Peer Review Report

A Proof-of-Concept Case Study Integrating Publicly Available Information to Screen Candidates for Chemical Prioritization under TSCA

May 2021

Table of Contents

Overview

EPA staff developed the report, "A Proof-of-Concept Case Study Integrating Publicly Available Information to Screen Candidates for Chemical Prioritization under TSCA," which presents a proof-of-concept approach to organizing large numbers of chemical substances using publicly available scientific data for further evaluation. This report was identified as Influential Scientific Information (ISI), under the definitions and guidelines of the EPA Peer Review Handbook[1]. After internal EPA technical review, the report was sent to five independent experts for external peer review. The process was managed by Eastern Research Group, Inc under contract by EPA. The charge to reviewers and the individual responses are contained in this report.

Summary of report

Regulatory agencies world-wide are looking to efficiently integrate information on chemical substances in order to inform priorities for decisions and data requests. This document presents the Public Information Curation and Synthesis (PICS) approach that integrates publicly available hazard, exposure, persistence, and bioaccumulation information for chemical substances. The PICS approach synthesizes information from traditional and new approach methods (NAMs) to understand the overall degree of potential concern related to human health and the environment as well as the relative coverage of potentially relevant human health and ecological toxicity and exposure information that could inform level of effort and resources that may be needed to evaluate that specific substance. This approach is not designed to replace any existing prioritization processes but aims to increase efficiency and focus expert review on substances that may have a greater potential for selection for further evaluation. A proof-of-concept case study was performed by applying the PICS approach to a subset of the TSCA active inventory. The PICS approach may be applied to large numbers of chemical substances and is an important tool for integrating and synthesizing large amounts of publicly available information.

Peer Review Process

EPA conducted the independent peer review process using a contract with Eastern Research Group, Inc (hereafter, "ERG"). The peer review process provided a documented, independent, and critical review of the report. For this review, EPA provided ERG with the draft report and a list of required expertise.

[1] U.S. Environmental Protection Agency Peer Review Handbook 4th Edition, 2015 (https://www.epa.gov/sites/production/files/2015-10/documents/epa_peer_review_handbook_4th_edition_october_2015.pdf)

Specifically, EPA asked for experts in human health toxicology, ecological toxicology, fate and transport, chemistry and exposure science; and that all reviewers should have broad expertise in the area of toxicology and/or exposure and in vitro methodology, as well as an understanding of new approach methodologies and other applicable guidance particularly as related to chemical risk assessment. ERG was charged with sole responsibility for recruiting qualified peer reviewers and conducting a thorough conflict of interest (COI) screening. During the selection process, ERG developed a list of 10 candidate reviewers, and ultimately selected five peer reviewers (see section 4). EPA provided consent for these reviewers, and ERG certified that these five peer reviewers had no real or perceived COI.

ERG also facilitated the peer review by distributing materials and managing the returned reviews. In consultation with EPA, 12 charge questions under five groupings were developed and provided to reviewers (see Section 5). ERG monitored the review and returned responses to EPA. After reviewing the responses, EPA asked ERG for a clarification from one reviewer. The original text and clarification are provided in Dr Edward Perkins' response for transparency. Section 6 of this Peer Review Report presents the reviewers' individual written comments.

List of peer reviewers and affiliations

Dr. Tara S. Barton-Maclaren, Health Canada
Dr. Weihsueh A. Chiu, Texas A&M University
Dr. Helen M. Goeden, Minnesota Department of Health
Dr. Kerry W. Nugent, AICIS (formerly NICNAS)
Dr. Edward J. Perkins, Department of Defense

Charge to Reviewers

1. OVERALL QUESTIONS

   Based on your knowledge and understanding of toxicology and/or exposure, chemistry, and risk assessment, please comment on the overall TSCA POC document.

   1A. Does this document address the purpose and aims as laid out in the introduction?

   1B. Are the ideas presented throughout the document clear and presented in a logical manner?

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

2. SCIENTIFIC DOMAINS

Based on your knowledge of toxicology, chemistry, risk assessment, and/or exposure science, please comment on the evaluation, workflow, and metrics developed for the individual scientific domains in the TSCA POC.

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

For each of the scientific domains, there is a discussion of limitations and longer-term options. Based on your knowledge of toxicology, chemistry, and/or exposure science:

2C. Are the appropriate limitations and long-term options included for each domain?

2D. Are there additional long-term options that could be included?

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

Peer Review Comments

Reviewer: Tara S. Barton-Maclaren, Ph.D.

Sr Research Manager, Emerging Approaches Unit, Health Canada,
Healthy Environments and Consumer Safety Branch, Ontario, Canada

Thank you for the opportunity to review the EPA TSCA Proof-of-Concept Case study. This is a well written and clear document outlining the data sources, methods and outcomes of the approach relative to the chemical space selected to illustrate the utility and sensitivity of the tool. Introducing automated approaches to enhance the efficiency of chemical screening and prioritization is an area under exploration and development is risk assessment programs internationally. The thoughtful integration of data and technical advancements described and tested in this PICS approach will provide a useful foundation to support modernizing approaches to priority setting in programs external to the EPA.

For transparency, I would like to acknowledge that my review focused on the details related to the human health hazard and exposure domains. The ecological domains are outside the scope of my scientific expertise.

1. OVERALL QUESTIONS

Based on your knowledge and understanding of toxicology and/or exposure, chemistry, and risk assessment, please comment on the overall TSCA POC document.

1A. Does this document address the purpose and aims as laid out in the introduction?

In the introduction, the EPA effectively delineates the key drivers behind the need for a more effective, rapid and consistent approach to screen chemicals for further evaluation – that being far too large an inventory to continue to manually collect, synthesize and review information that can be more efficiently processed using automated workflows. It is explicitly outlined that the approach is to include both traditional and NAMs in the scientific domains. The addition of the background section with relevant information set the stage well delineating the motivation and requirements of the presented approach.

The purpose and aims are clearly defined; that being to understand the information landscape of large inventory of chemicals, provide transparent and reproducible, as well as a flexible and sustainable process, increase efficiency and manage workload, and create a modular workflow that can be readily adapted. Each aim is thoroughly met as evidenced by the detailed descriptions of the data used, the considerations for interpretation, the development and application of the domain criteria as well as by the recognition of limitations and areas for further work. What the approach is not intended to do was also stated. This is important to acknowledge and adds clarity on purpose and scope. For consideration as an additional element of “not intended” I do wonder if it should be acknowledged that this approach does not include the comprehensive screening of scientific literature that may be available and used for subsequent risk assessments (i.e. PubMed, SciFinder, etc). The document indicates throughout that this approach integrates publically-available information, for transparency acknowledging the scope of information that is captured up front would also be useful as this will inherently limit the information availability metric of many chemicals that may have data outside the scope of the sources used.

1B. Are the ideas presented throughout the document clear and presented in a logical manner?

Generally, the document is clearly written, well organized and the style and format makes the document and technical information easy to follow. The overall approach is introduced to provide an overarching view and each of the domains are systematically described. The use of consistent tables and the inclusion of definitions and brief explanations in footnotes adds further clarity and transparency in the document. The use of schematics and graphical representations of the information and results effectively communicates the outcomes of the proof-of-concept evaluation.

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

Yes, given that the domain workflows are programmed to run in an automated fashion and search large publically-available curated datasets, I see no concerns in scaling this approach to address the TSCA inventory. Technology and the workflow, in my opinion, is not the limitation of the approach; this is what in fact makes the method very scalable to thousands of chemicals. Data availability from the Type 1 information sources used more broadly for the TSCA inventory is the more challenging element. In scaling the approach across the larger chemical space more emphasis may be needed on NAM data than was used in the proof of concept which included chemicals either with fairly high levels of information or those for which there is already an established level of concern.

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

Yes, many other chemical risk assessment programs internationally are seeking methods to introduce efficiencies, transparency and consistency in their screening, prioritization and assessment processes. The approach described provides a first-tier screening approach for prioritization but may also find utility for other programs, with some modification, as a strategy for automated data searching and collection of data for those chemicals already designated for risk assessment. The design and inclusion of the information gathering flags nicely supports early identification of data gaps which can be leveraged early in the problem formulation or risk assessment process to direct further information gathering or data generation as appropriate. The EPA has gone to great efforts to compile and curate a significant amount of data that is and undoubtedly will continue to be useful for other regulatory programs. The fact that the approach is designed in domains and the data sources are well documented allows the flexibility for others to adapt and customize as needed to meet program requirements or needs that might be different to those of the EPA.

2. SCIENTIFIC DOMAINS

Based on your knowledge of toxicology, chemistry, risk assessment, and/or exposure science, please comment on the evaluation, workflow, and metrics developed for the individual scientific domains in the TSCA POC.

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

The domain specific evaluations were logical and weighted appropriately based on tiers of information with *in vivo* scoring highest. This aligns with current risk assessment requirements and the use of animal studies for hazard characterization and point of departure derivation.

Designing the domain workflows to select more conservative options is appropriate as a first tier in the screening and prioritization process. Further refinement can be done during the expert review stage. The specific identification of the study types that are missing with the IG flag is a key element of the

reporting in particular if there are opportunities to address the data gaps in advance of starting the risk assessment.

For the Hazard-to-Exposure (HER) evaluation, there would be added value to include a more detailed description related to the interpretation and impact of this metric in the overall outcome of the scientific domain results. Given that this is the metric that provides the risk-based context, I wondered if the weight of this metric in the overall scheme should have a more prominent role. I've included more specific comments related to the chemical comparison in the results section below.

