

Chadwick M. Thompson, Ph.D.

SENIOR HEALTH SCIENTIST

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Chad M. Thompson is a senior health scientist with ToxStrategies and holds a doctorate degree in Biomedical Sciences. Dr. Thompson specializes in mechanistic and quantitative risk assessment, including dose-response modeling using global nonlinear regression, and BMD modeling using the U.S. EPA BMDS and BMDExpress. Dr. Thompson was aco-author of the U.S. EPA 2010 draft "Toxicological Review of Formaldehyde – Inhalation Assessment", and the 2009 document, "An Approach to Using Toxicogenomic Data in U.S. EPA Human Health Risk Assessments: A Dibutyl Phthalate Case Study."

In previous positions as a Risk Policy Fellow with the American Association for the Advancement of Science (AAAS) and the U.S. Environmental Protection Agency (EPA), and as a Health Scientist at the U.S. EPA, Dr. Thompson was involved with IRIS chemical risk assessments, the development of databases for physiological parameters suitable for application in physiologically-based pharmacokinetic (PBPK) modeling, as well as the development of risk assessment practices and policy documents for genotoxic compounds. He has extensive expertise in susceptibility issues – including those related to genetics (e.g. polymorphisms), age (e.g. children), and health.

Dr. Thompson has co-authored over 25 publications in the peer-reviewed literature, several of which represent work conducted while at the U.S. EPA and pertain directly to human health risk assessment. He is experienced with several software packages relevant to this project including Microsoft ACCESS and Excel, U.S. EPA BMD Software, BMDExpress, and Ingenuity Pathway Analysis.

EDUCATION AND DEGREES EARNED

MBA; Virginia Commonwealth University, Richmond, VA, 2001

PhD in Biomedical Sciences; University of Texas Health Science Center Houston, 1999

BS in Psychology (cum laude); Old Dominion University, Norfolk, VA, 1994

PROFESSIONAL ASSOCIATIONS

American Association for the Advancement of Science

Society of Toxicology

SERVICE/PEER REVIEW

Journal of Toxicology and Environmental Health

Environmental Health Perspectives

Regulatory Toxicology and Pharmacology

Chemosphere

International Journal of Medical Sciences

Expert Opinion on Drug Metabolism & Toxicology

SELECTED PROFESSIONAL EXPERIENCE

Risk Assessment

Coordinated and coauthored portions of IRIS chemical risk assessments – including all or portions of pharmacokinetics, hazard characterization, and dose-response analysis. Chemicals include reactive gases (e.g. formaldehyde) and systemically distributing compounds (methanol).

Evaluated Provisional Peer-Reviewed Toxicity Values (PPRTV) for benzene and propene derivatives for U.S. EPA's Superfund Program.

Served as a member of the U.S. EPA Pharmacokinetic Workgroup that provides expert consultation to EPA chemical managers regarding the application of PBPK models for ongoing assessments.

Regulatory Toxicology

Coauthored and coordinated the completion and review of several risk assessment documents – including those related to the use of PBPK models for application in risk assessment, qualitative and quantitative approaches to considering children's susceptibility, and the exploration of the use of "omics" data in hazard characterization and dose-response in risk assessment:

"Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment". (<http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=157668>)

"A Framework for Assessing Health Risks of Environmental Exposures to Children" (<http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158363>).

"An Approach to Using Toxicogenomics Data in EPA Risk Assessments."

Research & Development

Managed the development of ACCESS databases containing physiological data for supporting PBPK model development for humans of various life stages and health conditions, as well as laboratory species.

Collaborated and published with national and international academic scientists on the collection, characterization, and analysis of lifestage-specific physiological data and its application in PBPK modeling and risk assessment.

Collaborated and published with scientists at Karolinska Institute and the VTT Technical Research Centre of Finland on mechanisms of formaldehyde toxicity– including potential respiratory effects relating to the dual function of alcohol dehydrogenase 3 in the oxidation of formaldehyde and reduction of the endogenous bronchodilator S-nitrosoglutathione (GSNO).

Project Management

Served as the Technical Project Officer on several contracts with outside contractors. Responsibilities included developing cost estimates for bid proposals; managing and approving payments to contractors; writing statements of work, reviewing and selecting bid contracts; providing scientific consultation and judgment on technical issues related to contracts; and providing final approval on delivered contract products.

