

Polystyrene Health Effects

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ToxWorks

Incorrect Statement

- “polystyrene.....is a suspected human carcinogen.”
- Polystyrene is NOT a suspected carcinogen
- It should not be confused with styrene

Are You Confused ?

- Polystyrene is a solid; styrene is a liquid
- Polystyrene is unreactive; styrene is reactive

Chemical Reactions

- When chemicals react, the product has its own properties, not those of reactants.
- Example
 - Sodium – very reactive solid metal
 - Chlorine – poisonous gas
 - When sodium reacts with chlorine, table salt is produced (sodium chloride)

Polymers Differ from Monomers

- Polymers do not have the same properties as the monomers that compose them.
- Example
 - Glucose – sweet tasting
 - Polymerize by joining glucose molecules together,
Produces cellulose – wood or plant fiber
- Same for styrene and polystyrene

Sources of Styrene Exposure

- Ambient air (automobile exhaust, factory discharge, cigarette smoking, etc) – 80 ug/day
- Naturally occurring in foods – 9 ug/day
- Migration from polystyrene food packaging – 6.6 ug/day
 - Migration from foam food service items – 4 ug/day (of the 6.6 ug/day for all PS)
- 4 ug = 1millionth of a teaspoon

Styrene Health Effects

- US NTP (2011) lists styrene as “Reasonably Anticipated to be a Human Carcinogen”
 - Based on suggestive increases in reinforced plastic workers
 - Based on lung tumors in mice
 - No other tumors increased in mice
 - No tumors increased in rats

New Human Studies

- Since ROC listing, most human cohorts (groups of workers) have been re-examined as older workers have died
- Tumors suggested among earlier evaluations are no longer increased

