NTP
National Toxicology Program

NTP Study Nomination: 4,7,10-Trioxatridecane-1,13-diamine

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4,7,10-Trioxatridecane-1,13-diamine (TTD)

- Nominated by the NCI based on:
  - High production volume
  - Lack of adequate toxicity data
  - Potential worker exposures

- Wide variety of industrial uses
  - Amine curing agent (intermediate) in production of polymers, emulsfiers, corrosion inhibitors, textile and leather additives
  - 40-70% by weight in industrial epoxy adhesive
  - U.S. production 500M-1B lbs in 1998; <1M lbs in 2002
- Human exposure potential
  - Assumed only in workplace; no specific exposure data
- Toxicological data
  - Slight acute systemic toxicity by oral and dermal routes
  - Severe skin irritant in rabbits; potential eye and respiratory irritant
  - No genotoxicity, repeat dose toxicity or ADME studies

Data Gaps and Key Issues

- Some suspicion of carcinogenic potential based on QSAR prediction/chemical structure
- Little or no data describing the extent of exposure or the potential toxicity to humans
- Predicted metabolism not very informative regarding potential toxicity
  - Possible metabolism to glycol ether?
- No workplace regulations, but labeled as corrosive
- Nominated for testing in [ICCVAM-recommended] *in vitro* alternative test systems
  - Information on several endpoints (acute toxicity, corrosivity, ocular toxicity) generally available
  - Potential value as reference compound in future alternative test method validation activities

TTD Study Recommendations

- *In vitro* biomolecular screening studies
  - Integration with HTS Initiative
- *In vitro* genotoxicity studies
- No *in vivo* studies at this time
  - Irritancy and corrosivity would likely preclude humane *in vivo* toxicity studies by a relevant route of exposure at sufficiently challenging doses, though studies may be feasible at lower exposure levels

Questions and Comments