

Chadwick M. Thompson, Ph.D., M.B.A.

SENIOR MANAGING SCIENTIST
MECHANISTIC AND COMPUTATIONAL BIOLOGY

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Chad M. Thompson holds a doctoral degree in Biomedical Sciences and specializes in mechanistic and quantitative aspects of risk assessment. He has written extensively on the mode of action (MOA) of high-profile compounds such as formaldehyde, hexavalent chromium, and dioxin. He has also helped design, conduct, and analyze multimillion-dollar research projects with a focus on understanding the toxicity of environmental contaminants and application of such information to risk assessment. Dr. Thompson has extensive experience in dose-response modeling (including benchmark dose modeling), and he helped develop dose-response packages for the R statistical language (www.r-project.org). Dr. Thompson specializes in the integration of dose-response, toxicological, and mechanistic information in human health risk assessment. As a former health scientist at the U.S. Environmental Protection Agency (EPA), he is a co-author of multiple IRIS chemical risk assessments, as well as several agency documents on risk assessment practices and policies, including the application of physiologically based pharmacokinetic (PBPK) models, toxicogenomic data, and lifestage susceptibility information in risk assessment. Dr. Thompson is a coauthor of more than 50 publications in the peer-reviewed literature, many of which pertain directly to human health risk assessment. He is a former Risk Policy Fellow with the American Association for the Advancement of Science (AAAS).

EDUCATION AND DEGREES EARNED

- 2001 MBA, Virginia Commonwealth University, Richmond, VA
- 1999 Ph.D. in Biomedical Sciences, University of Texas Health Science Center, Houston
- 1994 BS in Psychology (*cum laude*), Old Dominion University, Norfolk, VA

PROFESSIONAL HONORS/AWARDS

- 2013 Society of Toxicology Risk Assessment Specialty Session (RASS) top 10 papers of 2012
- 2012 Society of Toxicology Risk Assessment Specialty Session (RASS) top 10 papers of 2011
- 2010 Society of Toxicology Risk Assessment Specialty Session (RASS) top 10 abstracts of the year award
- 2009 Level II Scientific and Technological Achievement Awards (STAA): Developing Guidelines for Physiologically Based Pharmacokinetic (PBPK) Modeling in Quantitative Risk Assessment
- 2009 Level III Scientific and Technological Achievement Awards (STAA): Outlining the Sensitivity of Inferences on Mode-of-Action and Cancer Risk Estimates using Clonal Growth Models
- 2009 Honorable Mention: A Groundbreaking Lifestage-Specific Approach to Health Risk Assessment of Environmental Exposures
- 2008 Superior Performance Award, cash award from U.S. EPA
- 2007 U.S. EPA Bronze Medal Award for preparing A Framework for Assessing Health Risk of Environmental Exposures to Children
- 2007 Superior Performance Award, cash award from U.S. EPA
- 2006 U.S. EPA Bronze Medal Award for preparing Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment
- 2006 Superior Performance Award, cash award from U.S. EPA
- 2004 2004–2005 AAAS Science & Technology Policy Fellowship
- 2003 2003–2004 AAAS Science & Technology Policy Fellowship
- 2003 Ruth L. Kirschstein National Research Service Awards for Individual Postdoctoral Fellows (declined in order to accept the AAAS Science & Technology Policy Fellowship)

PROFESSIONAL ASSOCIATIONS

American Association for the Advancement of Science
Society of Toxicology, RASS Specialty Section, Mechanisms Specialty Section, LSSOT Regional Chapter

