MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Acetonitrile (CAS # 75-05-8)

FROM: Robert Sills, AQD Toxics Unit Supervisor

SUBJECT: Screening level for Acetonitrile (ACN)

DATE: August 21, 2015

The screening level for acetonitrile (ACN) is as follows:
ITSL = 200 ug/m^3, annual averaging time (AT).

The basis for the ITSL is the EPA (1999; IRIS) assessment, which included an inhalation RfC = 60 ug/m^3. This RfC was based on mouse subchronic and chronic inhalation bioassays (NTP, 1996) which provided a NOAEL = 200 ppm (336 mg/m^3), a NOAEL(ADJ) = 60 mg/m^3, a NOAEL(HEC) = 60 mg/m^3, and a frank effect level (FEL) of 400 ppm (672 mg/m^3). The FEL(ADJ) and the FEL (HEC) were 120 mg/m^3. The critical effect was early mortality. EPA (1999) applied a total UF of 100 and a Modifying Factor (MF) of 10. The UF_T consisted of UF_H = 10 and UF_A = 3 for toxicodynamic differences, and a UF = 3 for database gaps (UF_{DB}) . When the previous ITSL was established based on this RfC on 3/3/99, the ITSL was set equal to the RfC and a default AT of 24 hours was applied. At this time the AT is being set at annual as appropriate considering that the key studies involved lifetime exposure. Also, it is regarded as unusual and inadequately supported to apply a database gaps UF of 3 in this particular case, together with a MF of 10. EPA (1999) rationalized that the UF_{DB} of 3 was based on, "…limited data on reproductive endpoints involving exposure of laboratory animals before and during mating through parturition and the absence of hematological measurements in either mouse study. A full factor of 10 was not considered necessary for the following reasons: (1) there is no evidence to suggest that ACN accumulates in the body, (2) the developmental effects observed seem to be marginal, and (3) these effects occur at concentrations that are lethal to dams." This rationale appears to indicate that there is no significant evidence that a more critical / sensitive effect exists for ACN for which the UF_{DB} is needed and justified. EPA (1999) applied a MF = 10, "…because of the uncertain role that inhalation may have played in the development of the concentration-related increase in the incidence of forestomach lesions in both male and female mice. A potential role of inhalation can be envisioned." AQD will defer to EPA (1999) and adopt this same MF, however it is noted that the conservatism of applying this MF appears to also address any concerns that EPA may have had for database gaps. Therefore, the ITSL is based on the EPA (1999) RfC but without the application of UF_{DB} = 3, resulting in an ITSL = 200 ug/m^3, with annual AT. The previous ITSL had an AT of 24 hours as the default value under Rule 232(2)(b). However the AT is being set at annual at this time, as allowed under Rule 229(2)(b), as appropriate given the chronic nature of the key bioassays and the discussion in EPA (1999) about the protectiveness of the risk assessment. The ITSL was derived as follows:

$$\text{ITSL} = \frac{\text{NOAEL(HEC)}}{\text{UF x MF}} = \frac{60{,}000\ \text{ug/m}^3}{30 \times 10} = 200\ \text{ug/m}^3 \text{ (annual AT)}$$

References

EPA. 1999. IRIS database. Chemical entry for acetonitrile. Inhalation RfC assessment. Last revised 3/3/1999. Still current as of 8/21/15.

NTP. 1996. Toxicology and carcinogenesis studies of acetonitrile (CAS No. 75-05-8) in F344/N rats and B6C3F1 mice (inhalation studies). NTP TR 447.