THE COST OF THE NEUROBEHAVIORAL EFFECTS OF TOLUENE EXPOSURE

[*]Vernon A. Benignus
[#]William K. Boyes
[#]Philip J. Bushnell

US EPA, ORD, NHEERL

[*]Human Studies Division
[#]Neurotoxicology Division

THE EFFECTS IN HUMANS OF ACUTE TOLUENE INHALATION

- Increases reaction time
- Decreases alertness
- Degrades vision
- Affects decision-making
- Wide range of other effects

SO WHAT? HOW IMPORTANT ARE THESE EFFECTS?

WE CAN MONETIZE THESE EFFECTS BY "COMPARING" THEM TO THE EFFECTS OF ALCOHOL INGESTION

Neurobehavioral effects of alcohol consumption are very similar to those of acute toluene inhalation

Acute effects of alcohol drinking have been monetized – (e.g., for automobile crashes)

Ethanol and toluene have similar mechanisms of action

HOW WE COMPARE THE EFFECTS OF TOLUENE WITH THOSE OF ALCOHOL

Compare dose-effect curves

Must have the same dose metric

we chose brain molar concentration or blood concentration

Must also have same metric for effects

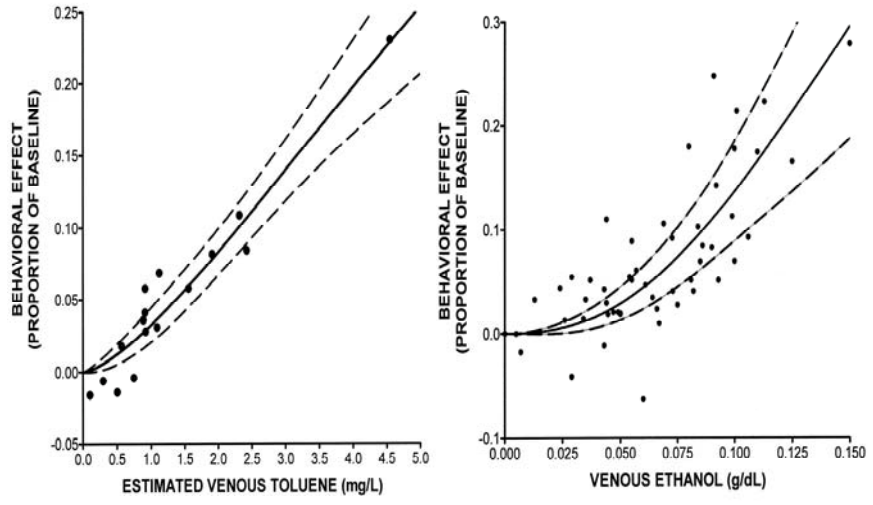
we chose an effect magnitude scale (E), given as percent of maximum possible value. thus when here is no effect, E=0.0 and when effect is at maximum possible, E=1.0

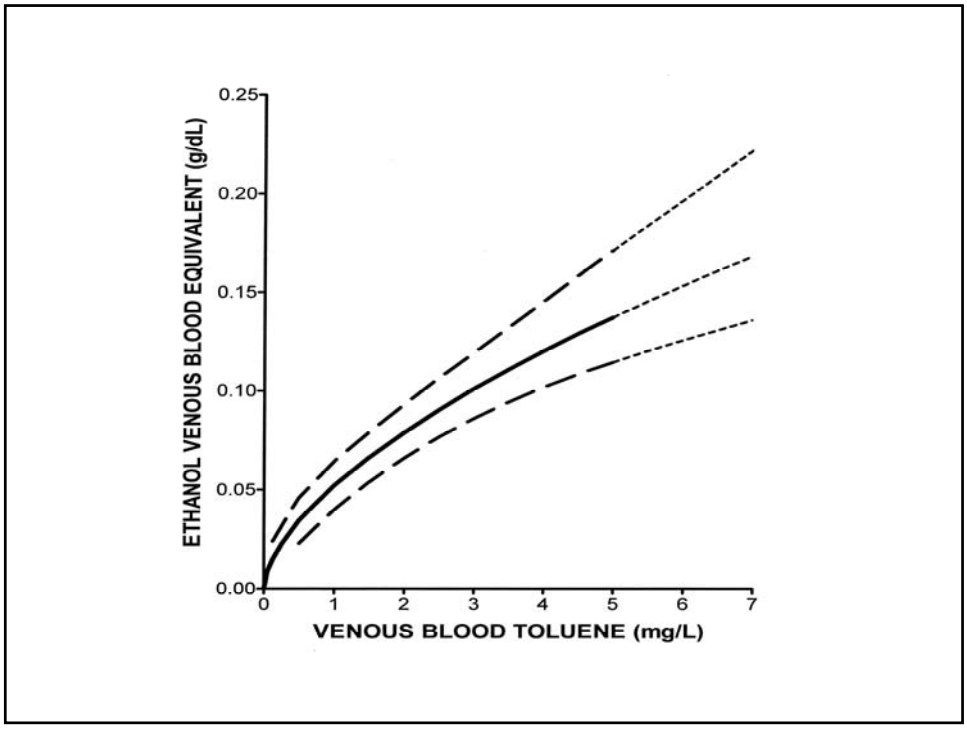
WE CAN NOW DERIVE A DOSE-EQUIVALENCE EQUATION (DEE)