SERVICE/PEER REVIEW

<i>Biomedical and Environmental Sciences</i>	<i>Food & Chemical Toxicology</i>
<i>Cell Biology & Toxicology</i>	<i>Human and Ecological Risk Assessment</i>
<i>Chemical Research in Toxicology</i>	<i>International Journal of Medical Sciences</i>
<i>Chemosphere</i>	<i>Journal of Toxicology and Environmental Health</i>
<i>Drug & Chemical Toxicology</i>	<i>Journal of Applied Toxicology</i>
<i>Environmental Research</i>	<i>Regulatory Toxicology and Pharmacology</i>
<i>Environmental Toxicology & Pharmacology</i>	<i>Toxicology and Applied Pharmacology</i>
<i>Expert Opinion on Drug Metabolism & Toxicology</i>	<i>Toxicology Letters</i>

SELECTED PROFESSIONAL EXPERIENCE

Toxicological Risk Assessment

Evaluated and interpreted toxicology data on a variety of environmental contaminants, including formaldehyde, methanol, chromium, nickel, dioxin and dioxin-like compounds (DLCs), brominated flame retardants, and various VOCs. Areas of expertise include hazard characterization, and dose-response analysis, pharmacokinetics, and developments of toxicity and safety values.

Conducted toxicological evaluations of chemical substances present or potentially present in vaccines, and also derived safe levels for excipients, detergents, surfactants, and other chemicals used in the production or inactivation of vaccine products.

Conducted comprehensive literature reviews on the toxicology of nickel compounds in support of registration under the Registration, Evaluation & Authorisation of Chemicals (REACH) initiative. Populated an International Uniform Chemical Information Database (IUCLID) for each substance. Evaluated key studies for reliability and relevance, synthesized large volumes of data, and generated integrative reports.

Developed, managed, analyzed, and published research into the mode of action (MOA) of intestinal tumors in mice exposed to hexavalent chromium [Cr(VI)] in drinking water. Analyzed *in vivo* and *in vitro* toxicological responses, including toxicogenomic and genotoxic endpoints.

Analyzed dose-response data pertinent to the development of safety values for oral exposure to Cr(VI) using benchmark dose and constrained nonlinear regression modeling techniques.

Communicated toxicological study findings on Cr(VI) to regulatory authorities across North America.

Collaborated with international researchers to develop methods for assessing the presence or absence of potential thresholds in the dose response of genotoxic endpoints both *in vitro* and *in vivo*.

Assisted in the development of an R language script (*viz.*, *drsmooth*) for using smoothing splines to determine point-of-departure values in toxicological dose-response data sets.

Explored techniques for deriving relative potency estimates for DLCs using toxicogenomics and dose-response modeling methods.

Prepared comments on several external review drafts developed by regulatory agencies, including draft risk assessments, toxicological bioassays, and risk assessment practices and policy documents.

Coordinated and co-wrote portions of U.S. EPA IRIS chemical risk assessments, including reactive gases (e.g., formaldehyde) and systematically distributing compounds (methanol).

Evaluated Provisional Peer-Reviewed Toxicity Values (PPRTVs) 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

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. Co-author of:

- 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 (<http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=213405>)

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 their application in PBPK modeling and risk assessment.

Collaborated and, with scientists at Karolinska Institute and the VTT Technical Research Centre of Finland, published 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

Assisted in the oversight of a multimillion-dollar research project on the mode of action of hexavalent chromium. Responsibilities included direct interaction with contract laboratories regarding aspects of final study design, contract review, schedule oversight, managing and authorizing payments to contractors, providing scientific consultation and judgment on technical issues, and providing final approval on delivered work products.

Served as the Technical Project Officer on several contracts with outside vendors. 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.

Litigation Support

Prepared (and rebutted) expert reports for formaldehyde litigation relating to alleged adverse health effects from formaldehyde and mobile home exposures.

Taught CLE course related to causation and Havner guidelines.

COMPUTER & LANGUAGE SKILLS

Ingenuity Pathways Analysis (IPA), IUCLID 5, U.S. EPA's Benchmark Dose Modeling Software (BMDS); PROAST, BMDEExpress, U.S. EPA's Regional Deposited Dose Ratio (RDDR) software v. 2.3, Multi-Path Model of Particle Deposition (MPPD) v. 2.1, Berkeley Madonna (ordinary differential equation solver); GraphPad Prism, @RISK Monte Carlo Software, Microsoft Office (including Access); Minitab Statistical Package, R statistical language.

