TCE and Fetal Heart Development

Linval R. DePass, Ph.D., DABT, ATS

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