

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

August 31, 1993

To: File for CEFTIOFUR HYDROCHLORIDE (CAS # 103980-44-5)

From: George Eurich, Toxics Unit - AQD

Subject: Screening Level for Ceftiofur Hydrochloride  
(CAS # 103980-44-5)

The following sources were searched for toxicity data:

RTECS  
IRIS  
EPB LIBRARY  
NIOSH  
ACGIH TLV  
NTP Management Status Report  
IARC Monographs  
HEAST  
CAS ONLINE  
NLM toxline data base  
UM-MEDLINE

The medline search provided the only database information on this chemical. An oral NOEL in newborn swine was determined to be 64 mg/kg, single oral dose (Yancey, R.J., et al., 1990.) The only data useful in determining the ITSL was taken from a summary of in-house toxicity studies done at Upjohn. The entire studies couldn't be acquired because they were deemed to contain confidential information by Upjohn. The summary included abstracts of a 4 hour inhalation study in rats, and a 90 day oral study in dogs. The dog study concluded the "no obvious effect level" (NOEL) to be 30 mg/kg/day. Both studies used ceftiofur sodium as the treatment compound.

The calculated screening level was based on an "ACUTE 4-HOUR DUST INHALATION TOXICITY STUDY ON CEFTIOFUR SODIUM (U-64,279E) IN ALBINO RATS", summary memo received from Upjohn, August 19, 1993. Five male and 5 female albino rats were exposed to a dust atmosphere of ceftiofur sodium at a concentration of 8.3 mg/l for 4 hours. During exposure most exhibited salivation and/or nasal discharge. Immediately following the 4 hr exposure, all demonstrated slight dyspnea. One hour post-exposure all but 1 of the rats appeared normal. Diarrhea was observed in 6 rats for 1-2 days between days 2 and 5 post-exposure. By day 6 post-exposure no pharmacotoxic signs were observed except for 1 male appearing unkempt between

days 4-10 post-exposure, and 1 female exhibiting a red material encrusted around the nares from days 10-12 post exposure. Rats showed no gross lesions when sacrificed and examined on day 14 post-exposure. Histopathology of lungs, liver, kidney, trachea, and nasal turbinates was also negative.

This study does not demonstrate the absolute LC50 since there were no animals that died at this exposure level. Therefore the value calculated below represents a conservative estimate of the ITSL.

$$\text{ITSL} = \frac{\text{LC50}}{500 \times 100} = \frac{8.3\text{mg/l} \times 1000 \text{ l/m}^3}{50000} = 166 \text{ ug/m}^3 \text{ based on annual average time.}$$

The ITSL calculated using the 90 day dog study NOEL (oral) as an RfD would be as follows:  $30\text{mg/kg/day}/1000 \text{ UF} \times 70\text{kg}/20\text{m}^3 = 105 \text{ ug/m}^3$  based on 24 hr averaging time. Considering the difference in averaging times, the use of the LC50 probably provides a more conservative estimate of the ITSL. Since Upjohn would not supply the entire 90 day study for DNR review, the ITSL will be based upon the acute inhalation study.

References:

Yancey, R.J., et al., 1990. Efficacy of ceftiofur hydrochloride for treatment of experimentally induced colibacillosis in neonatal swine. Am. J. Vet. Res. 51(3):349-353.