

No Additional THMs Should be Considered for Prioritization

Robert G. Tardiff, PhD., ATS
The Sapphire Group, Inc.

On Behalf of
Chlorine Chemistry Division
American Chemistry Council

20 November 2008



Evidence that THMs as a Group are Not Clearly Shown to Cause Reproductive & Developmental Toxicity

- USEPA & WHO
- Epidemiologic findings
- Toxicological findings



Studies Identified by OEHHA As “Increased Risk” from THM

- Hwang et al., 2008
 - ◆ Not significant for 3 endpoints: $LCI \leq 1$
 - ◆ Significant <all birth defects>
 - ☞ Low dose only; no dose-response
 - ☞ Overall: 5 studies not SS
- Toledano et al., 2005
 - ◆ Not significant: $LCI < 1$
 - ◆ Significant <LBW & VLBW>
 - ☞ Confounding w/ socio-economic status unadjusted
 - ☞ One H₂O district of 3
 - ☞ Not significant for 3 districts combined
 - ☞ Overall LBW = 2+ v 5-
 - ☞ Overall VLBW = 1+ v 3-
- Wright et al., 2004
 - ◆ Significant for SGA
 - ☞ No dose-response
 - ☞ Overall: 3+ v 11-



Studies Identified by OEHHA As “Increased Risk” from THM (cont)

- Windham et al., 2003
 - ◆ Not significant <menstrual cycle>: LCI <1
 - ◆ Poor participation
 - ◆ Self-reporting error

- King et al., 2000
 - ◆ Significant <stillbirth, 100 v 50 ppb>
 - ☞ No dose-response
 - ☞ Overall: 2+ v 2-

- Waller et al., 1998
 - ◆ Significant <SAB>
 - ☞ 1 of 3 H₂O supplies
 - ☞ Savitz et al. (2005) with improved design =
Not significant
 - ☞ EPA disqualified Waller study
 - ☞ Overall: 1+ v 2-



Other Considerations for Prioritization

- Chemical structure of THM group does not suggest reproductive toxicity
- Metabolism of THM group does not suggest reproductive toxicity



National and International Consensus: No Clear Evidence that THMs as a Group Cause Reproductive or Developmental Toxicity

- USEPA, 2006: “...concludes that a causal link between adverse reproductive health effects and exposure to chlorinated drinking water or DBPs has not been established ...”
- WHO, 2000: “... existing epidemiological data are insufficient to allow the importance of observed associations of chlorinated water or THMs and adverse reproductive outcomes to be assessed.”



No Clear or Consistent Association Between Reproductive or Developmental Toxicity and THMs as a Group

- Global review (Tardiff et al. 2006*): “... *The updated epidemiological weight of evidence demonstrated that that no associations with DBP exposure exists for over a dozen [reproductive] outcomes. ...*”

- Epidemiologic data since 2001:
 - ◆ 29 endpoints = no SS association
 - ◆ 8 endpoints = no distinction THMs from CBP
 - ◆ 3 endpoints = inconsistent findings
 - ◆ 1 endpoint = no confirmation, replication, dose-response

- *Reg. Tox Pharm 45, 185-205 (2006)



Comprehensive Epidemiologic Factors Do Not Support Prioritization of THM Group

- All negative and positive studies included
- Major study types included
- 40+ endpoints included
- Quality of studies including confounders addressed
- Dose-response sought
- Statistical analyses evaluated
- Criteria for positive associations applied



Toxicology Weight of Evidence = No Clear Cause of Reproductive or Developmental Toxicity by Group of THMs

- No studies



Conclusion

- No sufficient evidence to prioritize any additional THMs either as a group or individually