COMPUTER & LANGUAGE SKILLS

Ingenuity Pathways Analysis (IPA) 5.0, IUCLID 5, U.S. EPA Benchmark Dose Modeling Software (BMDS); PROAST, BMDEExpress, Berkeley Madonna (ordinary differential equation solver); GraphPad Prism, @RISK Monte Carlo Software, Microsoft Office (including ACCESS); Minitab Statistical Package

MANUSCRIPTS

Kopec, A.K., Kim, S., Forgacs, A.L., Zacharewski, T.R., Proctor, D.M., Harris, M.A., Haws, L.C, **Thompson, C.M.** (accepted) Genome-wide gene expression effects in B6C3F1 mouse intestinal epithelia following 7 and 90 days of exposure to hexavalent chromium in drinking water. *Toxicology and Applied Pharmacology*.

Thompson, C.M., Proctor, D.M., Suh, M., Haws, L.C., Hebert, C. D., Mann, J.F., Shertzer, H. G., Hixon, and Harris, M. A. (in press) Comparison of the Effects of Hexavalent Chromium in the Alimentary Canal of F344 Rats and B6C3F1 Mice Following Exposure in Drinking Water: Implications for Carcinogenic Modes of Action. *Toxicol Sci*.

Thompson, C.M., D.M. Proctor, L.C. Haws, C.D. Hebert, S.D. Grimes, H.G. Shertzer, A.K. Kopec, J.G. Hixon, T.R. Zacharewski and M.A. Harris. (2011) Investigation of the Mode of Action Underlying the Tumorigenic Response Induced in B6C3F1 Mice Exposed Orally to Hexavalent Chromium. *Toxicol Sci*. 123(1): 58-70.

Proctor, D.M., **Thompson, C.M.**, Suh, M., and Harris, M.A. (2011) A response to “A quantitative assessment of the carcinogenicity of hexavalent chromium by the oral route and its relevance to human exposure.” *Environmental Research*. 111(3):468-470.

Wilson, V.S., Keshava, N., Hester, S., Segal, D., Chiu, W., **Thompson, C.M.**, Euling, S.Y. (2011) Utilizing Toxicogenomic Data to Understand Chemical Mechanism of Action in Risk Assessment. *Toxicology and Applied Pharmacology* (in press).

Thompson, C.M., L.C. Haws, M.A. Harris, N.M. Gatto and D.M. Proctor. (2011) Application of the U.S. EPA Mode of Action Framework for Purposes of Guiding Future Research: A Case Study Involving the Oral Carcinogenicity of Hexavalent Chromium. *Toxicol Sci.* 119(1): 20-40.

Thompson, C.M. and R.C. Grafström. (2010) Considerations for the implausibility of leukemia induction by formaldehyde. *Toxicol Sci.* 120(1): 230-2.

Thompson, C.M., R. Ceder and R.C. Grafström. (2010) Formaldehyde dehydrogenase: beyond phase I metabolism. *Toxicol Lett.* 193(1): 1-3.

Thompson, C.M., Johns, D.O., Sonawane, S., Barton, H.A., Hattis, D., Tardif, R., and Krishnan, K. (2009) Database for Physiologically Based Pharmacokinetic (PBPK) Modeling: Physiological Parameters for Healthy and Health-Impaired Elderly. *Journal of Toxicology and Environmental Health, Part B.* 12:1–24.

Makris, S.L., **Thompson, C.M.**, Euling, S.Y., Selevan, S.G., Sonawane, B. (2008) A Lifestage- Specific Approach to Hazard and Dose-Response Characterization for Children's Health Risk Assessment, *Birth Defects Research, Part B.* 83, 530–546.

Thompson, C.M., Subramaniam, R.P., and Grafström, R.C. (2008) Mechanistic and Dose Considerations for Supporting Adverse Pulmonary Physiology in Response to Formaldehyde. *Toxicology and Applied Pharmacology.* 233, 355–359.

Thompson, C.M., Sonawane, B., Barton, H.A., DeWoskin, R.S., Schlosser, P., Lipscomb, J.C., Chiu, W., and Krishnan, K. (2008) Approaches for Applications of Physiologically Based Pharmacokinetic Models in Risk Assessment. *Journal of Toxicology and Environmental Health, Part B.* 11, 519–547.