A general observation regarding the scientific domains is that this is a sound data driven approach for substances that have a more fulsome dataset, existing hazard classifications and/or existing assessments. However, it is not as clear if the approach will support the identification of substances that have the potential to be of concern but that are lacking traditional (animal) data from the data sources currently incorporated. The goal of prioritizing substances with higher data availability has been effectively achieved. If there is a desire to also document those substances that (may) require further action but that do not have traditional data, then this may not have been achieved based on the designation of a value of 0 or IG flag when other than primary source animal data are considered. The noted exception is for the genotoxicity domain. Perhaps related to the comment above, this is where further details on the application of the HER, BER, TER could be expanded to better illustrate how this subset of chemicals will be defined. Expanding the POC test set to include chemicals based on the lower tiered data might help to delineate this aspect of the approach further.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

One element of the scientific domain that is not included is that of endocrine activity. The EPA has made much progress in this area in terms of developing tiered screening approaches for the prioritization of chemicals for potential endocrine disruption. The absence of this domain from the approach appears to be a gap that might also contribute to the expansion of considerations in the susceptible populations domain.

Carcinogenicity Domain - Based on the IG flags description in table 2 my interpretation is that there are a number of limited data sources that in fact would lead to the designation of a metric even if secondary source data or a determination by an authoritative source is not considered to contribute to the metrics. If this is true, it would be beneficial to provide a list or table of the data sources that are considered acceptable in the carcinogenicity determination. For further consideration, especially in the context of prioritization, would be how the sources of information currently noted as IG flags could contribute in a more quantitative manner to the metric as I would expect there could be substances missed through this exclusion (Table 10 indicates that only 3% of substances on the TSCA active inventory have carcinogencity data). Perhaps there is a strategy to look more closely at those substances with the IG flag that do have information other than an IARC classification or 2-year cancer bioassay, but this is not clear based on the current description. In that case, the value of 0 given in the "absence of data" may be a little misleading. Some further clarity here would be helpful.

Including further detail on how NAM will be used in the workflow would be useful. For example, in Section 5.5 and Table 11, including chemicals that use BER and TER as the domain metric and how these translate to positions on the graphical visualizations would be interesting. As a pre-prioritization exercise NAM may also be used to begin to identify those substances of potential emerging concern i.e., those

that have hazard flags, potential for exposure but for which higher tier information is not available. This could also support the identification of information gaps and accordingly, research and data needs.

In the case of the genotoxicity domain, secondary data sources were deemed acceptable and given an IG flag for awareness and presumably follow up as relevant. Why would this same approach not be considered acceptable for other hazard domains? This could be appropriate across the domains given the number of substances that will have very limited data. Perhaps this would require a metric scale of 5 to allow for these sources to have a metric = 1 rather than 0. 0 would then truly reflect no data / no flags as is done for sensitization and irritation. For consideration.

<u>For each of the scientific domains</u>, there is a discussion of limitations and longer-term options. Based on your knowledge of toxicology, chemistry, and/or exposure science:

2C. Are the appropriate limitations and long-term options included for each domain?

HER Domain - It is appreciated that the limitations regarding inhalation values are included. Could similar considerations and discussion be added for the derma routel? Exposure via the dermal route is often a key scenario and driver in risk characterizations for products. Are there complementary models or approaches that exist or that should be developed (in the future) to better include and characterize potential concern related to the dermal route of exposure?

Carcinogenicity -The discussion on limitations and longer-term options for the carcinogenicity domain triggered some thinking in the context on how one might better use predictive tools.
Regarding OncoLogic, some additional considerations are needed in order to incorporate the outcomes of this type of predictive system in an automated way. Some concerns would be the relevance of the flags to the parent query chemical based on OncoLogic only, as the system bases the prediction on chemical features that are common with chemical classes of carcinogenic concern and not the primary structure of interest. As such multiple chemical classes may be alerted for a single substance having many functional groups and in turn can lead to different levels of concern for the same chemical. Although it is acknowledged that OncoLogic is a valuable tool, it would be best incorporated into a consensus or weight of evidence approach with complementary predictions from other profilers.

OncoLogic Primary Classification profiler is included in the current OECD QSAR Toolbox, and can now accommodate batch runs; however, this would only provide a high-level flag as a starting point. Using the QSAR Toolbox functionalities, chemicals with OncoLogic flag would need further investigation to verify/justify the relevance of the cancer flag. This could also be done in the OECD Toolbox through the development of groups around the target chemicals but would require some expert driven evaluation.

Of note, (although likely a well know point) a lack of flag shouldn't or cannot be interpreted as absence of genotoxic or carcinogenic activity as the domain of OncoLogic is limited by its chemical classes.

Other profilers or databases in the Toolbox that might be considered in the development of a more automated approach include:

- Carcinogenic Potential Database (CPDB)
- Genotoxicity & carcinogenicity ECVAM database
- ECHA REACH database
- Cell transformation assay ISSCTA database
- Carcinogenicity & Mutagenicity (ISSCAN) database
- Carcinogenicity (genotox, nongenotox) alerts by ISS

It is acknowledged that the suggestions above may be beyond the goal of this domain and would require some development and validation work however may provide a more substantiated approach in the longer term for data poor chemicals.

Susceptible Populations - Agree that a limitation of the susceptible population domain is the sole focus on children. Expanding the metric to include additional susceptible populations would be of great value. Workers is mentioned; other populations for consideration could be pregnant women, sex-related susceptibilities, geographical location / hot spots and socio-economic considerations.

The approach mentions that data collection is ongoing to expand this domain. Kudos to the EPA and ORD for their tremendous efforts related to data collection and curation. These efforts have important utility for risk assessment programs beyond the EPA.

2D. Are there additional long-term options that could be included?

In addition to the above, a long-term consideration could be to continue to work toward integrating broader information sources such as through the development of natural language processing approaches. This would continue to expand the data sources and enable the screening of other published literature with the goal of getting a better idea on the amount of supporting information (even if in an qualitative manner) that could be available to support assessment.

Another consideration is complementing the approach with the ability to identify groups/clusters of substances that may warrant further exploration rather than the more single substance approach outlined in the current proof-of-concept.

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

It is clearly stated that the information availability domain is designed to automatically evaluate substances based on both the number and types of studies available. The manner by which the type of studies for each chemical is taken into account and how the amount of information available impacts the four modifying criteria could be more explicitly outlined in section 5.4. My interpretation of the description is that a value of "1" will be given to each scientific domain for which there is any single piece of experimental data to a maximum of 8 points for substances with a complete data profile in the context of the approach. This is equivalent to those chemicals for which there is an authoritative human health risk assessment. Whether "experimental data" implies in vivo experimental only is not clear. This could be defined for added transparency. An outstanding question is how each of the four modifying criteria are applied to the information availability metric derived based on the scientific domains? A low and high chemical specific example to illustrate the calculation would be informative.

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

The results of the POC clearly demonstrate the strength and consistency of this automated data driven approach when compared against chemicals with a previously characterized level of concern. Illustrating that the approach can distinguish high and low priority chemicals, when experimental data is available, using the various data plots and then providing specific chemical examples for the

calculation of the scores provides further transparency. The addition of the plot of frequency distribution of the IG flags for each of the scientific domain metrics for the POC238 set of substances was particularly interesting and gives a solid perspective on the actual data situation at hand even for what is likely a subset of the more data rich or better characterized (e.g. SCIL) chemicals. This is also acknowledged in the POC report.

Although the overall evaluation and communication of the results are well written and clearly presented, I offer a few comments for consideration.

In the opening sentence it is noted that out of the active TSCA inventory of 33, 092 substances only 15, 987 are unique organic chemical substances. If this is the defined chemical space of applicability for the PICS approach that could be stated. Also, if true, and mixtures or chemicals with greater complexity are not included, then future work may be to explore ways that an automated screening approach could be applied to the other 52% of chemicals on the active inventory. This is an area where there is likely an imperative need to apply the various NAM tools and grouping approaches that have been developed and demonstrated to have application to begin to address the more complex contexts related to screening and assessment.

Based on figure 16 (distributions of metric scores for selected substances) the whiskers span of the distributions are very large in some cases. What was interesting is that in the case of the TSCA high and the TSCA low, the lower and upper bounds for each respectively, do not overlap suggesting that it might be possible to suggest regions within the priority matrix that result in high, moderate and low priority for further work. Although this part of the evaluation is implicit in the analysis there is not a discussion on where soft thresholds could be placed on the plots to inform future activities. It may be of interest to think of these types of thresholds, or zones, to inform both priority for prioritization for risk assessment as well as priority for possible research and data generation.

The addition of the examples to illustrate the process is valuable. The example chemicals are shown to clearly separate high vs low based on the differential values of the scientific domain however based on the HER metric values of 2.7 and 2.3 for benzene and 3-methoxybutyl acetate, respectively, they are similar. In this case, the driver for the high designation is flags across hazard domains, including cancer classification, however this doesn't necessarily mean that the repeat dose toxicity flag is insignificant for 3-methoxybutyl acetate in terms of possible toxicity of concern. Could the impact and utility of the HER (or BER, TER) be further discussed in the overall context of the SDM? The chemical examples included focus on chemicals with fairly clear outcomes. Would it be possible to include another example, or 2, to also illustrate the application and impact of the BER and/or TER on outcome?

Further to the previous comment, perhaps another level of priority in the context of endpoint severity could be introduced to distinguish priority substances with existing classifications (e.g. CMR) – again just food for thought as this might be considered beyond the scope of a pre-prioritization effort.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

Yes. As outlined above, the selection of chemical space was relevant and appropriate to address the aim and purpose of the approach. Further, the level of analysis conducted was in-depth enough to demonstrate with examples that the conclusions are well supported for those chemicals that have *in vivo* data. The area that could be further expanded on is the inclusion of experimental data other than animal guideline studies in the case of some of the scientific domains however this does not contradict the fact the results presented support the conclusions.

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

Editorial or additional comments have been included in **Table 1** below.