MANUSCRIPTS

Thompson CM, Dewhurst N, Moundous D, Borghoff SJ, Haws LC, Vasquez MZ. 2024. Assessment of the genotoxicity of tert-butyl alcohol in an *in vivo* thyroid comet assay. *Environ Mol Mutagen* 65(3–4):129–136; doi: 10.1002/em.22601.

Thompson CM, Heintz MM, Cullen JM, Haws LC. 2024. Letter to the Editor of *Environmental Pollution*: In regard to Wan et al. (2024), "GenX caused liver injury and potential hepatocellular carcinoma of mice via drinking water even at environmental concentration." *Environ Pollut*, May 20:124171; doi: 10.1016/j.envpol.2024.124171.

Vincent MJ, Fitch S, Bylsma L, **Thompson C**, Rogers S, Britt J, Wikoff D. 2024. Assessment of associations between inhaled formaldehyde and lymphohematopoietic cancer through the integration of epidemiological and toxicological evidence with biological plausibility. *Toxicol Sci* 199(2):172–193; [open access](#).

Heintz MM, Klaren WD, East AW, Haws LC, McGreal SR, Campbell RR, **Thompson CM**. 2024. Comparison of transcriptomic profiles between HFPO-DA and prototypical PPAR α , PPAR γ , and cytotoxic agents in wild-type and PPAR α knockout mouse hepatocytes. *Toxicol Sci* 200(1):183–198; doi: 10.1093/toxsci/kfae045. PMID: 38574385.

Heintz MM, Klaren WD, East AW, Haws LC, McGreal SR, Campbell RR, **Thompson CM**. 2024. Comparison of transcriptomic profiles between HFPO-DA and prototypical PPAR α , PPAR γ , and cytotoxic agents in mouse, rat, and pooled human hepatocytes. *Toxicol Sci* 200(1):165–182; doi: 10.1093/toxsci/kfae044. PMID: 38574381.

Thompson CM, Brorby G, Keig-Shevlin Z, Smith R, Franzen A, Ulrich K, Blanchette AD, Doepker C. 2023. Assessment of the *in vivo* genotoxic potential of three smoke flavoring primary product mixtures. *Environ Mol Mutagen* 64(8–9):420–431; doi: 10.1002/em.22576.

Thompson CM, Kirman C, Harris MA. 2023. Derivation of oral cancer slope factors for hexavalent chromium informed by pharmacokinetic models and *in vivo* genotoxicity data. *Regul Toxicol Pharmacol* 145:105521, doi: [10.1016/j.yrtph.2023.105521](https://doi.org/10.1016/j.yrtph.2023.105521).

Thompson CM, Proctor DM, Harris MA. 2023. Letter to "Chepelev et al. Establishing a quantitative framework for regulatory interpretation of genetic toxicity dose-response data: Margin of exposure case study of 48 compounds with both *in vivo* mutagenicity and carcinogenicity dose-response data." *Environ Mol Mutagen* 64(4):259–260; doi: [10.1002/em.22537](https://doi.org/10.1002/em.22537).

Heintz MM, Haws LC, Klaunig JE, Cullen JM, **Thompson CM**. 2023. Assessment of the mode of action underlying development of liver lesions in mice following oral exposure to HFPO-DA and relevance to humans. *Toxicol Sci*. 192(1):15–29. doi: 10.1093/toxsci/kfad004. PMID: 36629480; PMCID: PMC10025879.

Thompson CM, Heintz MM, Wolf J, Cheru R, Haws LC, Cullen JM. 2023. Assessment of mouse liver histopathology following exposure to HFPO-DA with emphasis on understanding mechanisms of hepatocellular death. *Toxicol Pathol*. 1926233231159078, doi: 10.1177/01926233231159078. Epub ahead of print. PMID: 36987989.