Subramaniam, R.P, Chen, C., Crump, K.S., Devoney, D., Fox, J.F., Portier, C.J., Schlosser, P.M., **Thompson, C.M.**, White, P. (2008) Uncertainties in Biologically-Based Modeling of Formaldehyde-Induced Respiratory Cancer Risk: Identification of Key Issues. *Risk Analysis* 28, 907–923.

Thompson, C.M. and Grafström, R.C. (2008) Mechanistic Considerations for Formaldehyde- Induced Bronchoconstriction Involving S-Nitrosoglutathione Reductase. *Journal of Toxicology and Environmental Health, Part A.* 71, 244–248.

DeWoskin, R.S. and **Thompson, C.M.** (2008) Renal Clearance Parameters for PBPK Model Analysis of Early Lifestage Differences in the Disposition of Environmental Toxicants. *Regulatory Toxicology and Pharmacology.* 51, 66–86.

Chiu, W., Barton, H.A., DeWoskin, R.S., Schlosser, P., **Thompson, C.M.**, Sonawane, B., Lipscomb, J.C., and Krishnan, K. (2007) Evaluation of Physiologically Based Pharmacokinetic Models for Use in Risk Assessment. *Journal of Applied Toxicology.* 27(3), 218–37.

Barone, S. Jr., Brown, R.C., Euling, S., Cohen Hubal, E., Kimmel, C.A., Makris, S., Moya, J., Selevan, S.G., Sonawane, B., Thomas, T., and **Thompson, C.M.** (2006) Visión General De La Evaluación Del Riesgo En Salud Infantil Empleando Un Enfoque Por Etapas De Desarrollo. *Acta Toxicol. Argent.* 14(Sup), 7–10.

Thompson, C.M., Wojno, H., Greiner, E., May, E.L., Rice, K.C., and Selley, D.E. (2004) Activation of G-proteins by Morphine and Codeine Congeners: Insights to the Relevance of O- and N-Demethylated Metabolites at μ - and δ -Opioid Receptors. *Journal of Pharmacology and Experimental Therapeutics.* 308(2), 547–554.

Strobel, H.W., **Thompson, C.M.**, Antonovic, L. (2001) Cytochromes P450 in brain: function and significance. *Current Drug Metabolism*. 2(2), 199–214.

Thompson, C.M., Capdevila, J.H., and Strobel, H.W. (2000) Recombinant P450 2D18 Metabolism of Dopamine and Arachidonic Acid. *Journal of Pharmacology and Experimental Therapeutics*. 294(3), 1120–1130.

Thompson, C.M., Kawashima, H., and Strobel, H.W. (1998) Isolation of partially purified P450 2D18 and characterization of activity towards the tricyclic antidepressants imipramine and desipramine. *Archives of Biochemistry and Biophysics*. 359(1), 115–121.

Gerhardt, B., Kordas, T.J., **Thompson, C.M.**, Patel, P., and Vida, T.V. (1998) The vesicle transport protein, Vps33p, is an ATP binding protein that localizes to the cytosol in an energy dependent manner. *Journal of Biological Chemistry*. 273(25), 15818–15829.

Kawashima, H., Kusunose, E., **Thompson, C.M.**, and Strobel, H.W. (1997) Protein expression, characterization, and regulation of CYP4F4 and CYP4F5 cloned from rat brain. *Archives of Biochemistry and Biophysics*. 347(1), 148–154.

Thompson, C.M., Bernhard, A.E., and Strobel, H.W. (1997) Barbiturate-induced expression of neuronal nitric oxide synthase in the rat cerebellum. *Brain Research*. 754, 142–146.

Huber, K.M., Mauk, M.D., **Thompson, C.M.**, and Kelly, P.T. (1995) A critical period of protein kinase activity after tetanic stimulation is required for the induction of long-term potentiation. *Learning & Memory*. 2, 81–100.

BOOK CHAPTERS

Johns, D.O., E.O. Owens, **C.M. Thompson**, B. Sonawane, D. Hattis, and K. Krishnan. 2010. Chapter 5: Physiological Parameters and Databases for PBPK Modeling, in *Quantitative Modeling in Toxicology*. K. Krishnan and M. Andersen (eds.). p. 107.