The existing substances bureau has also been conducting a review of data sources that are relevant for hazard identification and assessment. A supplementary excel document (**Table-2-14 Jan 2020.xlsx**), including a crosswalk of data sources in ToxValDB with those included in our in-house search strategy has been shared in case there are other data sources that may be incorporated into the EPA automated approach. In the table, those sources highlighted in red may be novel sources to consider. Some caveats are that this list has not been carefully scrutinized in detail to rule out any possible redundancies to all sources that the EPA may have already included and there are some sources that may not be amenable to automation as bulk data downloads are not possible. This would need follow up from EPA scientists.

Table 1.

Section / Page / Line Number	Comment
4.1 / pg 12 / 294	Figure 1. There is added value in introducing the scheme at a high level as an introduction to the overall approach however the elements listed within the figure are too small to read in the schematic. Suggest increasing font size and perhaps adjusting arrangement in the vertical directions to allow for each of the SDM and IAM figures to be slightly increased in size for readability.
5.0 / pg 15 / footnote 25	Please check formatting – appears that there may be additional numerical values in the text (footnotes within footnotes?) (e.g. a direct query such as SQL20, or webservice APIs21. EPA's National Center for Computational Toxicology's Chemistry Dashboard22 is one of the several examples of a Type 1 source. The Chemistry Dashboard integrates information across various sources mapped to an expert-reviewed chemical structure23)
5.0 / pg 15 / 80	It is noted that SOPs are being implemented in a software system – Can the system be named? Is it public software or an in-house system?
5.1 / pg 15 / 392 - 395	DTXSIDs are appropriate identified however in our experience the InChI keys tend to be the most reliable substance identified. The EPA may want to consider including these as a secondary or complementary source of identifiers for mapping to CAS numbers.
5.1 / pg 16 / 418 - 419	The statement related to overall information availability implies that the exercise was conducted for the entire inventory, is this correct? If yes, could quantification of this statement be added?
5.2 / pg 17 / 452	Please define "…for making a determination…." – is this a determination of potential hazard or speaking to the overall determination of high vs low priority for each of the scientific domains?
5.2 / pg 19 / Figure 4	The tiered approach to data selection and application is well outlined however, I offer a few suggestions for further refinement. - Exposure estimate? I understand this as estimate coming from ExpoCast only – what could lead to a "no" estimate? And how does a value of zero impact the overall outcome for the HER if that is still intended to be described based on flow in figure 4?

	- Suggest to use a third colour box to outline IG flag - Suggest that "lowest appropriate[2] POD" be defined – I suspect this was intended but it appears to be missing in the Figure description. I would also suggest that these are different for in vivo and in vitro PODs respectively.
5.2 / pg 20 / 497	For purposes of priority setting would it not be more protective from an early screening perspective to use 95th percentile estimates to capture possible susceptible populations as well as general population (median estimates)?
5.2 / pg 20 / 500	It is noted that "other routes of exposure are included if the units had been converted appropriately…". Dermal exposure is often a key driver for concern for products used by consumers. It is understood that dermal studies are often lacking however, is it possible to include IG flags for those chemicals where the exposure models predict likely dermal use / exposure scenarios? This could be an important trigger for further evaluation to ensure critical exposure scenarios are not missed in the screening step.
5.2 / pg 20 / 506 - 508	Additional publication for consideration to add to references - Paul Friedman K, Gagne M, Loo LH, Karamertzanis P, Netzeva T, Sobanski T, Franzosa JA, Richard AM, Lougee RR, Gissi A, Lee JJ, Angrish M, Dorne JL, Foster S, Raffaele K, Bahadori T, Gwinn MR, Lambert J, Whelan M, Rasenberg M, Barton-Maclaren T, Thomas RS. Utility of In Vitro Bioactivity as a Lower Bound Estimate of In Vivo Adverse Effect Levels and in Risk-Based Prioritization. Toxicol Sci. 2020 Jan 1;173(1):202-225. doi: 10.1093/toxsci/kfz201. PMID: 31532525; PMCID: PMC7720780.
5.2 / pg 20 / 537	Should the first term read log10(HER/BER/TER)?
5.2 / pg 20 / 544-545	If the value of zero is given as a result of no exposure information but there are (high) hazard flags is there a specific annotation that could be provided to direct the info gathering flag? I am thinking in the context of being able to better inform targeted info gathering and/or prioritizing info gathering and/or data generation efforts.
5.2 / pg 20 / Table 1	For clarity suggest including in the table interpretation of the continuum, i.e. 1 = highest HER (lowest concern); 4 = lowest HER (highest concern)
5.2 / pg 22 / 555 - 556	"…uses hazard information from *in vivo* repeat dose studies." It should be clear that "repeat dose" studies includes a broader scope such as reproductive and developmental studies. Perhaps a specific note to this nature earlier in the section would provide useful clarification regarding the breadth of study types included. Also, is this information restricted to guidelines studies? I suspect not necessarily if PODs that are available from an authoritative regulatory agency may be used, but this would also be a useful detail to include.

5.2 / pg 22 / 568	"…used to identify a minimum potency value showing bioactivity" – consider adding that although this is an area for refinement current evidence supports that this global bioactivity approach is protective/conservative and that further efforts to refine may provide additional pathway specific PODs (increase relevance / credible).
5.2 / pg 22 / 570	"…other sources of high-throughput bioactivity data, …". Suggest providing some example to pre-empt the application, e.g. high throughput transcriptomics, high content phenotypic data and others as relevant.
5.2 / pg 23 / 585 - 587	Carcinogencity Domain - In addition to the sources noted here (e.g., IARC, IRIS) it is suggested that GHS classification categories could also be included here as a flag indicative of the ability of an agent to cause cancer. I note that GHS is later noted as a flag for sensitization and irritation and would suggest that it could also be used for other classifications.
5.2 / pg 25 / Genotoxicity Domain	Relevant citation that may be of interest: Catrin Hasselgren, Ernst Ahlberg, et al. Genetic toxicology in silico protocol, Regulatory Toxicology and Pharmacology, Volume 107, 2019, 104403, ISSN 0273-2300, https://doi.org/10.1016/j.yrtph.2019.104403. (http://www.sciencedirect.com/science/article/pii/S0273230019301655)
5.2 / pg 29 / Table 3	Metric 1 and 2 – should these both indicate predicted "or" measured. Or is there an intentional difference between 1 – predicted and measured with 2 0 predicted or measured?
5.2 / pg 32 / 772	Typo - …"calculated in the same way as for human HER…
5.5 / pg 50 / 1269	Typo - benzene, 70.5~~.0~~
5.5 / pg 50 / 1370	The PICS replies on a large database developed from many source databases. If there is a need for ongoing screening and prioritization in a cyclical manner is there a proposed frequency and plan for updating the data sources? Or is the workflow pulling directly from the primary sources as possible?
5.5 / pg 55 / Table 11	A few comments on Table 11. - Benzene HER metric in the text indicates 2.8 and is 2.7 in the table. - HER repeat dose values – it is not clear how these values are derived. Suggest adding explanation to the narrative comparison of the 2 chemicals.

Reviewer: Weihsueh A. Chiu, Ph.D.
Professor, Department of Veterinary Integrative Biosciences
College of Veterinary Medicine and Biomedical Sciences, Texas A&M University
College Station, Texas

1. OVERALL QUESTIONS

Based on your knowledge and understanding of toxicology and/or exposure, chemistry, and risk assessment, please comment on the overall TSCA POC document.

1A. Does this document address the purpose and aims as laid out in the introduction?

Yes, overall, this document addresses the purpose and aims as laid out in the introduction. However, a major limitation is in how the 238 POC238 substances were selected, and the degree to which they are representative and the results generalizable. Some of the "expected" results for the POC238 are described on pages 52-53, and page 57 (paragraph lines 1352-1365). However, the fact that this is at the very end suggests that this reasoning may be somewhat post-hoc. Thus, while the POC238 may be a useful exercise in showing the feasibility of the process involved in the PICS approach, it has less utility with respect to showing that the results are useful. For instance, more formal analysis of the discriminatory power of the PICS approach – including its stated goal of allowing more false positives while reducing false negatives – may be useful before proceeding to apply it across the whole TSCA inventory. Additionally, perhaps a depiction of the chemical space covered by the POC238 as compared to the entire inventory may be useful (e.g., principal components, phys/chem descriptors such as molecular weight, log P, polar surface area, etc.).

1B. Are the ideas presented throughout the document clear and presented in a logical manner?

Yes, overall, the ideas in the document are clear and logically presented.

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

Yes, overall, this method appears to be scalable to the thousands of individual chemicals on the TSC inventory. However, it should be noted that because of the QC requirements, it is not "fully automated," but will still require knowledgeable staff to implement. Additionally, it was noted that "the majority of the substances on the inventory are mixtures of varying complexity" – so it is very unclear that this approach is scalable to address those substances.

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

Yes, overall, as a whole, this method appears to be adaptable to other large-scale chemical prioritization efforts other than TSCA, as long as only individual chemicals are prioritized.

2. SCIENTIFIC DOMAINS
Based on your knowledge of toxicology, chemistry, risk assessment, and/or exposure science, please comment on the evaluation, workflow, and metrics developed for the individual scientific domains in the TSCA POC.