Rogers JM, Heintz MM, **Thompson CM**, Haws LC. 2023. A putative adverse outcome network for neonatal mortality and lower birth weight in rodents: Applicability to per- and polyfluoroalkyl substances and relevance to human health. *Birth Def Res* 115:1011–1062.

Heintz MM, Chappell GA, **Thompson CM**, Haws LC. 2022. Evaluation of transcriptomic responses in livers of mice exposed to the short-chain PFAS compound HFPO-DA. *Front Toxicol* 4:937168, <https://doi.org/10.3389/ftox.2022.937168>.

Lea IA, Pham LL, Antonijevic T, **Thompson C**, Borghoff SJ. 2022. Assessment of the applicability of the threshold of toxicological concern for per- and polyfluoroalkyl substances. *Regul Toxicol Pharmacol* 133:105190, [open access](#).

Chappell GA, Wolf JC, **Thompson CM**. 2021. Crypt and villus transcriptomic responses in mouse small intestine following oral exposure to hexavalent chromium. *Toxicol Sci*, kfab152, doi: 10.1093/toxsci/kfab152. Epub ahead of print. PMID: 34935971.

Thompson CM, Aardema MJ, Heintz MM, MacGregor JT, Young RR. 2021. A review of mammalian in vivo genotoxicity of hexavalent chromium: implications for oral carcinogenicity risk assessment. *Crit Rev Toxicol* 51(2), <https://doi.org/10.1080/10408444.2021.2000934>.

Thompson CM, Bhat VS, Brorby GP, Haws LC. 2021. Development of updated RfD and RfC values for medium carbon range aromatic and aliphatic total petroleum hydrocarbon fractions. *J Air Waste Manag Assoc* 71(12):1555–1567, doi: 10.1080/10962247.2021.1974123.

Proctor DM, Bhat V, Suh M, Reichert H, Jiang X, **Thompson CM**. 2021. Inhalation cancer risk assessment for environmental exposure to hexavalent chromium: Comparison of margin-of-of exposure and linear extrapolation approaches. *Regul Toxicol Pharmacol* 124:104969, <https://doi.org/10.1016/j.yrtph.2021.104969>.

Felter SP, Zhang X, **Thompson C**. 2021. Butylated hydroxyanisole: Carcinogenic food additive to be avoided or harmless antioxidant important to protect food supply? *Regul Toxicol Pharmacol* 121:104887.

Chappell GA, Wikoff DS, **Thompson CM**. 2021. Assessment of mechanistic data for hexavalent chromium-induced rodent intestinal cancer using the key characteristics of carcinogens. *Toxicol Sci* 180(1):38-50, <https://doi.org/10.1093/toxsci/kfaa187>.

Gentry R, **Thompson CM**, Franzen A, Salley J, Albertini R, Lu K, Greene T. 2020. Using mechanistic information to support evidence integration and synthesis: A case study with inhaled formaldehyde and leukemia. *Crit Rev Toxicol* 50(10):885–918, <https://doi.org/10.1080/10408444.2020.1854678>.

Thompson CM, Gentry R, Fitch S, Lu K, Clewell HJ. 2020. An updated mode of action and human relevance framework evaluation for formaldehyde-related nasal tumors. *Crit Rev Toxicol* 50(10):919–952, <https://doi.org/10.1080/10408444.2020.1854679>.

Thompson CM, Donahue DA, Hobbs C, Costecalde Y, Franzen A, Suh M, Proctor DM, Harris MA. 2020. Exposure to environmentally-relevant concentrations of hexavalent chromium does not induce ovarian toxicity in mice. *Regul Toxicol Pharmacol* 116, open access: <https://doi.org/10.1016/j.yrtph.2020.104729>.

