



American Chemistry Council Ethylbenzene Panel

Presentation to HEAC, CA Dept. Industrial Relations

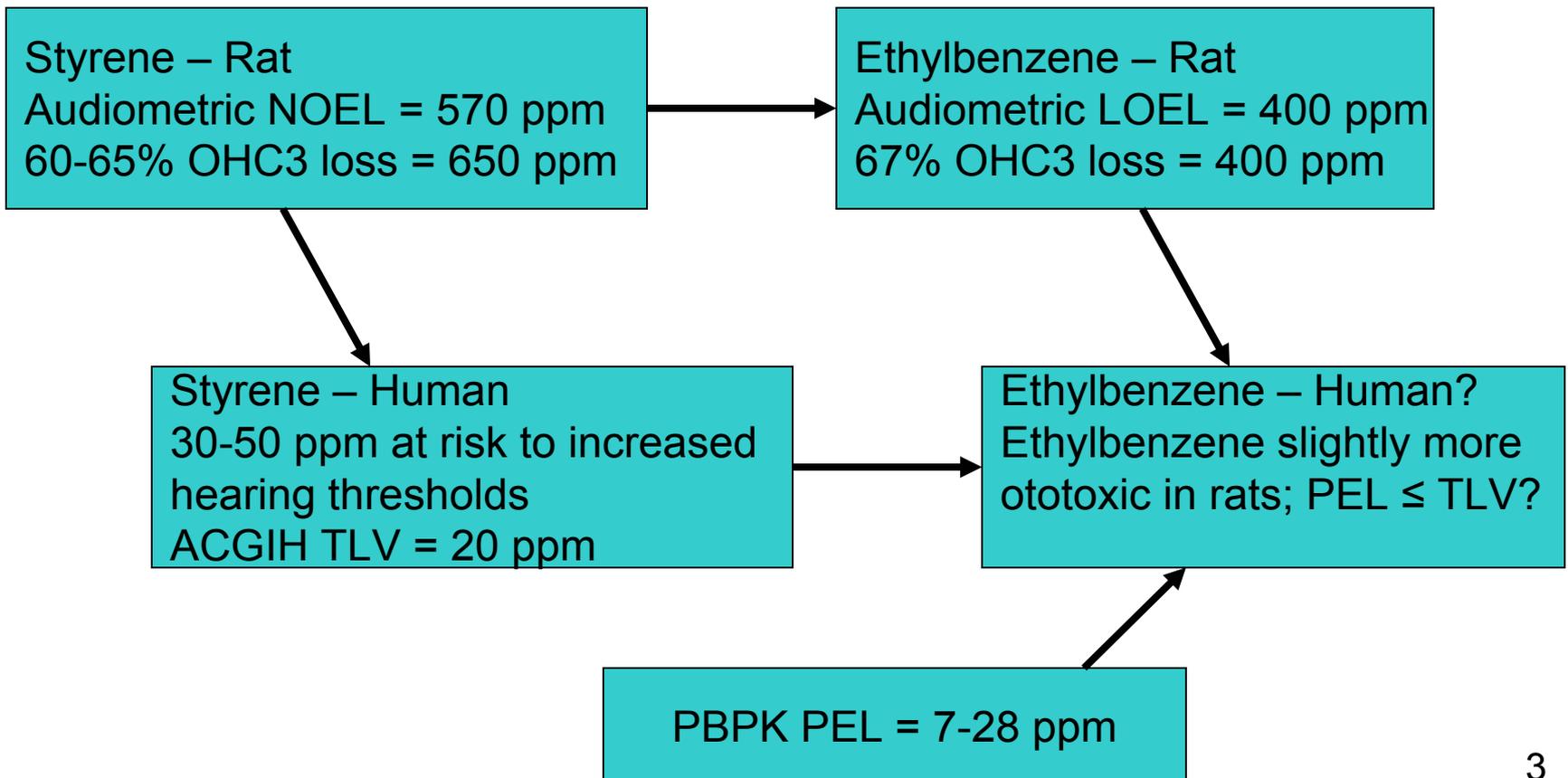
James S. Bus, Ph.D., DABT, Fellow ATS
The Dow Chemical Company

June 24, 2009

Physiologically Based Pharmacokinetic Model (PBPK): Informing Ethylbenzene PEL

- PBPK approach proposed for N-methylpyrrolidone PEL
- Published PBPK models available for rat and human for ethylbenzene
- National Academy of Sciences used PBPK to develop draft AEGL for ethylbenzene
- Ethylbenzene PBPK-estimated PELs:
 - Mouse lung tumors: 28 ppm
 - Liver effect: 7 ppm
 - Ototoxicity: 7-28 ppm

Ototoxicity: Overlay of Ethylbenzene PBPK PEL estimate with “Read-across” to Styrene





Conclusions

A weight-of-evidence analysis of the toxicology, genotoxicity, mode of action, and PBPK information for ethylbenzene indicates:

- **HEAC PEL should be based on a non-linear assessment of the mouse lung tumor response, mouse liver effects, and/or rat ototoxicity;**
- **PEL of 7-28 ppm is supported by PBPK**