

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY
WATER BUREAU

TOXICOLOGICAL ASSESSMENT FOR
2-CHLOROANILINE (CASRN 95-51-2)
HUMAN NONCANCER VALUE (HNV)

Literature Review Date: March 20, 2008

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The key study for the derivation of the HNV was a 13 week study of 2-chloroaniline in male and female rats and mice (NTP, 1998). In this study, 10 male and 10 female F344/N rats and B6C3F1 mice were administered 2-chloroaniline by gavage at 0, 10, 20, 40, 80, or 160 mg/kg/d for 13 weeks. Animals were evaluated for hematology clinical chemistry, histopathology, and reproductive system effects (vaginal cytology and sperm motility evaluations). Results showed 2-chloroaniline had no effect on survival but produced significant decreases in body weights for male rats and female mice in the high dose group. Also, 2-chloroaniline administered to rats at 80 and 160 mg/kg/d and mice at 160 mg/kg/d produced tremors. Additional adverse effects observed only in rats included a transient bluish discoloration of the genital and footpad regions at doses of 40 mg/kg/d and greater. Methemoglobin concentrations were elevated in rats and mice at all doses and resulted in secondary anemia which had a dose-dependent severity. * Minimal to mild hemosiderin pigmentation was observed microscopically in the spleen, liver, and renal cortex of male and female rats in the 160 mg/kg groups and in the spleen of females in the 80 mg/kg group. Hemosiderin pigmentation in the spleen was also reported for most female mice administered 40 mg/kg or greater, in all male mice in the 160 mg/kg group, and one male mouse in the 80 mg/kg group. Hematopoietic cell proliferation and capsule fibrosis of minimal to mild severity occurred in the spleens of male and female rats in the 80 and 160 mg/kg groups, in male mice administered 40 mg/kg or greater, and in female mice in the 80 and 160 mg/kg groups. All male and female rats administered 80 or 160 mg/kg and one male rat administered 40 mg/kg had minimal to mild hyperplasia of the bone marrow erythroid cells. For both rats and mice, there were no significant differences in sperm motility or vaginal cytology parameters between dosed and vehicle control males or females. The LOAEL for rats and mice was reported as 10 mg/kg/d based on elevated methemoglobin concentrations resulting in secondary anemia.

The HNV was calculated from the LOAEL of 10 mg/kg/d reported for rats and mice by NTP (1998). An uncertainty factor of 3,000 was used based on uncertainty factors of 10 each for the interspecies, intraspecies, and the sub-chronic to chronic extrapolation. An additional uncertainty factor of 3 was applied to account for using a LOAEL with minimal effects.

References

NTP. 1998. Technical Report on comparative toxicity studies of o-, m-, and p-chloroaniline administered by gavage to F344/N rats and B6C3F1 mice. National Toxicology Program, Research Triangle Park, NC. NIH/PUB-98-3943.

HUMAN NONCANCER VALUE WORKSHEET

Chemical Name: 2-chloroaniline CAS No. 95-51-2
 Developed By: S. Briggs
 Reviewed By: D. Bush Verification Date: 9/26/08

Key Study: NTP (1998) reported a LOEL of 10 mg/kg/d for 2-chloroaniline in rats and mice. Animals were dosed with 0, 10, 20, 40, 80, or 160 mg/kg of 2-chloroaniline for 13 weeks.

ADE = 0.00333 mg/kg/d

$$\text{ADE} = \frac{10 \text{ mg/kg/d}}{3,000}$$

Where UF = 3,000 based on 10x for each intraspecies, interspecies, and sub-chronic to chronic extrapolation and 3x for using a LOAEL with minimal effects.

drinking water

$$\text{HNV} = \frac{(0.00333 \text{ mg/kg/d}) (70 \text{ kg}) (0.8)}{(2 \text{ L/d}) + (0.0036 \text{ kg/d} \times 2.5 \text{ L/kg}) + (0.0114 \text{ kg/d} \times 3.6 \text{ L/kg})} = 91.06 \text{ ug/L}$$

HNV for drinking water = 91 ug/L

non-drinking water

$$\text{HNV} = \frac{(0.00333 \text{ mg/kg/d}) (70 \text{ kg}) (0.8)}{(0.01 \text{ L/d}) + (0.0036 \text{ kg/d} \times 2.5 \text{ L/kg}) + (0.0114 \text{ kg/d} \times 3.6 \text{ L/kg})} = 3,109.0384 \text{ ug/L}$$

HNV for non-drinking water = 3,100 ug/L