

Thyroid Mechanistic Study on *tert*-Butanol in Female B6C3F1 Mice

J. Fowles, Ph.D.

Tox-Logic Consulting
Santa Rosa, CA



Cytochrome P450 Enzyme Activities Induced by TBA Drinking Water Exposure in B6C3F1 Female Mice.

	TBA 2 mg/mL		TBA 20 mg/mL	
	Day 3	Day 14	Day 3	Day 14
Total P450	+11%	+15%	+11%	+56%**
EROD	+/- 0%	+10%	-3%	+5%
PROD	-3%	+10%	-4%	+110%**
BROD	+7%	+66%**	+54%	+1100%**
LAH	-4%	+/-0%	+11%	+18%

** p < 0.01

Source: Blanck O, et al., 2010. *J. Appl. Toxicol.* 30(2).

Conclusion: TBA is an inducer of specific CYPs relevant to PB-type induction

Phase I and II Enzyme Transcripts Relevant to PB-Type Induction and to Thyroid Hormone Elimination Were Weakly Induced

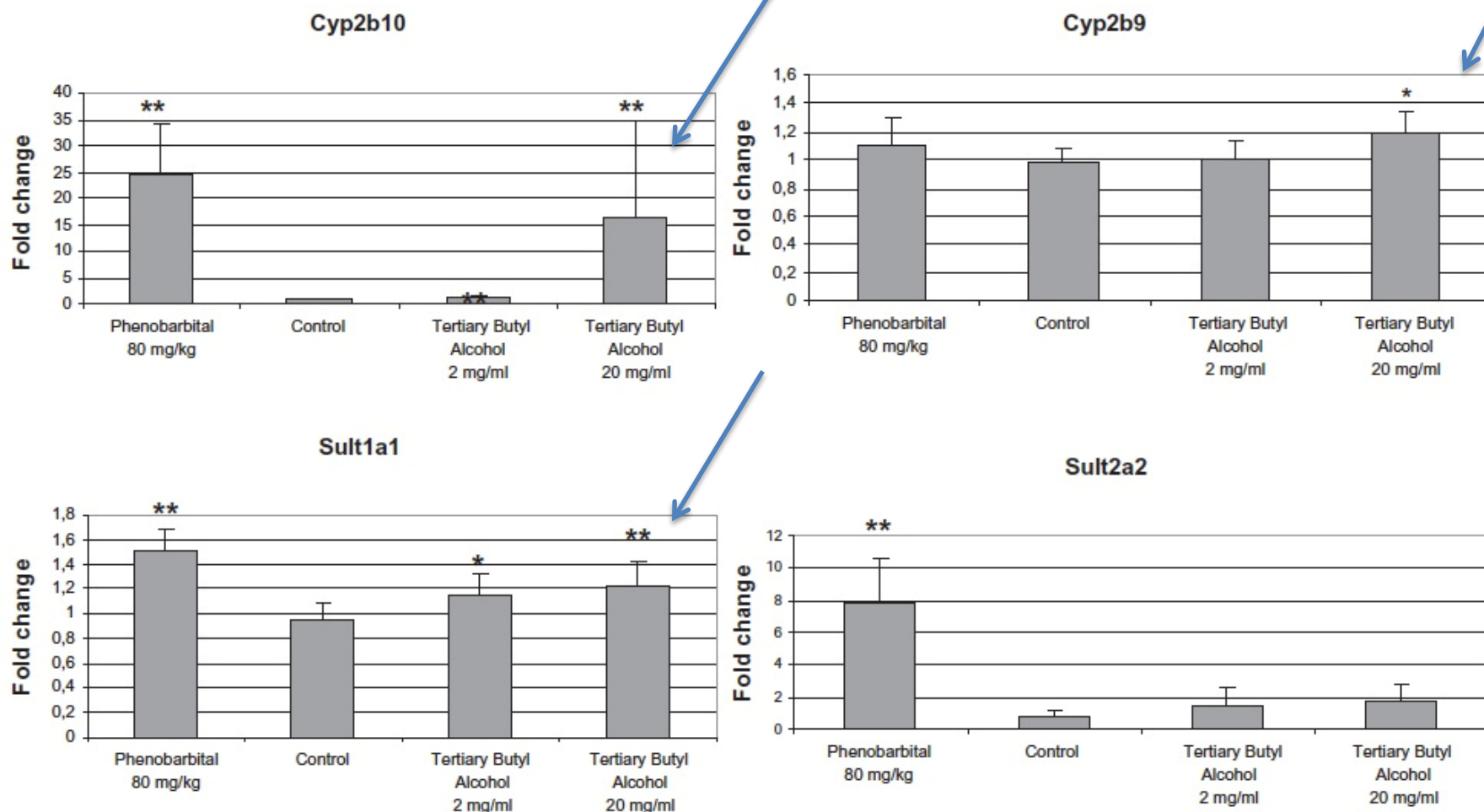


Figure 4. QPCR results showing the gene transcripts that were the most strongly affected by TBA administration to female B6C3F1 mice after 14 days of treatment.

Study Findings:

- TBA did not cause thyroid pathology after 14 days in B6C3F1 female mice.
- TBA did cause mild to slight centrilobular hypertrophy at 20 mg/mL
- TBA caused a slight but significant reduction in T3/T4 by 14 days at 2 and 20 mg/mL
- TBA induced specific CYP and Sulfotransferases at 2 and 20 mg/mL.

Study Conclusions:

TBA is a weak CYP and SULT liver enzyme inducer in female B6C3F1 mice, sharing some PB and CAR like induction elements.

Thyroid effects of TBA are likely secondary to a high dose hepatic enzyme induction effect on thyroid hormone elimination and homeostasis in mice.