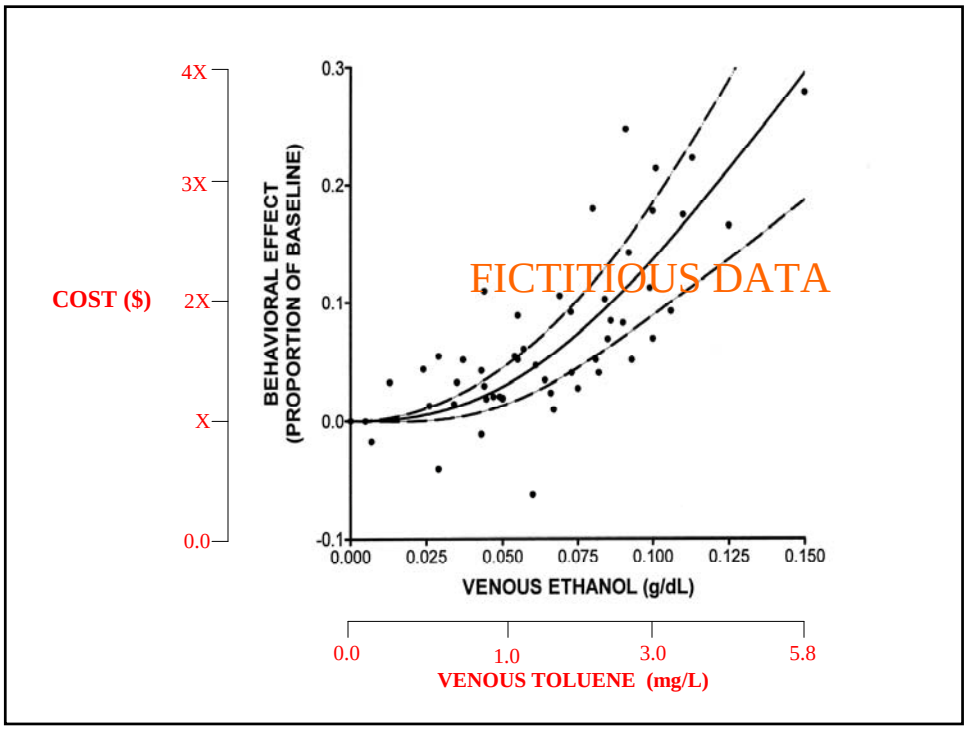
The DEE gives the doses (brain concentrations) of ethanol which produce the same E as a range of doses of toluene.

Plotting the DEE gives a graph with toluene brain concentration on the horizontal axis with alcohol brain concentration on the vertical axis.

All **pairs of brain concentrations** (toluene and ethanol) that lie on the plotted line give the same E.




ETHANOL VENOUS BLOOD EQUIVALENT (g/dL)
0.25
0.20
0.15
0.10
0.05
0.00
0
1
2
3
4
5
6
7
VENOUS BLOOD TOLUENE (mg/L)


COST ($)
4X
3X
2X
X
0.0
BEHAVIORAL EFFECT
(PROPORTION OF BASELINE)
0.3
0.2
0.1
0.0
-0.1
0.000
0.025
0.050
0.075
0.100
0.125
0.150
VENOUS ETHANOL (g/dL)
FICTITIOUS DATA
0.0
1.0
3.0
5.8
VENOUS TOLUENE (mg/L)

ASSUMPTIONS AND CONSEQUENCES

No inherent assumptions about data in the method

Assumptions can be added to suit the goals of work

Example 1: Assume that toluene and ethanol produce neurobehavioral effects *via* the same mechanism of action.

Then the suite of effects for each would be the same

Therefore, if the DEE were determined for one of the suite of effects, that DEE would hold for the whole suite

Example 2: Assume that the mechanisms of the two substances in the DEE were mechanistically dissimilar.

Then the suite of neurobehavioral effects might differ

A DEE for one effect could only be considered to be a lower bound for any cost estimate.

Could construct DEEs for more of the suite of effects and add the costs.

SUMMMARY:

Given a toxicant, the effects of which have been monetized
Given <u>another</u> toxicant, the effects of which have <u>not</u> been monetized

A DEE may be derived by which the previously un-monetized toxicant may be implicitly monetized

The completeness of the monetization depends on the assumptions which may be justified

REPRISE OF THE QUESTION OF THE IMPORTANCE OF ACUTE NEUROBEHHAVIORAL EFFECTS

Chronic effects accumulate over a long period, gradually increasing the probability of health effects or perhaps deaths

Acute neurobehavioral effects occur after only a short exposure and the injuries, property damage and deaths accumulate over time

If the accumulation period for chronic and acute effects were equal, would costs be comparable?