSH) criteria document (NIOSH, 1977). Skin disorders have also been reported in hard metal workers, but again, Co, rather than WC, has been been implicated as the cause (Beliles, 1994).

In addition, laboratory animal studies lend support to the relatively minor effect of WC on the development of pulmonary fibrosis in hard metal disease, compared to the effects of Co or mixtures of WC and Co. Some fairly recent studies have attempted to assess the separate contributions of WC and Co to the pulmonary toxicity of cemented WC. An abstract by Costa and coworkers (1990) describes their work, in which groups of 24 ten week-old F344 rats were exposed for thirteen weeks (six hours/day, five days/week) to clean air, Co dust (at 1 mg/m^3), WC (at 15 mg/m^3) or a WC-Co combination (at 1 mg Co and 15 mg WC/m^3). Exposures were chosen to simulate the common ratio of WC and Co found in an occupational setting (cutting and grinding tool production); mass median aerodynamic diameter (MMAD) of the generated particles was $\approx$ 4.1 μm (σ_g = 1.9). Six days after the final exposure, each rat underwent a series of pulmonary function tests which included assessments of lung volumes, static and dynamic mechanics, and carbon monoxide diffusing capacity. Following termination, lungs were excised and prepared for histopathological and compositional examination, including dry lung weights, total hydroxyproline and elastin, and total tissue protein and DNA. There were no significant effects on lung function in any group. Small increases in hydroxyproline and elastin were noted in the Co and WC-Co groups, along with increases in wet and dry lung weights (~12%) and (to a lesser extent) protein increases which were disproportionate to increases in DNA content. The WC and WC-Co groups exhibited some evidence of end airway inflammation, accompanied by mild to moderate interstitial thickening, in excess of that seen with Co alone. The authors concluded that there was no evidence of toxic interaction between WC and Co on any of the studied endpoints. Conversely, Lasfargues *et al.* (1992) found the acute lung toxicity of WC-Co mixtures to be much higher than that of the individual components, and Co significantly more toxic than WC alone. In this study, groups of ten female Sprague-Dawley rats, 2-3 months old, were intratracheally injected with sterile saline (negative control), WC (15.67 mg/100 g body weight; median particle size (d_{50}) = 2 μm), Co (1 mg/100 g body weight; d_{50} = 4 μm), or WC-Co (16.67 mg/100 g body weight [Co 6.3%, W 84%, C 5.4%]; d_{50} = 2 μm) in saline. The groups were checked for mortality at 24 hours post-dose, and the lungs excised and subjected to histopathology. In a second series of experiments, groups of five animals were intratracheally instilled with somewhat lower doses (0.06 mg/100 g body weight for Co, 1 mg/100 g body weight for WC, WC-Co and crystalline silica [positive control; d_{50} < 5 μm]) and after 24 hours bronchoalveolar lavage (BAL) was performed. Cytology and biochemical tests (lactate

dehydrogenase [LDH], total protein [TP], serum albumin (ALB), plasminogen activity and *p*-nitroaniline [pNa]) were performed on the fluids obtained. Mortality (%) was 10, 10, 20 and 60 in the negative control, WC, Co and WC-Co groups, respectively. "The microscopic examination of the lungs of animals instilled with WC did not reveal marked changes; there was no edematous reaction, only a mild infiltration of macrophages in the alveolar duct walls". Histopathology of the Co group showed "scattered sites of exudative alveolitis" in both lungs and cellular proliferation at the origin of the alveolar ducts. The reaction in the WC-Co group was prominent, producing "an acute and diffuse inflammatory reaction with generalized oedematous alveolitis" with substantial interstitial thickening. The BAL results revealed no significant differences between the negative control, WC and Co groups on any of the measured parameters, while the WC-Co groups showed significant differences from control for most of the cytological (numbers of total cells, macrophages and neutrophils) and half of the biochemical (LDH, TP, ALB) endpoints. These results confirmed what this same group of investigators had found in *in vitro* tests previously, that the acute lung toxicity of the WC-Co mixture exceeded that of either component, and that Co was somewhat more toxic than pure WC. The authors concluded that WC somehow increases the bioavailability of Co. These (Lasfargues *et al*, 1992) and other authors (Morgan, 1984) have suggested that WC in the absence of cobalt, and tungsten metal itself (Schepers, 1955) are essentially inert in the lung.

No literature supporting tungsten carbide as a carcinogen was found during screening level development. One reference (Helmes et al., 1983) lists WC as having been nominated to the Chemical Selection Working Group (CSWG) of the National Cancer Institute (NCI) for carcinogen bioassay, but this recommendation was "based on the considerable potential for human exposure" rather than on preliminary evidence of carcinogenicity. NIOSH (1977) notes two case reports of hard metal workers, one of whom was diagnosed with bronchiolar carcinoma, and another with pulmonary fibroadenomatosis. However, neither report implicated WC as causal, and both individuals were subject to mixed exposures from the various hard metal components. Given the rarity of these cancer reports among the many exposed individuals and the possible confounding exposure to nickel, a known carcinogen, it seems unlikely that WC exposure was responsible for these cases. NIOSH apparently concurs, noting (with respect to WC) that "no carcinogenic, mutagenic, teratogenic or reproductive effects in humans have been reported".

