

Science Question 5: Database for Reproductive and Developmental Effects

Key Points

1. **Repro/dev NOAELs in NTP studies provide sufficient data for risk assessment**
2. **Studies with repro/dev LOAELs that are lower than NTP NOAELs are of lower quality and of questionable utility for risk assessment**
3. **All repro/dev LOAELs are higher than liver and intestinal LOAELs**
4. **Repro/dev endpoints are less sensitive than liver and intestinal endpoints observed in NTP chronic bioassay**

Deborah Proctor

ToxStrategies, Inc.

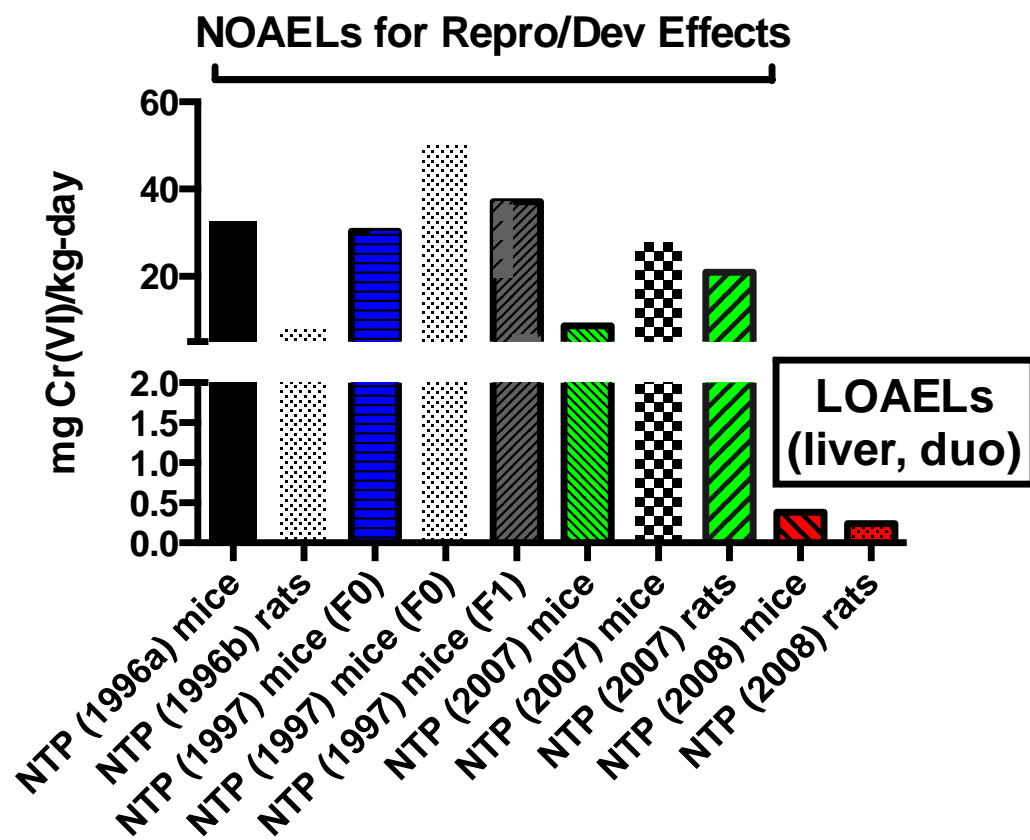
June 25, 2014

The logo for ToxStrategies, Inc. features the company name in a white, sans-serif font. The letter 'x' in 'Tox' has a small dot above it. The text is set against a green background that is shaped like a semi-circle or a rounded arch, with a gradient from light green at the top to a darker green at the bottom.

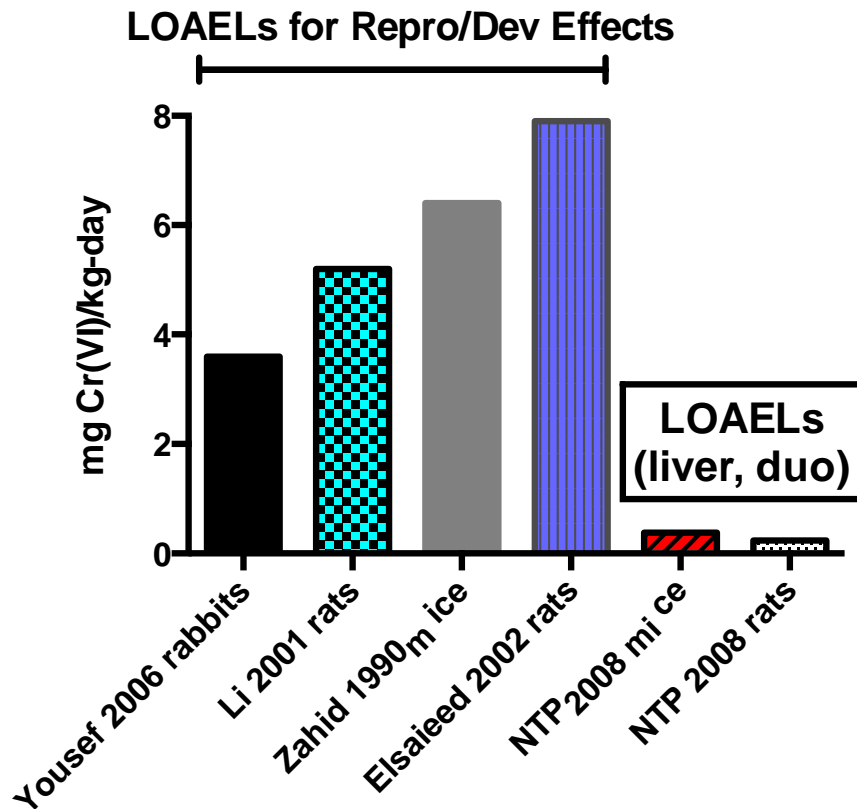
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Reproductive and Developmental Effects of Cr(VI) in the NTP Studies

- No significant reproductive or developmental toxicity observed at Cr(VI) levels tested by NTP
- LOAELs for liver and duodenum in NTP chronic bioassay are much lower than reproductive and developmental NOAELs



Reproductive and Developmental Effects of Cr(VI) Reported in Other Studies



NTP NOAELs

- **Repro: 8.5-32.5 mg/kg-day**
- **Dev: 30-50 mg/kg-day**
- **No effects observed**

- **4 studies cited in the EPA Preliminary Materials have LOAELs that are lower than NOAELs in the NTP studies**
- **LOAELs for repro/dev are still much higher than for LOAELs for intestinal and liver effects in NTP (2008)**

Study Feature Comparison to NTP

Study	Effect/ Species	GLP or OECD design	Gavage/Natural Administration	Doses Single/Multi ple	Quality Questioned by ATSDR ¹
Yousef (2006)	Male repro/ Rabbits	No	Gavage	Single	No
Li (2001)	Male repro/ Rats	No	Gavage or Feeding (?)	Multiple	Yes
Zahid (1990)	Male repro/Mice	No	Natural	Multiple	Yes
Elsaieed (2002)	Develop- mental/Rats	No	Natural	Single	No
NTP 1996a;b; 1997; 2007	Male and female repro, develop- mental/ Rats & Mice	Yes	Natural	Multiple	No—used as point of comparison for other studies

¹ ATSDR (2012) Toxicological Profile for Chromium