

MECHANISTIC INVESTIGATION OF LOW-DOSE METABOLIC INTERACTIONS

Issue: Risk Management

Department: RASA

Program: Risk Management

Task Force/Staff: Tox & Benzene TF/
Bruce Jarnot

Segment(s): Multi-segment

Y2008 Budget Amount: \$75K

Prior Cost: New

Future Cost (2009–2013)*: \$0K

Project Description:

Preliminary results from API- and ExxonMobil-funded rodent co-exposures to mixtures of toluene and benzene suggest differences in metabolism / metabolic interaction between these compounds at high doses (e.g., those used in toxicology bioassays) versus interactions observed at low doses (e.g., relevant to current occupational exposures). Differences in low-dose interactions have been similarly suggested for benzene interaction with paraffinic hydrocarbons.

API Toxicology and Benzene Task Forces will jointly manage this project, which straddles the boundary between these groups. CIIT has agreed to match funds and to use these seed monies to develop a multi-year research program to address questions regarding high dose vs. low dose interactions. Based on CIIT progress toward this goal, API anticipates receiving a proposal from CIIT in 2008 along with an invitation to join a multi-stakeholder program that appeals to a wider audience, yet retains API significance toward understanding metabolic mechanisms responsible for concentration-dependent coexposure health effect differences.

Benefit to Industry:

This project should also increase our understanding of risk from low-dose mixed hydrocarbon exposures as seen with such complex mixtures as light & middle distillate fuels, petroleum streams, etc.

***Future Costs Over Next 5 Years (2009-2013; in 2007 dollars):**

At the present time, it is unclear whether additional funding associated with this project will be sought between 2009 and 2013.

Anticipated Research Needs Based on Regulatory and Legislative Issues Beyond 2013:

We do not foresee additional research activity associated with this project beyond 2013, given our level of current understanding of the issue(s), approach and API relevance.

Program Priority: 5