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

Overall, the decisions in each domain-specific evaluation appear logical and based on sound science.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

There are several significant issues that I would like to elaborate on:

i. First, the PICS approach should strongly consider adding QSAR-derived PODs to the tiered workflow for the Human Hazard-to-Exposure Ratio domain. For instance, Li et al. (2020) [https://doi.org/10.1289/ehp6483] recently performed screening assessments that incorporated PODs from the Wignall et al. (2018) [https://doi.org/10.1289/ehp2998] QSAR model for toxicity values. Similarly, Jolliet et al. (2020) [https://doi.org/10.1111/risa.13604] also used this QSAR model in its high throughput risk and impact screening approach when in vivo values are not availab le. Additionally, it was shown in Wignall et al. (2018) that the QSAR model performed better (in terms of precision and accuracy) at predicting PODs than

the ToxCast+HTTK approach employed in PICS. It should also be noted that QSAR is used in some of the other domains (e.g., genotoxicity, bioaccumulation), so there should be no reason to exclude it here.

ii. Second, the issue of metals and metalloids may need special treatment. From a screening approach (minimizing false negatives, allowing more false positives), it may be more appropriate to simply group metal and metalloid-containing compounds by the element of metal or metalloid it contains. Effects of speciation and different chemical forms is a level of detail that is probably better conducted under the "expert review and analysis" step.

iii. The determination of when data are "negative" (e.g., carcinogenicity and genotoxicity domains) needs to be made more transparent. In particular, the distinction between "inadequate"/"inconclusive" and "evidence of low likelihood" is not described. It is generally very difficult to "prove a negative" so my suggestion for both of these is that for "evidence of low likelihood" be removed as a category. Thus, "inadequate" or "inconclusive" would be the lowest level with data, and then a separate category of course for "no data." Additionally, it seems that "inadequate" or "inconclusive" would also merit some sort of flag for information availability, though not to the same degree as "no data."

iv. For the susceptible population domain, it is unclear how the "cutoffs" were determined between the value from 1-18 and the metric of 1-4. See comment below about using percentiles.

v. For persistence, the relationship between the experimental half-lives and the half-lives in the persistence criteria column is unclear. Why would biodegradation half-life of 2.75-5 weeks have the same rating as persistence half-life of >180 days? What is the justification for this correspondence?

vi. Finally, particularly for the "Ratio" metrics but maybe also for some of the others (maybe "Susceptible population, for instance), I wonder whether a percentile-based metric would be more useful, since we are really talking about relative ranking throughout the entire process. The problem with the direct use of the ratio metric is that, even on log scale, a few "outliers" can mean that the results are bunched up.

For each of the scientific domains, there is a discussion of limitations and longer-term options. Based on your knowledge of toxicology, chemistry, and/or exposure science:

2C. Are the appropriate limitations and long-term options included for each domain?

Except for those issues identified above in 2B, the appropriate limitations appear to be included for each domain.

2D. Are there additional long-term options that could be included?

It may be useful to include a discussion of what options are available for mixtures for each domain.

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

The description of the information availability domain calculations is not very clear. It would be useful to have a more extensive flow-chart as to how the determinations are made for each domain and how they are added together. Additionally, it is odd that the IG flags "do not directly impact the information availability metric" – it seems that this information could be integrated. Finally, the 0 or 1 only for each

domain seems overly coarse, so perhaps including the IG flags could provide a more graded score for each domain.

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

My main concern as to the description of the results is that by aggregating all the scores together, one loses the information on the individual domains. Additionally, this does not distinguish between cases of "high score" in a few domains and "moderate score" in many domains. The "rule" for moving to more detailed evaluation could be a combination of total score and "maximum score" (or "top 3" or something like that).

Additionally, a graphical visualization may be easier for communication. For instance, the ToxPI methodology (most recent published version: Marvel et al. 2018 [https://doi.org/10.1186/s12859-018-2089-2] has been used at EPA and elsewhere to help visualize multi-domain information. I would imagine actually that two ToxPIs – one for the Scientific Domains and one for the Information Availability – would be useful. You can still have an overall aggregated ToxPI Score, but having the "pie" visualization would better describe evidence for each domain. For instance, in example with Benzene and 3-Methoxybutyl acetate, a ToxPI for each chemical would very easily show the differences between the two chemicals in terms of the different metrics.

Finally, providing some idea as to the distribution across chemicals for each metric would be useful (e.g., histograms). This will help to identify whether there are certain domains where the metrics are too coarsely categorized and therefore not useful for discrimination between "higher potential" and "lower potential" substances.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

As I mentioned in the "overall" comments, the main issue is whether the PICS approach offers discriminatory power as to the potential for high and low priority. Thus, it seems that a more rigorous, statistically-based analysis with some prior expectation as to the results would be useful. This could be a two-stage approach, in which PICS is used on a set of chemicals, but the results blinded, and then the expert judgment process is applied to ALL those chemicals, and then the discriminatory power is analyzed (how well does PICS predict "high" and "low" priority, with the desired higher sensitivity at the expense of lower specificity).

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

I do not have any additional or editorial comments.

Reviewer: Helen M Goeden, Ph.D.
Principal Toxicologist, Health Risk Assessment Unit
Minnesota Department of Health, Saint Paul, Minnesota

1. OVERALL QUESTIONS

Based on your knowledge and understanding of toxicology and/or exposure, chemistry, and risk assessment, please comment on the overall TSCA POC document.

1A. Does this document address the purpose and aims as laid out in the introduction?

This document describes an approach (PICS), which integrates publicly available information in such a way that can efficiently provide screening level information on potential concern within the context of how much relevant information is available. The purpose of the document is not explicitly stated. By reading through section 2 one can surmise that the purpose is to describe why the PICS approach was developed and the aims are to describe how the PICS was developed and tested using a Proof-of-Concept (POC) case study. The POC case study illustrated the ability of the PICS approach to separate lower and higher potential concern chemicals while also acknowledging the limitations of the available relevant information.

1B. Are the ideas presented throughout the document clear and presented in a logical manner?

The document steps through each individual domain in a logical and generally clear manner. The scope of the domains and integration are quite large but the authors should be commended on writing a concise document that is quite readable. Some of the sections could benefit from additional information, especially for readers who may not be as familiar with TSCA activities. Some of these suggestions are provided below as well as in the comments on the individual metrics.

Figure 2. Schematic of the PICS Approach in Relation to Identifying High- and Low-Priority Candidate Substances – as it is currently presented indicates that PICS is not only compiling and integrating information in a useful way but that it is the only factor going into identifying a subset of the TSCA Active Inventory for additional expert review and analysis? If this is correct – what criteria is used to identify this subset? If PICS is just one of several tools the Figure should be modified.

Section 5.1 Chemical Substance Selection, Curation and Quality Control.

Since the quality of the data was not evaluated the use of the phrase Quality Control is inappropriate and should be completely avoided throughout the document. A term such as “Data Verification” appears to be more accurate and should replace the phrase “Quality Control”.

The bulleted list under Chemical Substance Selection should include mention of TSCA10 and 90. Presumably the TSCA 10 are included within the first bullet “Initial proposed set of 20 high- and 20-low-priority candidate substances” and likewise, the second bullet – “Chemical substances from the 2014 update to the TSCA Work Plan” includes the TSCA 90 list.

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

The automated method described in the document appears to be scalable to a much larger group of chemicals. The POC list, however, was enriched in the high priority regulatory substances, and the remaining chemical substances were largely selected because of knowledge of some toxicological concern. It is not clear whether the information required to calculate a valid Scientific Domain Metric (SDM) exists for the thousands of chemicals, which would be necessary for the PICS approach to be applied in a meaningful way.

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

The PICS approach does appear to be adaptable for other large-scale evaluations within EPA that are focused on identifying chemicals that may be of higher concern. Again, the key factor will be availability of information to inform SDM. In addition to prioritization, the approach may also be useful in identifying common data gaps across large groups of chemicals, which could facilitate research efficiencies.

2. SCIENTIFIC DOMAINS

Based on your knowledge of toxicology, chemistry, risk assessment, and/or exposure science, please comment on the evaluation, workflow, and metrics developed for the individual scientific domains in the TSCA POC.

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

Within each domain the evaluation as described was logical and were science-based. The overall decision on the selection of the individual domains appears, at least in part, to be based on past practice. Section 5.2 explains that the domains were selected based on their importance to understanding human and ecological hazard and human exposure based on past use in TSCA prioritization activities and/or statutory language in the Frank R. Lautenberg Chemical Safety for the 21st Century Act.

In particular, it is not entirely clear why separate carcinogenicity and genotoxicity domains are identified. While it is true that cancer can occur in absence of gentoxicity that in itself is not sufficient rationale for having two of the seven individual SDM in essence assigned to the same endpoint. A single potential carcinogenicity score that incorporates genotoxicity and the available cancer data would suffice. If the goal of the selected individual domains is to identify endpoints that are of particular concern developmental/reproductive hazard should also be a separate domain. Developmental and reproductive hazards can have generational impacts. The susceptible population assessments appears to focus on exposure and does not address toxicological susceptibility.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

The workflows appear logical and the concepts are easy to follow. I did not identify significant issues but do have some suggestions or comments some of the individual domains.

Human Hazard-to-Exposure –

Formula 1 should be formatted in equation format to increase readability. The opposing directions of the metrics will undoubtedly cause confusion - - chemical with the lowest HER (highest concern) is set to the highest domain value of 4 and highest HER (lowest concern) is set to the lower domain value of 1. This domain would greatly benefit from having an example - the chemicals with the largest and smallest HERs are mentioned in the paragraph. Using one or both as an example to demonstrate how the equation calculations work should be beneficial. Alternatively, 3-methoxybutyl acetate and benzene, the two compounds listed in Table 11 could be used as the chemical examples throughout the document.

5.3 Scientific Domain Metric Calculation

Combining individual domain no data chemicals with those given a value of 1 (low concern) could result in a misleading SDM value. However, this is apparently addressed in the visual by the size of the dot – as noted in the title/description of Figure 14. This statement should also be explicitly stated in Section 5.3. as it is absolutely critical context, especially when the individual domain metrics of zero are set to 1.

For each of the scientific domains, there is a discussion of limitations and longer-term options. Based on your knowledge of toxicology, chemistry, and/or exposure science:

2C. Are the appropriate limitations and long-term options included for each domain?
2D. Are there additional long-term options that could be included?

I commend the authors for including a limitations and longer-term options discussion for each of the domains. I have combined my comments 2C and D below for each domain.

- ***Human Hazard-to-Exposure Ratio (HER) Domain***

  There are a variety of types of PODs, with some representing no effect levels while others may represent effect levels (e.g., NOAEL 'vs' LOAEL). This is not mentioned in the discussion but distinguishing between types of PODs is critical in providing context to the magnitude of the HER. Limitations should include identification of chemical class for which in vitro bioassays (the basis of the BER) or TTC (the basis of the TER) do not perform well.

