MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Polyvinyl Pyrrolidone (CAS# 9003-39-8)

FROM: Michael Depa, Toxics Unit

SUBJECT: Initial Threshold Screening Level

DATE: October 29, 1993

The initial threshold screening level (ITSL) for polyvinyl pyrrolidone (PVP) is being established at 4 µg/m^3 based on an annual averaging time.

PVP is a polymer which ranges in molecular weight from 2,500 to 1,200,000. PVP is categorized according to its average molecular weight and then assigned a K-number. Commonly used PVPs are K-25 (MW = 23,000-32,000), K-30 (MW = 35,000-51,000) and K-90 (MW = 900,000-1,300,000). The compounds known as PVP are thought to have similar toxicological properties and will be regulated as if they were identical. Until information becomes available that would support using a different regulatory approach, all PVPs will be assigned the ITSL of 4 µg/m^3 based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL for PVP: IRIS, RTECS, ACGIH Threshold Limit Values, NIOSH Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, IARC Monographs, CAS Online (1967-September 4, 1993), and NTP Management Status Report. Review of these sources found that EPA has not established an RfC for polyvinyl pyrrolidone. Occupational exposure limits from NIOSH, OSHA, or ACGIH were not available for polyvinyl pyrrolidone. There were no chronic inhalation studies available on PVP toxicity.

Summaries of chronic oral toxicity studies found in Robinson (1990) were available for review. The first study reviewed was conducted by Shelanski (1957), who administered PVP K-30 to 50 male and 50 female Sherman-Wistar rats at 0, 1% or 10% by weight of the diet over a 2-year period. The body weights of the top dose group were within 10% of the control weights throughout the study. Hematological parameters at 15, 18, 21, and 24 months were all within the normal range. Urine analysis at the same time intervals, including pH, sugar albumin content and density, showed no differences up to 15 months. Albumin was present in the urine of the top dose group at 18 months and in all groups including controls at 21 months. Although special attention was given to histological investigation of the lymphatic system, no gross or histopathological effects attributable to PVP were found in these or any other organs. With the exception of fluid stools, no other effects were observed. The author concluded that PVP administered to albino rats in quantities up to 10% by weight of the diet was harmless.

In a second study summarized in Robinson et al, the corporation BASF (1978) performed toxicity testing using PVP K-25, where 0, 5% or 10% by weight was administered in the diet over a 2-year period to Sprague-Dawley rats (50/sex/group). A second control group was fed 5% cellulose in the diet. No effect was found on food intake or body weight. No substance related differences were found in hematological, clinical or urine analysis parameters. No gross

histopathological effects were found related to treatment, and there was no evidence of PVP storage in mucous membranes of the duodenum or intestine or in mesenteric lymph nodes.

There were no inhalation studies available which meet the minimum criteria for establishing an RfC. However, there was a subchronic animal inhalation study available for review where 8 Sprague-Dawley rats were exposed to an aerosolized PVP (K-30) water solution (93.3% mean particle size < 4 µm) at 146 mg/m^3 for 8 hours a day, 5 days a week for 6 weeks (Lowsma, 1966). These animals were sacrificed two at a time at intervals of 1, 3, 4, and 6 months after exposure. The lungs of the animals sacrificed at 3 and 4 months revealed mild lymphoid hyperplasia or fibroplasia in the peribronchial, perivascular, and subpleural lymphatics, and an occasional giant cell was also seen in the hyperplasia. One shortcoming of this study was that there was only one dose group. Other shortcomings included the small number of animals used, the lack of statistical analysis, and the absence of an evaluation of organs other than the lungs and respiratory lymphatics. However, this study did provide adequate data on which to base an ITSL. The ITSL was determined from the exposure concentration used in this study as follows:

$$ITSL = LOAEL/(UF_1 \times UF_2 \times UF_3 \times UF_4) \times 8\ hrs/24\ hrs \times 5\ days/7\ days$$

$$ITSL = 146\ mg/m^3 / (10 \times 10 \times 10 \times 10) \times 8/24 \times 5/7 = 0.004\ mg/m^3$$

$$ITSL = 4\ \mu g/m^3$$

Where: $LOAEL = 146\ mg/m^3$,

UF_1 = Uncertainty factor used to protect sensitive individuals in the human population,

UF_2 = Uncertainty factor used to extrapolate human toxicity from animal studies,

UF_3 = Uncertainty factor used to extrapolate a NOAEL from a LOAEL, and

UF_4 = Uncertainty factor used to extrapolate chronic toxicity from a subchronic study

Rule 230(d) provides for the use of a 35-fold uncertainty factor to account for the duration of the study for a 7-day study. This subrule also states that the ITSL may be determined on a case-by-case basis from repeated dose studies other than 7-day studies. Typically, for a 90-day study, a 10-fold uncertainty factor is used to account for duration of the study. Since the study by Lowsma is greater than 7 days, but less than 90 days, an uncertainty factor between 10 and 35 is suggested. A factor of 10 was selected for UF_4 because the duration of the Lowsma study is closer to 90 days than 7 days, and the additional uncertainty from the shorter term study may be accounted for in the 10-fold uncertainty factor for extrapolation from a LOAEL to NOAEL. An additional uncertainty factor due to the shortcomings of the study for Lowsma could be used; however, considering the low toxicity by the oral route of exposure, and the combined magnitude of all the uncertainty factors, it was decided that such an uncertainty factor was not necessary.

Lowsma, H., Jones, R., and Prendergast, J. 1966. Effects of respired polyvinylpyrrolidone aerosols in rats. Toxicology and Applied Pharmacology. 9:571-582.

Robinson, B. 1990. PVP: A Critical Review of the Kinetics and Toxicology of Polyvinyl Pyrrolidone. Lewis Publishers, Inc., Chelsea, Michigan.