Thompson, C., Nong, A., Sonawane, B. and Krishnan, K. Considerations for Applying Physiologically Based Pharmacokinetic Models in Risk Assessment in *Toxicokinetics and Risk Assessment*, J.L. Lipscomb and E.V. Ohanian, eds. 2006, Informa Healthcare USA, Inc: NY. P. 123–139.

DeWoskin, R., Lipscomb, J., **Thompson, C.**, Chiu, W.A., Schlosser, P., Smallwood, C., Swartout, J., Teuschler, L., and Marcus, A. Pharmacokinetic/Physiologically Based Pharmacokinetic Models in Integrated Risk Information System Assessments in *Toxicokinetics and Risk Assessment*, J.L. Lipscomb and E.V. Ohanian, eds. 2006, Informa Healthcare USA, Inc: NY. P. 301–348.

PRESENTATIONS AND ABSTRACTS

2011. Thomas, R.S., Rowlands, J.C., Budinsky, R.A., **Thompson, C.M.**, Urban, J.D., Dombkowski, A. Genomic approaches for relative potency assessment. Dioxin 2011, August 21-25, 2011. Brussels, Belgium.

2011. Wikoff, D.S., **Thompson, C.**, Walker, N., DeVito, M., Harris, M., Birnbaum, L. Haws, L. Derivation of relative potency estimates using benchmark dose modeling: a case study with TCDF. Dioxin 2011, August 21-25, 2011. Brussels, Belgium.

2011. Ceder, R., M. Merne, J.-A. Nilsson, C. Staab, J.-O. Höög, **C.M. Thompson**, and R.C. Grafström. Toxicogenomic profiling of formaldehyde-exposed normal and transformed human oral keratinocytes. Society of Toxicology's 50th Annual Meeting, March 6-10, 2011. Washington, D.C.

2011. Haws, L., D. Proctor, **C. Thompson**, and M. Harris. Research Plan to Fill Data gaps in the Mode of Action for Cancer Risk Assessment of Hexavalent Chromium in Drinking Water. Society of Toxicology's 50th Annual Meeting, March 6-10, 2011. Washington, D.C.

2011. Kim, S., **C.M. Thompson**, A.K. Kopec, M.A. Harris, and T.R. Zacharewski. Comparison of basal and CrVI-mediated solute carrier gene expression in rodent duodenal epithelium. Society of Toxicology's 50th Annual Meeting, March 6-10, 2011. Washington, D.C.

2011. Proctor, D., **C. Thompson**, L. Haws, and M. Harris. Use of Mode of Action and Pharmacokinetic Findings to Inform the Cancer Risk Assessment of Ingested Cr(VI): A Case Study. Society of Toxicology's 50th Annual Meeting, March 6-10, 2011. Washington, D.C.

2011. **Thompson, C.**, C. Perry, D. Gaylor, A. Tachovsky, B. Burkhalter, and L. Haws. Derivation of an oral reference dose and drinking water screening level for sulfolane using benchmark dose modeling. Society of Toxicology's 50th Annual Meeting, March 6-10, 2011. Washington, D.C.

2010, Mode of Action For the Cancer Risk Assessment of Ingested Hexavalent Chromium: Identifying and Resolving Data Gaps. **C.M. Thompson**, D. Proctor, L. Haws, M. Harris, Annual Meeting of the Society of Toxicology. (Blue Ribbon Award)

2010, Development of a Physiological Parameters Database for Physiologically-Based Pharmacokinetic (PBPK) Modeling. D. Johns, R. Dewoskin, **C.M. Thompson**, K. Krishnan, H.A. Barton, B. Sonawane. Annual Meeting of the Society of Toxicology.

2008, Evaluation of Physiological Parameters in Adult Rats and Mice for Populating an ACCESS Database. B. Sonawane, D. Johns, **C.M. Thompson**, H. Barton, D. Hattis, R. Tardif, and K. Krishnan. *Annual Meeting of the Society of Toxicology*. Seattle, WA. (Blue Ribbon Award)

2007, Dosimetric Adjustments Across Lifestages in Risk Assessment in symposia session Considering Lifestage in PBPK Modeling for Risk Assessment, *2007 Society for Risk Analysis Annual Meeting*, San Antonio, TX.