  Use of TTC values – current TTC values have a large overlap of toxicity distributions within each category, and therefore is of limited value for separating chemicals of different toxicity potential. FDA has been working on an enhanced decision tree (EDT) for several years. An overview of the improvements were presented at the Jan 2020 Tox Forum Session: Update to the Cramer et al., Decision Tree and Thresholds of Toxicological Concern to Improve Safety Assessment and Prioritize Chemicals for Testing. The presentations were publically available for a limited time and appear to no longer be available. I do have a copy which I can make available. Alternatively, Dr Stice The three TTC classes are based on 613 compounds whereas the EDT will be based on over 1900. The large overlap between classes of different toxicity potential is vastly improved in the EDT. Based on personal communication with Dr. Stice (Szabina.stice@fda.hhs.gov), who leads this effort, there are two manuscripts under development. The first contains what, why and how and was to be submitted to Regulatory Tox and Pharm fall of 2020. The second manuscript (also to be submitted to Reg Tox and Pharm in approximately Feb of 2021) will contain the actual decision tree with over 100 example substances.

  An additional tool for estimating $NOAEL_{chronic}$ is that should be considered is the application of a LD_{50}-to-$NOAEL_{chronic}$ or $NOAEL_{subacute}$-to-$NOAEL_{chronic}$ extrapolation factor (Kramer et al Conversion Factors Estimating Indicative Chronic No-Observed-Adverse-Effect Levels from Short-term Toxicity Data. Reg Tox Pharm 23: 249-255, 1996). The Minnesota Department of Health has evaluated this methodology and has found that it performed better than the TTC approach. The performance of TTC vs LD_{50} extrapolation was summarized in a 2017 SOT poster presentation and in project reports (an executive summary of the most recent report can be found at https://www.health.state.mn.us/communities/environment/risk/docs/guidance/dwec/execsumm2015.pdf).

  ATSDR has also assessed the use of LD_{50} by assessing LOAELs, NOAELs and MRLs from ATSDR's MRL dataset (personal communication with Siwakoti, 2016 SOT poster). The strength of association between log-LOAELs and log-LD_{50}s in molar units was evaluated using correlation analysis and regression. The 90^{th} percentile LD_{50} to $NOAEL_{chronic}$ Conversion Factor was very consistent with the 95^{th} percentile CF reported in Kramer et al 1996.

The Texas Commission on Environmental Quality utilizes LD_{50} extrapolation to derive NOAEL-to-LD_{50} ratio-based toxicity values for chemicals with limited toxicity data (TCEQ Guidelines to Develop Toxicity Factors, Sept 2015. Accessed at: Guidelines to Develop Inhalation and Oral Cancer and Non-Cancer Toxicity Factors (texas.gov))

Regarding the exposure parameter - it is not clear why NHANES is the sole source of biomonitoring data. Biomonitoring data is the most direct measure of human exposure and data is available from additional sources such as California (Explore Results | Biomonitoring California) and Canada (Human Biomonitoring of Environmental Chemicals - Canada.ca). If these sources do not allow for automated compilation of the data that should be acknowledge in the document.

- **Carcinogenicity and Genotoxicity Domains**
  While it is true that carcinogenicity may be associated with nongenotoxic as well as genotoxic mechanisms it is not clear what the value added is by having separate domains. Many chemicals will not have cancer data - nearly half of the chemicals in the test set have no cancer data. Whereas only ~8% of the test compounds did not have genotoxicity data. Chemicals with higher cancer scores also typically had higher genotox scores. From a risk perspective chemicals with no cancer data but high genotox scores would be of concern not only for cancer but for developmental toxicity as well. Development of a carcinogenicity potential domain, that incorporates both cancer data and genotox data would provide a better metric.

  Having two of the seven SDM domains focused on carcinogenic potential seems unnecessary. In addition, other health effects of high concern such as developmental or reproductive toxicity, which can have generational consequences should be consider as a separate domain. In the absence of developmental toxicity test data the EPA TEST could be used to predict developmental toxicity along with other tools.

- **Ecological Hazard Domain**
  This domain is outside my area of expertise. I have the same comment re: formula 2 as for formula 1 – put the formula into equation format and provide example(s) to demonstrate how the domain metric value is calculated.

  Although consideration only of aquatic ecotoxicity is consistent with the GHS approach ecotoxicity for other terrestrial organisms (e.g. amphibians, birds, reptiles, etc) should be pursued as a longer-term option. The human hazard domain evaluation does not address terresterial ecotoxicity concerns.

- **Susceptible Human Population Domain**
  Although susceptible subpopulation is defined as a group of individuals within the general population who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture this domain only focuses on the exposure aspect and does not address greater toxicological susceptibility. This focus should clearly be acknowledged in the limitations. A domain name of Susceptible Human Population Exposure Domain would be more accurate. In the absence of developmental toxicity test data the EPA TEST could evaluated as a potential predictor of developmental toxicity along with other tools.

- **Persistence and Bioaccumulation Domain**
  Glad to see that EPA is in the process of adopting new approach that includes partitioning, as well as acknowledging the current inability to adequately predict bioaccumulation of ionizable compounds. In addition to identifying this inability the relative magnitude of this problem should be conveyed (e.g., many or few substances commonly exist in the ionized state at environmental pH values).

In addition to persistence (how long a substance may remain in the environment) there should be at least two additional considerations:

1) magnitude of use. Widely used substances result in a 'constant' environmental presence and therefore are persistent in the environment, and
2) the ease or difficult for removing the substance (e.g., remediation) should also be considered.

- **Skin Sensitization and Skin/Eye Irritation Domain**
  This area is outside expertise. Multiple limitations are clearly stated.

  Longer-term options – EPA OPP has a major effort to use alternative approaches for skin sensitization and skin/eye irritation. Why are these efforts (e.g., Adopting 21st-Century Science Methodologies - Replacement Strategies | Pesticide Science and Assessing Pesticide Risks | US EPA) not mentioned here?

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

The description of the IAM calculation is straightforward. Within the PICS approach the information availability metric (IAM) is designed to automatically evaluate chemical substances based on the number and type of studies available to inform this analysis. Missing information is flagged but the IG flags do not directly impact the IAM and only identify specific information gaps. If the chemical substance has a human risk assessment from one of six authoritative bodies it is given a point for each of the human information availability study types. However, the existence of a human risk assessment does not indicate that information is available for each of the study types. In fact, the risk assessment from some of the authoritative bodies listed may conclude that the information available is insufficient to assess potential risk to human health. Rationale for assigning a point for each human information study type needs to be provided.

It is not clear why the IAM section does not include a Limitations and Longer-term Options discussion. Limitations in the methodology and potential longer-term options for improvement should be identified and discussed.

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

The results of the POC are clearly described and presented. The results of the POC study demonstrated that while the SDM and IAM were correlated, the PICS approach was able to segregate the recently released TSCA high- and low-priority candidate substances.

Only a small fraction of the chemical substances in the non-confidential active TSCA inventory have some in vivo mammalian data and ecotoxicological data. The data included in the PICS approach was limited to publically available data and excludes industry submitted CBI studies. The PICS approach also did not include data extracted from the literature beyond what is included in the Type 1 data sources currently being utilized. Given the dearth of publically available data and the clear association between SDM and IAM (i.e., more information tends to produce a higher value) an explanation for excluding industry submitted CBI should be provided.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

The results of the POC support the conclusions. Automation of data gathering and compilation to more efficiently and accurately inform chemical selection is an admirable goal. Since the POC list was enriched in the high priority regulatory substances, and the remaining chemical substances were largely selected because of knowledge of some toxicological concern it raises the question of whether sufficient data exists for PICS to achieve this goal given that there may be insufficient data to inform a SDM. This concern should be acknowledged. The PICS approach may only be useful for a subset of chemicals that have at least minimal data. If data is missing from the majority of the individual domains a reasonable estimate of an SDM is not possible.

Inclusion of 2-methoxybutyl acetate and benzene as illustrations of how the process works is very important. If possible these chemicals should be used as examples of how values are calculated using Formula 1 and 2.

[Note several of the specific scores noted in the text do not match the values in Table 11. For example, HED metric for benzene is identified as 2.8 in text but 2.7 in table.]

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

I have several suggested edits to add clarity to several sections.

Executive Summary –
Regulatory agencies world-wide are looking to efficiently integrate information on chemical substances in order to inform priorities for decisions and data requests. This document updates the US Environmental Protection Agency's (EPA) long-term strategy described in the Working Approach for Identifying Potential Candidate Chemicals for Prioritization and presents the Public Information Curation and Synthesis (PICS) approach that integrates publicly-available hazard, exposure, persistence, and bioaccumulation information for chemical substances. The PICS approach is based on two dimensions. The first dimension, Scientific Domain Metric (SDM) synthesizes information from traditional and new approach methods (NAMs) to understand the overall degree of potential concern related to human health and the environment. The second dimension, Information Availability Metric (IAM)reflects the relative coverage of potentially relevant human health and ecological toxicity and exposure information that could inform level of effort and resources that may be needed to evaluate that specific substance. The PICS approach is not designed to replace the prioritization process described in TSCA but aims to increase efficiency and focus expert review on substances that may have a greater potential for selection as a high- or low-priority candidate.

A proof-of-concept case study was performed by applying the PICS approach to a subset of the TSCA active inventory. The results demonstrate that the approach discriminated between high- and low-priority candidate substances and identified potential information gaps. The PICS approach may be applied to large numbers of chemical substances and is an important tool for efficiently integrating and synthesizing large amounts of publicly-available information. Aspects of the approach could also be adapted and applied to other prioritization decision contexts (e.g., biosolids).