Chappell GA, **Thompson CM**, Wolf JC, Cullen JM, Klaunig JE, Haws LC. 2020. Assessment of the mode of action underlying the effects of GenX in mouse liver and implications for assessing human health risks. *Toxicol Pathol* 48(3):494–508, doi: 10.1177/0192623320905803. PMID: 32138627.

Pham LL, Borghoff SJ, **Thompson CM**. 2020. Comparison of threshold of toxicological concern (TTC) values to oral reference dose (RfD) values. *Regul Toxicol Pharmacol* 113:104651 [open access], <https://doi.org/10.1016/j.yrtph.2020.104651>.

Bhat VS, Cohen SM, Gordon EB, Wood CE, Cullen JM, Harris MA, Proctor DM, **Thompson CM**. 2020. An adverse outcome pathway for small intestinal tumors in mice involving chronic cytotoxicity and regenerative hyperplasia: A case study with hexavalent chromium, captan, and folpet. *Crit Rev Toxicol* (open access), <https://doi.org/10.1080/10408444.2020.1823934>.

Chappell G, Rager J, Wolf J, Babic M, Leblanc, Ring C, Harris MA, **Thompson CM**. 2019. Comparison of gene expression responses in the small intestine of mice following exposure to three carcinogens using the S1500+ gene set informs a potential common adverse outcome pathway. *Toxicol Pathol* 47(7):851–864, <https://doi.org/10.1177/0192623319873882>.

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- Proctor DM, Suh M, Chappell G, Borghoff SJ, **Thompson CM**, Wiench K, Finch L, Ellis-Hutchings R. 2018. An adverse outcome pathway (AOP) for forestomach tumors induced by non-genotoxic initiating events. *Regul Toxicol Pharmacol* 96:30–40, doi: 10.1016/j.yrtph.2018.04.016.
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- Thompson CM**, Kirman CR, Hays SM, Suh M, Harvey SE, Proctor DM, Rager JE, Haws LC, Harris MA. 2018. Integration of mechanistic and pharmacokinetic information to derive oral reference dose and margin-of-exposure values for hexavalent chromium. *J Appl Toxicol* 38:351–365. doi: 10.1002/jat.3545.
- Thompson CM**, Wolf, JC, McCoy A, Suh M, Proctor DM, Kirman CR, Haws LC, Harris MA. 2017. Comparison of toxicity and recovery in the duodenum of B6C3F1 mice following treatment with intestinal carcinogens captan, folpet, and hexavalent chromium. *Toxicol Pathol* 45(8):1091–1101. DOI: 10.1177/0192623317y4324.
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- Thompson CM**, Rager JE, Suh M, Ring CL, Proctor DM, Haws LC, Fry RC, Harris MA. 2016. Transcriptomic responses in the oral cavity of F344 rats and B6C3F1 mice: Implications for risk assessment. *Environ Mol Mutagen* 57:706–716.
- Thompson CM**, Bichteler A, Rager JE, Suh M, Proctor DM, Haws LC, Harris MA. 2016. Comparison of *in vivo* genotoxic and carcinogenic potency to augment mode of action analysis: Case study with hexavalent chromium. *Mutat Res* 800:28-34.
- Thompson CM**, Suh M, Mittal L, Wikoff D, Welsh B, Proctor DM. 2016. Development of linear and threshold no significant risk levels for inhalation exposure to titanium dioxide using systematic review and mode of action considerations. *Regul Toxicol Pharmacol* 80:60–70.
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ABSTRACTS, PRESENTATIONS, POSTERS

Heintz MM, Buerger AN, Haws LC, East AW, Cullen JM, **Thompson CM**. Comparison of phenotypic and transcriptomic profiles between HFPO-DA and prototypical PPAR α , PPAR γ , and cytotoxic agents in wild-type and PPAR α knockout mice. Abstract 3972, Society of Toxicology 64th Annual Meeting, Orlando, FL, March 2025.

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