TCE and Fetal Heart Development

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Does TCE Cause Heart Defects?

• Epidemiology data are suggestive but inconclusive
• Mechanistic studies are suggestive but relevance to mammals and humans is unclear
Mammalian Studies

• Five inhalation studies on mice, rats and rabbits were uniformly negative
• A high-dose (500 mg/kg) gavage study was negative
• A drinking water study was positive for heart defects, but there are study design and reporting issues
Mammalian Studies

• Fisher et al. (2001)
  – High gavage dose (500 mg/kg/day)
  – Adequate power to detect a treatment effect
  – Dawson method used to examine fetuses as was used in the positive drinking water study(ies)
  – No evidence of heart defects
Mammalian Studies

• Carney et al. (2006)
  – High inhalation exposure (≤600 ppm)
  – Exposure exceeded EPA test guideline by 50%
  – Adequate power to detect a treatment effect
  – Accepted regulatory method (Staples) used to examine fetuses
  – GLP-compliant
  – No evidence of heart defects
Conclusions and Recommendation

• Negative inhalation and oral studies cannot refute a positive drinking water study because the maternal plasma and fetal exposures may be significantly different
• Recommend a drinking water study in rats conducted by an expert teratology team under GLP regulations
• Conduct fetal examinations using an accepted regulatory method familiar to the team