Figure 1. Schematic of the PICS approach
This figure should be simplified to provide an initial 'big picture' view of the approach. Strongly recommend providing a simplier and more general visual. The IAM part is completely unreadable due to the level of detail provided, a less detail visual could be used accompanied by a footnote that a more details are provided in Figure 12. Presenting the results of the POC without the accompanying details can create confusion. TSCA 10 and TSCA 90 are not even defined until page 51. With a lower level of detail in the text additional visual enhancements that convey that higher metric scores convey higher concern/greater levels of relevant information.

Section 4.1, last paragraph needs to be broken up to enhance readability:

The PICS approach is based on two dimensions allowing visualization and separation of the chemical substances along each dimension (Figure 1). The first dimension reflects the overall degree of potential concern related to human health and the environment and is the integration of the individual results from the domain-specific workflows. In the PICS approach, this dimension is referred to as the Scientific Domain Metric (SDM).

The second dimension reflects the relative coverage of potentially relevant human health and ecological toxicity and exposure publicly-available information that could inform level of effort and resources that may be needed to evaluate that specific substance. This dimension is referred to as the Information Availability Metric (IAM). The level of effort and resources is typically context specific and informed by expert judgment; however, an expert driven approach is not scalable to apply to the thousands of substances on the TSCA active inventory at the initial screening stage. Therefore, a set of modifying criteria were used to inform the set of potentially relevant human health and ecological toxicity information. The modifying criteria were modeled after considerations used in the EPA New Chemicals program and include a combination of functional use considerations, environmental half-life, water solubility, molecular weight, and whether the chemical substance is an exempt polymer. The existence of an authoritative human health assessment would also contribute to this metric. In the PICS approach, the summary result constitutes IAM.

The SDM and IAM are combined into a graphical representation of the PICS approach for the substances on the TSCA active inventory. In response to public comments, the PICS approach moved away from the defined 'bins' of chemical substances that had been proposed in the Working Approach. The PICS approach does not determine what a result for a specific chemical substance represents, rather it provides a synthesis of the public information available for individual substances.

Reviewer: Kerry W. Nugent, Ph.D.

Principal Scientist
Australian Industrial Chemicals Introduction Scheme (AICIS)
Gymea Bay, New South Wales, Australia

Background

This review takes into account experience gained during prioritization and assessment activities undertaken by the Australian industrial chemicals regulator. This organization and the relevant program changed names on 1 July 2020. The past work referenced herein was undertaken within the Inventory Multitiered Assessment and Prioritisation (IMAP) program of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Future work is under the Evaluations program of the Australian Industrial Chemicals Introduction Scheme (AICIS). The Evaluations program is effectively a continuation of the IMAP

program, with revisions of the chemical selection methodology, to account for most of the highest priority chemicals being addressed under IMAP.

1. OVERALL QUESTIONS

1A. Does this document address the purpose and aims as laid out in the introduction?

I am of the opinion that the document is very informative. It lays out a methodology for prioritizing chemicals for assessment in an automated manner, to reduce the amount of time-intensive manual data collection and review. This will only be required for chemicals selected by the automated process, for final decision making. It addresses methodologies for integrating data from animal experiments with data from new approach methodologies (NAMs), quantitative structure activity relationships (QSAR) and authoritative classification systems.

One critical aspect is that the document lays out what the approach is not intended to do. When this is taken into account, it is clear that the tools used in the PICS approach are highly relevant.

1B. Are the ideas presented throughout the document clear and presented in a logical manner?

The background information on the development of the ideas for prioritization of TSCA active chemicals is very useful for understanding the context of the remainder of the document. Following this, the basic architecture of the PICS approach is laid out. The individual constituents of the PICS approach are then described in detail, followed by a worked example. This reads clearly and was understandable on the initial reading. However, the Excel worksheet demonstrating the entire proof of concept working is difficult to follow and could be redesigned to maximise the logic flow of the presentation.

The approach has one novel and very useful component. That is the use of two separate dimensions, effectively one of known risk, and one of the available information. This allows decisions to be based not only on the likely risk, but also on the ability to fully characterize the risk.

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

This may be a problem given the current day data landscape. Given that the phase-in period of the European Union (EU) REACH program is now effectively complete, the availability of more animal data for incorporation in the approach is unlikely to increase dramatically. This leads to the situation pictured on Page 53, where the information availability metric for TSCA active chemicals is very much lower than that for the proof-of-concept set. This leads to a corresponding decrease in the scientific domain metric, not because the larger group of chemicals (TSCA active) is inherently safer, but because many of the chemicals have a default position for many hazards, associated with information gathering flags.

The future developments in QSAR predictivity and NAM information collection will go some way towards addressing this issue, although there remains a hurdle relating to quantification of results from these methods, and in gaining acceptance of the relevance of these methods for regulatory rulemaking.

One aspect of the risk assessment toolkit which is not greatly used in the PICS approach is read across. This is understandable, as read across normally requires significant expert input to ensure that it is used appropriately. However, in a limited sense, read across might be automated with higher reliability. This is where substances are ionizable, and their toxicity can be assigned to a summation of the toxicity of the individual component parts. This is particularly relevant for certain endpoints such as carcinogenicity. For example, the International Association of Research on Cancer (IARC) classifies component parts, rather than individual chemicals, for carcinogenicity. An example is lead compounds.

One simple way to incorporate this idea is to expand "lead compounds" to the group of individual lead compounds within the TSCA active group. More automated solutions could also be considered; I would normally consider a potassium salt to be well characterized if there is sufficient information on its equivalent sodium salt.

Specifically, for carcinogenicity, for which there is little available data, an expert system to identify chemical comprised of only low risk groups (such as alkanes, simple esters) might be of value.

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

The split between likely risk and data availability to fully characterize the risk should be useful in other chemical prioritization exercises, for example of environmental chemicals or pesticides, as well as in other jurisdictions for industrial chemicals. However, in a broader sense, this may be useful beyond chemical prioritization, with adjustment of the scientific domain tools.

2. SCIENTIFIC DOMAINS

Human Hazard-to-Exposure Ratio Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

This looks appropriate. It uses very new exposure estimate developments from ExpoCast and will serve as a stringent test of this methodology. I agree with the chosen group of exposure pathways. However, I consider that it would be better to include worker exposure under this domain, rather than as a sensitive population, where there is some incongruity. Dermal toxicity and inhalation toxicity are very relevant but may require different exposure models to be fully utilized. Reproductive toxicity point of departure (POD) estimates may also be used within this domain.

Use of TER as a conservative substitute for missing POD values is supported.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

Workflow appears appropriate. The ranking system, Formula 1, seems a convenient way of assigning scores that reflect the relative risk of the chemicals. There is a minor issue with Formula 1; it would be better to include within the formula an indication the maximum and minimum POD values are across the entire set, rather than just including this in the note below. Possibly a subscript "global" might be appropriate.

2C. Are the appropriate limitations and long-term options included for each domain?

There is discussion of use of acute toxicity data. This often relates to different modes of toxicity to those seen in repeat dose studies and should probably be used to develop their own HER values, in conjunction with relevant short term exposure scenarios, to fully consider chemicals such as carbon monoxide.

If sufficient exposure scenarios are included (including inhalation), the difference between systemic and local effects in animal studies by inhalation is of less importance.

The value of BER values to this domain is likely to increase as high throughput bioactivity data gathering is refined and in vitro/in vivo extrapolation methodology improves.

2D. Are there additional long-term options that could be included?

Development of further ExpoCast models to fully utilize dermal and inhalation data, particularly for workers, and selection from this expanded range of HER values.

Carcinogenicity Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

I agree with treating carcinogenicity separately from genotoxicity, in part because of the existence of non-genotoxic modes of carcinogenicity; also to the great public concern about chemical carcinogenicity. Separation of the carcinogenicity and genotoxicity domains gives increased weighting to genotoxic carcinogens, but I consider this to be a positive outcome.

This is an extremely difficult metric, due to the severe lack of data, the difficulty in predicting non-genotoxic carcinogenicity, and the lack of potency considerations in the main available data sources (classifications). Classifications are based on the quality of available evidence, rather than carcinogenic potency. There are some issues relating to this which cause difficulty in maximally utilizing this domain.

As an example, I will use the chemical 3,3'-dichlorobenzidine, which is one of the chemicals included in the POC set. Animal experiments suggest that this chemical is probably similarly potent to the IARC Class 1 chemical, benzidine. However, there are no quality human data for this chemical, probably due to most cohorts having exposure to carcinogens apart from this chemical. Accordingly, IARC considered it to be Class 2B. There is a Globally Harmonised System (GHS) harmonized classification which has been developed within the EU, which considers it to be GHS Class 1B (more similar to IARC Class 2A). An EU harmonized classification should be considered similarly reliable to an IARC classification.

Taking this into consideration, it remains hard to envisage a better scientific basis for this determination.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

As discussed above, the simple workflow based on existing classifications seems to be the best available option. Higher level data, such as slope factors, which could serve as potency-based indicators, are available only for a prohibitively small set of chemicals.

2C. Are the appropriate limitations and long-term options included for each domain?

The limitations of current automated prediction systems are an important focus of ongoing work.

2D. Are there additional long-term options that could be included?

Two additional steps could be considered. First is expansion of group classifications by IARC (for example, lead compounds) into a set of classified chemicals within the TSCA active set. Second, there are very few reliable data available on "low likelihood of carcinogenicity", and it may be possible to develop a simple expert system to identify chemicals for which we consider the likelihood low. This would be more straightforward than full development of a prediction system.

Development of an expert system based on principles such as the Benigni-Bossa rules could also serve as a screening level prediction tool.