2007, Children's Risk Assessment and PBPK Modeling in symposia session Physiological Parameters and PBPK Modeling for Children's Risk Assessment, *Annual Meeting of the Society of Toxicology*, NC.

2007, Physiologically Based Pharmacokinetic (PBPK) Modeling in the Elderly. **C.M. Thompson**, B. Sonawane, and K. Krishnan. *Annual Meeting of the Society of Toxicology*. Charlotte, NC.

2007, Physiological Parameters in Healthy and Diseased Elderly. B. Sonawane, **C.M. Thompson**, D. Hattis, R. Tardif, and K. Krishnan. *Annual Meeting of the Society of Toxicology*. Charlotte, NC.

2007, Use of Toxicogenomics Data in Risk Assessment: A Case Study on Dibutyl Phthalate and Male Reproductive Developmental Effects. S.Y. Euling, S. Makris, B. Sen, A. Kim, B. Benson, K. Gaido, V. Wilson, C. Keshava, N. Keshava, L. White, P. Foster, I. Androulakis, M. Ovacik, M. Ierapetritou, L.E. Gray, **C.M. Thompson**, S. Barone, W. Chiu, W. William, and G. Panos. *Annual Meeting of the Society of Toxicology*. Charlotte, NC.

2006, Noncytotoxic Cell Proliferation as a Subcomponent of the Mode of Action for Formaldehyde-Induced Carcinogenesis. **C.M. Thompson** and R.C. Grafström. *Annual Meeting of the Society of Toxicology*. San Diego, CA.

2006, Proposed Cancer Mode of Action for Formaldehyde Based on EPA Cancer Guidelines. J.E. Whalan, D. DeVoney, **C.M. Thompson**, P. White, and J.J. Vandenberg. *Annual Meeting of the Society of Toxicology*. San Diego, CA.

2005, PBPK Model Simulations of Kidney Physiology and Variability in Renal Clearance. R.S. DeWoskin and **C.M. Thompson**. *Annual Meeting of the Society of Toxicology*. New Orleans, LA.

2005, Development of A Children's Health Risk Assessment Framework Using a Life-Stage Approach S. Barone, R. Brown, S. Euling, E. Cohen-Hubal, C.A. Kimmel, S. Makris, J. Moya, S. Selevan, B. Sonawane, T. Thomas, **C.M. Thompson**. *Annual Meeting of the Society of Toxicology*. New Orleans, LA.

2004, Population Distribution of ALDH2 Genetic Polymorphism: Implications for Risk Assessment & Genetic Polymorphism in CYP2E1: Population Distribution of CYP2E1 Activity. *Evolving Genetics and Its Global Impact*. Bangkok, Thailand.

2002, Pharmacodynamics of Codones and Morphones at mu and delta Opioid Receptors. **C.M. Thompson**, H. Wojno, and D.E. Selley. *International Narcotics Research Conference*. Monterey, California.

1999, P450 2D18-Mediated Metabolism of Dopamine and Arachidonic Acid. **C.M. Thompson**, J.H. Capdevila, and H.W. Strobel. *29th Annual Gordon Research Conference on Drug Metabolism*. Plymouth, New Hampshire.

1998, Protein Expression and Purification of P450 2D18 and Analysis of Activity Towards the Tricyclic Antidepressants Imipramine and Desipramine. **C.M. Thompson**, H. Kawashima, and H.W. Strobel. *28th Annual Gordon Research Conference on Drug Metabolism*. Session A. Plymouth, New Hampshire.

1996, Barbiturate-Induced Expression of Neuronal Nitric Oxide Synthase in the Rat Cerebellum. **C.M. Thompson**, A.E. Bernhard, and H.W. Strobel. *XIth International Symposium on Microsomes and Drug Oxidations*, pp. 205. Los Angeles, California.

1995, The VPS33 Protein is Membrane Associated and Functions in Vacuolar Protein Transport. P.R. Patel, **C.M. Thompson**, and T.A. Vida. *Yeast Cell Biology*, pp. 73. Cold Spring Harbor, New York.