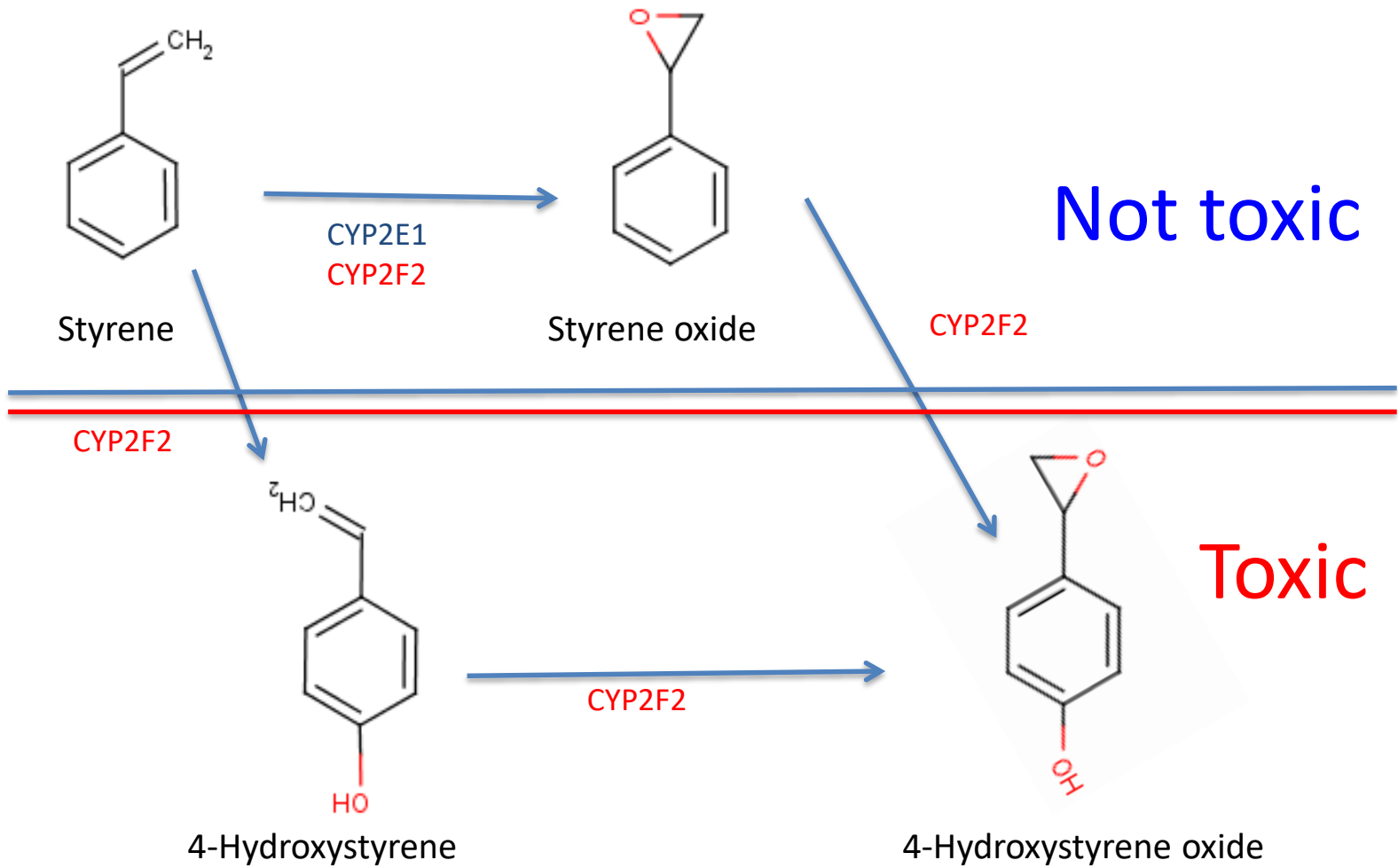
Mouse Lung Tumors

- 55 of 70 (78%) normal mice had preneoplastic or neoplastic lesions in lung after lifetime (2 years) exposure to 120 ppm styrene by inhalation.
- 0 of 70 mice without CYP2F2 had lung lesions

Mode of Action

- Key Events
 - Metabolism by CYP2F2
 - No evidence of genotoxicity
 - Metabolites damage and kill some lung cells
 - Metabolites stimulate production of new lung cells
 - Increased cells produce hyperplasia (excessive cells lining airways)
 - In some mice, tumors develop

- Normal metabolism of styrene is catalyzed by CYP2E1 – produces styrene oxide
- Mouse lung – CYP2F2 metabolizes styrene to different metabolites – oxidation of aromatic ring
- Styrene oxide is not toxic to mouse lung cells without further CYP2F2 metabolism



Summary of MOA

- Lung tumors in mice, not in rats
- Lung toxicity in mice, not in rats
- Toxicity and metabolism in Club (Clara) cells in mice, not rats
- Lung toxicity from 4HS in mice, not rats
- Elimination of lung toxicity from styrene and SO in CYP2F2-KO mice
- 80% reduction on ring-oxidized metabolites in CYP2F2-KO mice
- Lower level of CYP2F4 in rats does not produce toxicity
- Greater lung toxicity in mice from 4HS than from SO
- Limited toxicity from 4HS in 2F2-KO mice
- 3- or 4-methylstyrene do not cause lung tumors in mice
- Enhanced expression of cell cycle genes in WT mice
- No enhanced gene expression from styrene in KO mice

Human Relevance of Mouse Lung Tumors

- Rats have less CYP2F than mice; no toxicity, no lung tumors
- Humans have less CYP2F than rats; no toxicity no lung tumors

Risk Assessment

- Reinforced plastics workers – 2,000,000 ug/day
- Ambient styrene – 80 ug/day
- Food-derived styrene – 9 ug/day
- Polystyrene food service styrene – 4 ug/day
- Total non-occupational exposure – 96 ug/day

- Banning ps foodservice reduces styrene exposure by less than 5%

Risk Assessment

- “Let me put your mind at ease right away about polystyrene foam*” ... [the levels of styrene from polystyrene containers] “are hundreds if not thousands of times lower than have occurred in the occupational setting...In finished products, certainly styrene is not an issue.” Linda Birnbaum, Director NTP, 2011.
- "The risks, in my estimation, from polystyrene are not very great. It's not worth being concerned about." John Bucher, Associate Director NTP, 2011.

Conclusion

- Very high exposures to styrene may or may not present a risk
- USEPA acceptable exposure 20,000 ug/day; exposure from PS 4 ug/day
 - 5000-fold safety factor
- No government agency considers PS to be carcinogenic
- Styrene from polystyrene products do not present a measurable risk.