Genotoxicity Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

It may be of value to include additional genotoxicity test result types, rather than limit the data set to three study types. Studies such as sister chromatid exchange, unscheduled DNA synthesis and comet assays (in vitro and in vivo) would help to enlarge the data set. Inclusion of QSAR predictions, particularly those which utilize predictions of metabolism, is appropriate.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

I agree with the workflow. Chemicals classified as known mutagens should be specifically flagged. Where there are positive mutagenicity flags, it is appropriate that the PICS system should not count positive and negative results – these tests often relate to different modes of mutagenicity and in is normally not the case that uniformly positive results are obtained even for known mutagens. This determination should be left for expert consideration.

2C. Are the appropriate limitations and long-term options included for each domain?

The report notes than genotoxicity data are reasonably available, but often in secondary sources. It is appropriate that expert judgement is invoked by the scores given when any positive results are reported.

2D. Are there additional long-term options that could be included?

It is probable that data will continue to be generated for this endpoint, whether by in vitro methods or by QSAR.

Ecological Hazard Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

It is noted in the report that this domain is restricted to hazard, and data limitations restrict it to aquatic toxicity. The effect of missing data (acute and chronic, three trophic levels) is not adjusted by uncertainty factors but will be evident in the Data Availability Domain. One key consideration is that QSAR predictions of aquatic hazard data have a particularly long history and are therefore comparatively advanced.

The use of a factor of 10 for comparison of acute and chronic POD values is supported.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

The ranking system, Formula 2, seems a convenient way of assigning scores that reflect the relative hazard of the chemicals. As for Formula 1, I would like to see a subscript “global” against the maximum and minimum POD terms in Formula 2. It is pleasing to see that POD values above the maximum water solubility of the chemical are discounted by giving these chemicals a score of 1.

2C. Are the appropriate limitations and long-term options included for each domain?

Key limitations are described. Firstly, an automated system of environmental exposure estimation is flagged as a high priority. This would improve the quality of the environmental score by giving it a risk basis. Secondly, the limitation to aquatic data is raised. This is much more difficult to address, as there is paucity of data on other environmental compartments, and exposure estimation for these compartments is likely to be difficult. Consistent with current environmental screening, it is probable that the important aquatic compartment will remain the main focus. However, chemicals having

terrestrial toxicity (animals or plants) are likely to generally have higher scores in the human toxicology sections, or aquatic toxicity, and expert review of terrestrial data may occur in higher level screening.

2D. Are there additional long-term options that could be included?

Environmental assessment is not my main area of work, and so I am not aware of forthcoming developments which may add to this approach.

Susceptible Human Population Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

Similarly to carcinogenicity, this is a very difficult metric, but of high public interest. The approach used here is to identify potential scenarios which may lead to higher exposure of children compared with adults. Uses of the chemical leading to their presence in exposure sources relevant to these scenarios are then identified. The approach is therefore largely a list-based expert system, which appears to be unavoidable. Accounting for different bioavailabilities for individual chemicals for the same type of exposure source would be more complex than can be addressed at this screening level.

Currently, the metric is limited to excess exposure of children, for whom the factors leading to higher exposure can be reasonably well defined. Other susceptible populations, such as pregnant women and the elderly, would be much more difficult to narrow down in this way.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

Within the limitations described above, the workflow seems appropriate. As the data do not allow quantitative estimation of the excess exposure at this screening level, the assignment of scores to represent the likely exposure differential compared with adults seems the best compromise. I do not think that disproportionate weight should be placed on monitoring data (such as dust or breast milk), as this is largely influenced by the choice of analytes in a given study. Analytes not chosen to be studied may be missed if monitoring data is too large a component of the score.

2C. Are the appropriate limitations and long-term options included for each domain?

As stated above, I would prefer the worker exposure to be treated in the risk based Human Hazard-to-Exposure Ratio Domain. The limitation arising from the incomplete nature of the main data sources is acknowledged, and it is probable that the quality of this domain score will improve over time.

2D. Are there additional long-term options that could be included?

Any identification of further factors or behaviours giving rise to greater exposure of children or of other susceptible populations should be taken into account in development of this metric. An example may be products (non-therapeutic) with disproportionate use in hospitals or aged care homes.

Persistence and Bioaccumulation Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

The methods used in this domain scoring are consistent with normal assessment practice.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

One issue which I have identified is within Table 8. I consider that a combined score of 1, which can only arise when one or the other score is 0, should be translated to a score of 0, rather than 1.

2C. Are the appropriate limitations and long-term options included for each domain?

There are major issues when a chemical is not a neutral organic. Some of these issues, for example for perfluorinated substances, will require more work.

2D. Are there additional long-term options that could be included?

It should be practicable to define relevant scoring tables for the key inorganic ions, such as Pb, Cd (suggest metric score of 4) and Na, K (probably 1). Common anions could be treated similarly, with the maximum score for cation or anion being taken forward.

Skin Sensitization and Skin/Eye Irritation Domain

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

While these are quite different toxicological outcomes, having two separate domains would give excess weighting compared with the other toxicological domains. Compared with my previous comment about genotoxic carcinogens, in this case excess weighting is not warranted.

The scoring system is effectively aligned with the presence of GHS classifications, and requires confidence in the existing GHS classification. Alternate scoring systems would be difficult to implement, as there are multiple test methods with different scoring methodologies. These are already accounted for in the GHS classification system. However, it is valid to use raw data from more common test types (Draize, LLNA) and apply GHS rules where necessary.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

The biggest issue is with lack of reporting of GHS classifications for chemicals which do not meet the classification criteria. For this reason, lack of a classification is ambiguous, meaning either no data or not meeting criteria. This is a rationale for including the mapping of result summary sentences from REACH dossiers. The sentences in the classification section of the dossiers ("data conclusive but not sufficient for classification") can also serve as sources for identifying negative test results. However, for the many chemicals without dossiers, this remains an issue.

I note that sensitization category 1 maps to the same result as category 1a. This is appropriate, as the older guinea pig test methods are still major data sources, and these do not allow subcategorization of positive sensitization results.

Use of the most conservative of the individual score metrics (skin sensitization, skin irritation, eye irritation) is the most appropriate way to combine the scores in this domain. However, consideration could be given to changing the sensitization score table, for example scores of 0, 1, 3 and 4, so that strong sensitizers give scores similar to the highest irritancy classifications. These chemicals can have major morbidity outcomes.

2C. Are the appropriate limitations and long-term options included for each domain?

Quality issues with REACH dossiers will have some impact, but the current ECHA activities will lead to improvement over time. Over-classification is not likely to be a major issue, but under-classification can lead to missed chemicals. The biggest limitation is lack of listing of negative classification results.

2D. Are there additional long-term options that could be included?

In the short term, the Hazardous Substance Information System (HSIS) maintained by Safework Australia can be considered a reliable source of classifications. These derive either from harmonized EU classifications or classifications determined through NICNAS assessments. Future AICIS assessment are likely to become Type 1 sources. Existing IMAP assessments are not machine readable, but the classifications available from HSIS can be used.

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

The purpose of this domain is clear, and the decision-making process is described sufficiently. The subcategories appear logical.

One issue which does arise is that low scores may be obtained for some chemicals where assessment can still be carried out satisfactorily. These are cases where either some of the data types are not relevant (for example, carbon monoxide) or where individual hazards are so high that exposures related to other hazards will not occur (for example, potent genotoxic carcinogens). It is not clear how the second case could be addressed, but a separate category for gasses could be established.

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

The summary results in the Word document are sufficiently clear. Figure 16, in particular, is very informative. The presentation of the individual substances in the plot of Scientific Domain versus Information Availability is a visual guide to selection for assessment priority.

The use of a worked example is useful.

The Excel supporting data are not presented in a user-friendly form; identification of the key result columns is difficult, and the scores for each scientific domain could also be highlighted.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

The summary accurately reflects the data presented.

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

I noted an interesting pair of chemicals in the test set. These are 3,3’-dichlorobenzidine and the corresponding hydrochloride. From an assessor point of view, these would largely be considered interchangeable, with possible differences only in skin and eye irritation. Given the critical importance of the carcinogenicity potential of these chemicals, these differences would be of little importance. Based on the interchangeability of data between these two chemicals, I would like to see in the longer term

that the system can converge them to the same results for both scientific domain and for data availability.

Reviewer: Edward J. Perkins, Ph.D.
U.S. Army Senior Research Scientist
Environmental Networks and Genetic Toxicology
U.S. Army Engineer Research and Development Center (ERDC)
U.S. Army Corps Engineers (USACE)
Vicksburg, Mississippi

1. OVERALL QUESTIONS
Based on your knowledge and understanding of toxicology and/or exposure, chemistry, and risk assessment, please comment on the overall TSCA POC document.

1A. Does this document address the purpose and aims as laid out in the introduction?

In section 2, the introduction lays out the purpose of the document to be to describe the Public Information Curation and Synthesis (PICS) approach for integrating publicly-available information on the more than 33,000 chemical substances on the non-confidential TSCA active inventory to efficiently select substances for expert review prior to prioritization. The document aims to do this using a proof-of-concept case study to show how the PICS approach can help streamline the evaluation of chemical substances by transparently and reproducibly synthesizing available information and identify potential data gaps. Additionally, other sections (1) indicate that the document aims to demonstrate that the PICS approach can discriminate between high- and low-priority candidate substances, (4.1) aims to present potential options for future work to improve the approach, as well as caveats and limitations and (4.2) aims to describe what the PICS approach is and is not intended to accomplish.

Overall, the document does a thorough job addressing the purpose and aims described above. It would be helpful if the purpose and aims were also more explicitly and succinctly described in the executive summary rather than summarizing the document as if it were a research project. The document presents a potentially complex approach where one could get lost in the details. However, providing practical examples through the use of case studies and specific chemical comparisons was very helpful in explaining and demonstrating how the PICS approach works and can help streamline chemical evaluations.

1B. Are the ideas presented throughout the document clear and presented in a logical manner?

