EXECUTIVE SUMMARY

DIETHANOLAMINE - Oral Risk Assessment -CAS # 111-42-2			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEL (no-observed-adverse-effect level)	14	mg/kg-day	From a 13-week drinking water study in female F344 rats.
Oral RfD (oral reference dose)	0.01	mg/kg-day	From a 13-week drinking water study in female F344 rats with a 1,000x total uncertainty factor.
TAC (total allowable concentration)	0.1	mg/L	For a 70 kg adult drinking 2 L/day with a default 20% Relative Source Contribution for drinking water.
SPAC (single product allowable concentration)	0.01	mg/L	For a 70 kg adult drinking 2 L/day assuming the default 10 drinking water sources of diethanolamine.
STEL (short term exposure level)	0.5	mg/L	From a 13-week drinking water study in female F344 rats for a 10 kg child drinking 1 L/day.

KEY STUDY	NTP (National Toxicology Program). 1992. NTP Technical Report on Toxicity Studies of Diethanolamine (CAS No. 111-42-2) Administered Topically and in Drinking Water to F344/N Rats and B6C3F1 Mice. Department of Health and Human Services, National Institutes of Health. NIH Publication No. 92-3343, October 1992.
CRITICAL EFFECT	Subchronic drinking water exposure to diethanolamine was associated with clear evidence of hematotoxicity in the form of a dose-related reduction in erythropoiesis in Fischer rats at doses preceding and including general toxicity. Subchronic drinking water exposure to diethanolamine was also associated with some evidence of nephrotoxicity in the form of non dose-related exacerbated spontaneous nephropathy.
UNCERTAINTY FACTORS	• 10x for interspecies extrapolation • 10x for intraspecies extrapolation • 3x for extrapolation from a less-than-lifetime study to a lifetime exposure duration • 1x for extrapolation from a LOAEL to a NOAEL • 3x for database deficiencies Therefore, the total uncertainty factor is 1,000x.
TOXICITY SUMMARY	Human data were limited to case reports of occupational asthma or contact dermatitis caused by metalworking fluids containing diethanolamine. Limited human data also suggest that oral diethanolamine can alter blood cholesterol. Adverse systemic effects in laboratory animals attributed to diethanolamine exposure were not appreciably influenced by route or exposure duration. Short-term and subchronic repeated drinking water, gavage and dermal exposure to diethanolamine was associated with reduced erythropoiesis and exacerbated nephropathy in male and female Fischer rats at doses preceding and including general toxicity (NTP, 1992a, 1992b, 1999a). These effects were the most sensitive adverse effects in rodents, since they occurred at doses preceding other effects, which included general toxicity (reduced body weights of greater than 10%), hepatotoxicity (increased liver weights and hepatocellular cytologic alteration), immunotoxicity, reproductive toxicity (degeneration of the seminiferous tubules) and maternal and/or fetotoxicity in rats and/or mice orally administered diethanolamine. Mice were less sensitive to the effects of diethanolamine than rats. The weight of evidence suggests that diethanolamine has some genotoxic potential *in vitro*. Although mixed results were obtained in cell transformation assays *in vitro*, diethanolamine was not mutagenic in *Salmonella typhimurium*, *Escherichia coli*, *Saccharomyces cerevisiae*, mouse lymphoma cells, or Chinese hamster cells. Further, diethanolamine did not produce sister chromatid exchanges and/or chromosomal aberrations in hamster ovary or rat liver cells *in vitro*, was negative in a DNA damage test in *Escherichia coli*, and did not induce micronuclei in peripheral blood erythrocytes of mice *in vitro*. *In vivo* data were limited to a negative micronucleus assay in peripheral blood erythrocytes of mice exposed by topical application for 13 weeks (NTP, 1992a, 1999a). When evaluated according to U.S. EPA (2005) guidelines, there is *inadequate information to assess carcinogenic potential* of oral exposure to diethanolamine in humans, due to the lack of chronic human epidemiological data or chronic toxicity data in animals.
CONCLUSIONS	The RfD was based on the NOAEL for reduced erythropoiesis and supported by exacerbated nephropathy in rats after 13-week drinking water exposure to diethanolamine. Female rats were more sensitive than male rats for both effects based on the lower doses they received and the magnitude of their responses. Based on selection of the most sensitive endpoint in the more sensitive species and sex, and the uncertainty factors applied, the action levels derived herein are protective of public health.