Both ACGIH (1992) and NIOSH (1977) have set Occupational Exposure Limits (OELs) for WC as insoluble tungsten; both are set at 5 mg/m^3, as a time-weighted average (TWA). The ACGIH Short Term Exposure Limit (STEL) is 10 mg/m^3 as insoluble tungsten. The ACGIH Threshold Limit Value (TLV) appears to be based on two unpublished letters to the TLV committee (Demehl, 1966: McDermott, 1966) which suggest that long industrial exposures to insoluble tungsten at concentrations of about 5 mg/m^3 have not resulted in pneumoconioses. NIOSH, while setting an identical limit for insoluble tungsten, has modified its Recommended Exposure Limit (REL) for W to account for the toxicity of components of cemented WC other than pure WC. Those criteria state that "when cobalt content exceeds 2%, its contribution to the potential health hazard is judged to *exceed that of tungsten carbide and all other components* [italics mine], and the recommended standard for such mixtures is based on the current U.S. federal standard for occupational exposure to cobalt. If nickel is used as a binder rather than cobalt and the nickel content of the mixture exceeds 0.3% then the NIOSH recommended occupational exposure limit for nickel...shall apply".

Considering the preference for the use of human data, the extensive occupational exposure to tungsten carbide that has occurred and been monitored over the last 50 years (ACGIH, 1992; NIOSH, 1977), and the lack of an EPA RfC/RfD or adequate long term rodent inhalation studies, the OELs for WC represent the best data currently available with respect to human exposure and health effects. Consequently, they are used to drive the derivation of the ITSL. The ITSL for pure WC (as insoluble W) is derived below.

ITSL Derivations: Per Article II, Chapter 1, Part 55, Rule 230(8)(b) of Act 451:

$$\textbf{ITSL } (\textit{pure WC}) = \text{OEL} \times \frac{1}{100} = 5 \text{ mg/m}^3 \times \frac{1}{100} = 0.05 \text{ mg/m}^3 \times \frac{1000 \text{ µg}}{1 \text{ mg}} = \mathbf{50 \text{ µg/m}^3}$$

where the factor of 1/100 is a safety factor to account for: 1) differences in susceptibility between the healthy, adult worker population as compared to the general population which may include individuals or subpopulations more sensitive to the effects of exposure to tungsten carbide and 2) the difference in exposure duration for the worker population as opposed to the general population. The factor is derived as follows:

$$\text{Safety factor} = \frac{40 \text{ hours}}{168 \text{ hours}} \times \frac{30 \text{ years}}{70 \text{ years}} \times \frac{1}{10} = \frac{1}{100}$$

The first factor adjusts for the difference between a 40 hour work week and the total hours in a week; the second factor adjusts for the difference between an assumed working life of 30 years and an assumed total lifespan of 70 years; and the third factor is a standard ten-fold uncertainty factor to extrapolate from the healthy worker to sensitive individuals in the general population.

Consistent with 232(2)(a), since the OEL used here is based on a time-weighted average, an **8 hour averaging** time is considered appropriate.

Following NIOSH recommendations, the ITSL for cobalt (0.2 $\mu g/m^3$, 8 hour averaging) will apply to cemented WC having a Co content >2%:

$$\underset{\textit{(cemented WC > 2\% Co)}}{\textbf{ITSL}} = \textbf{ITSL } \textit{(for Cobalt)} = \text{OEL} \times \frac{1}{100} = 0.02 \text{ mg/m}^3 \times \frac{1}{100} = 0.0002 \text{ mg/m}^3 \times \frac{1000 \text{ µg}}{1 \text{ mg}} = \mathbf{0.2 \text{ µg/m}^3}$$

Also following NIOSH recommendations, the IRSL for nickel (0.0042 $\mu g/m^3$, annual averaging) will apply to cemented WC having a Co content < 2% and a Ni content > 0.3%:

$$\underset{\textit{(cemented WC < 2\% Co \& > 0.3\% Ni)}}{\textbf{IRSL}} = \textbf{IRSL } \textit{(for Nickel)} = \frac{1 \times 10^{-6}}{\text{EPA Inhalation Unit Risk for Ni refinery dust}} = \frac{1 \times 10^{-6}}{2.4 \times 10^{-4} \ (\mu g/m^3)^{-1}} = \mathbf{0.0042 \text{ µg/m}^3}$$

Finally, it should be noted that an ITSL for tungsten *per se* is not established here. While the ITSL for pure WC should be sufficiently protective of health effects from exposures to other insoluble tungsten compounds, it may not be protective for those exposed to the soluble compounds of tungsten, which are more toxic and probably more likely to result in systemic effects.

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