Yes, in general I thought they were presented clearly and logically. Section 4 was much appreciated as it helped to clearly set expectations for the rest of the document. The figures provide nice summaries of the different sections, but would be even more helpful if the fonts were larger (e.g. figure 1). While acronyms can be helpful to reduce overuse of words, the document could have more clarity with less use of acronyms and spelling out infrequently used acronyms/jargon. The inclusion of workflow diagrams in several of the scientific and information domain sections were informative. It would help with clarity if a high-level workflow chart figure were provided at the beginning of section 5 that illustrates the various overall steps of the proof-of-concept case - similar to figure 1, but with more details.

1C. Is the method described in this document appropriate to be scalable to the thousands of chemicals on the TSCA inventory?

Yes, this approach should be scalable to assessing information associated with thousands of chemicals. The demonstration examined 238 chemicals and the number of chemicals that approach can examine seems to only be limited by the ability to access the appropriate information in the structure used by PICS (e. g. type 1 data). These limitations can be overcome by transforming data/information into the correct structures[1] prior to analysis in addition to the cleaning and curation of data.

1D. Is this approach adaptable to other large-scale chemical prioritization efforts other than for TSCA?

Yes, the approach seems to be very flexible. Since PICS reproducibly synthesizes available information and identify potential data gaps it could be used in many different efforts. Designation of what characteristic (e.g. good, ok, bad, very bad) 1 to 4 scale could be assigned different metrics that may be more relevant to other efforts. For example, the approach could be used to inform prioritization of chemicals of emerging concern for human health in drinking water and ecological health in the environment. The approach appears flexible enough so that other scientific domains could be added or removed where/when appropriate. For example, the addition of a scientific domain describing partitioning of a chemical into biosolids and/or soil matrix would help identify what chemicals introduced through use of biosolids may pose the greatest a health hazard or identify chemicals that should be studied more because of lack of information and potential for persistence and greater exposure.

2. SCIENTIFIC DOMAINS

Based on your knowledge of toxicology, chemistry, risk assessment, and/or exposure science, please comment on the evaluation, workflow, and metrics developed for the individual scientific domains in the TSCA POC. Please explain and justify your rationale for your responses to the charge questions.

2A. Were the decisions in each of the domain-specific evaluations logical and based on sound science?

In general, they were logical, well described and based on sound science. In many cases they have taken common practices and used them as different tiers of workflow.

The human hazard relative to exposure domain follows the accepted paradigm for relevance of toxicity data for human risk: in vivo human>in vivo animal repeat dose toxicity>in vitro assay>in silico (threshold of toxicological concern or TTC).

The carcinogenicity domain takes a logical approach that minimizes confusion on information by scoring if authoritative source has determined that a chemical causes human carcinogenicity, then if there is evidence of animal carcinogenicity. This approach simplifies assessment of carcinogenicity and flags chemicals that display the potential for causing cancer for expert assessment.

The Genotoxicity domain takes the logical approach of using the standard tests for genotoxicity recommended by the Organization for Economic Cooperation and Development (OECD) for in vitro experimental determination of genotoxicity as the first tier of the workflow followed by in silico prediction of genotoxicity if no test data is available. This creates a tiered assessment of measured evidence for genotoxicity> prediction of genotoxicity> inconclusive evidence of genotoxicity> low likelihood of genotoxicity> no data. Each tier of assessment is backed by sound science.

[1] **Clarification:** Yes I meant the correct data structure. The correct structure means that the data would be already be formatted and compiled in manner such that no data cleaning or reformatting would be needed (e.g. type one data). The data would be immediately usable for analysis without further manipulation.

The Ecological hazard domain scheme is logical and follows a standard approach in ecotoxicological testing by first considering chemical effects on three major trophic groups (fish, invertebrate (crustacean), and a plant/algae). If no in vivo acute or chronic data is available, then Quantitative Structure Activity Relationships (QSAR) models are used to predict toxicity. Although, as discussed in the document, exposure is not considered in the evaluation which could lead to higher numbers of chemicals with higher hazard scores.

The Susceptible populations domain presents a logical approach for assessing if a chemical has the potential for a differential exposure between children and the general population. Media/environments where children are likely to experience a high exposure to a chemical, if it were present (e.g. breastmilk), are given higher scores than media/environments where children not expected to have high exposures (e.g. far field sources). The approach taken to sum scores for each media/environments that a chemicals may be present in is consistent with scientific understanding that exposures have cumulative effects.

Persistence in the persistence and bioaccumulation domain is based on a conservative "ultimate biodegradation" or mineralization to CO2 and water. This is a reasonable approach as incomplete mineralization could result in reduction of a chemical of concern but increase levels of daughter products that could be hazardous. Basically, ultimate biodegradation simplifies assessment by not having to consider potential hazards of daughter products. The bioaccumulation component takes a logical approach by first assessing whether or not a high-quality Bioaccumulation factor (BAF) or bioconcentration factor (BCF) is present. If no high-quality data are present then a BCF is predicted using accepted modeling approaches. A major reasonable assumption is that chemicals are neutral at environmental PHs – necessary as the modeling components can't accurately predict behavior of ionized chemicals.

The skin sensitization and skin/eye irritation takes the logical approach of tiering authoritative values at the first level, then screening level values at the second level, then QSAR or other modeling values at the third level. At each level the most conservative value is selected to ensure potential hazards are not underreported.

2B. Do you see any significant issues with any of the tiered workflows and metrics developed for these scientific domains? If so, please identify and explain those issues.

In general, the tiered workflows and metrics are reasonable given the purpose of the effort and limitations described in each domain area.

The workflow for the persistence sub-domain seems to be lacking in analysis of partitioning in different media, desorption rates and other factors that could increase persistence or decrease bioavailability of a chemical. It appears that Ionizable chemicals such as the PFASs would lack information in several domains that use QSARs. Specifically, PFASs would not be modeled well in domains using QSARs, especially in the persistence and bioaccumulation domain. Both of these issue/limitations were noted in the document.

As noted in the document the ecological hazard domain assessment does not include an exposure factor. This could make it more difficult to discern between hazardous chemicals. Without exposure factors, some chemicals will appear to be more hazardous than when a risk-based approach including exposure is used.

Currently the susceptible population domain only assesses exposure of children. This ignores other susceptible populations such as elderly, low income or ill subpopulations. As a result this may result in chemicals that these subpopulations are disproportionately exposed too being overlooked.

For each of the scientific domains, there is a discussion of limitations and longer-term options. Based on your knowledge of toxicology, chemistry, and/or exposure science:

2C. Are the appropriate limitations and long-term options included for each domain?

Yes, appropriate limitations and long-term options are included for each domain. In general, a good job is done in describing current limitations and potential longer term options for improving the effort.

Human hazard relative to exposure domain: In the description of human hazard relative to exposure depicted in figure 4 (line 480) New approach methodologies (NAM) are noted in the figure but could be pointed out in the text. Identification of the TTC as an in silico NAM would help illustrate how this class of information could be integrated into the overall scheme. Given the importance of NAMs it would be good to mention whether or not the workflow would handle other NAMs such as alternative species or *in chemico* assays. How will other models and NAMs be used in the long term?

2D. Are there additional long-term options that could be included?

Other long-term options for human and ecological domains would be to include assessment of specific pathways (estrogenic, etc) or Adverse Outcome Pathways based on in vivo, in vitro and or in silico data. Development of models predictive of hazards based on structure that can provide more accurate assessments than current models. Development of methods that can predict biomagnification.

3. INFORMATION AVAILABILITY

3A. How clearly and concisely are the descriptions of purpose and methodology of the information availability presented? Please identify areas where additional clarity is needed.

In general, I feel that, given the goals of the effort, the descriptions of purpose and methodology of the information availability were very clear and understandable. The examination/comparison of the two chemicals benzene and 3-methoxybutyl acetate were very helpful in understanding the process.

On line 1269, its unclear if the number after benzene represents the SDM values- is 70.5.0 a typo or is it another item? Based on table 11 it's a typo. It may help to present SDM values the same way as the IAM values (Benzene = 93%).

4. RESULTS and CONCLUSIONS

4A. Are the results of the TSCA POC clearly described and presented? If no, please identify areas where clarity is needed.

Yes, I felt that the results of the TSCA POC were clearly described and presented. I appreciated the comparison with other chemical groupings which had different levels of information (e.g. Safer Choice Ingredients List) or had expert driven assessments (e.g. TSCA Hi and Low). While the PICS approach has limitations and potential biases to accessible datasets and conservative estimates, PICS successfully identifies data relevant to chemical hazard and risk assessment in several area and manages to collapse this into two interpretable metrics that can be easily explored.

4B. Do the results presented adequately support the conclusions? If no, please identify and explain those issues.

The results of the POC do support the conclusions that the PICS approach can help inform chemical prioritization and identify possible data needs. Comparison of the POC238 to other chemical groupings (e.g. Figures 14 and 16. TSCA 90, TSCA Hi/Low, SCIL, food ingredients) demonstrated that PICS can identify chemicals with evidence of high impact versus those with low impact. These figures also show that PICS can identify chemicals with evidence of high impact that have low information availability. Chemicals with high SDM/ low IAM could be prioritized in future investments so that evidence can be developed to better define the hazard/risk of chemicals. Chemicals with high levels of information and evidence for high impact/hazard/risk could be priority for expert assessment due to the availability of information and need to understand hazard/risks of chemicals with high SDMS.

5. EDITORIAL OR ADDITIONAL COMMENTS

5A. Please provide any editorial or additional comments you would like to make here. These should be any comments that are not in direct response to the technical charge questions above.

Overall, I found the document clear and easy to read. EPA did a great job assembling the document and performing the POC study. I especially appreciated the flow charts describing what is being done in each section. Several acronyms have not been defined before use. For example: Need to define LLNA (Line 1068). OCSPP (line 1287).

CVs

Tara S. Barton-Maclaren, Ph.D.
Citizenship: Canadian
Date of Birth: November 08, 1977
Substantive Group: REM-02
Employment Status: Indeterminate
Languages: Fluent in English; E-C-C French Language Proficiency
Address: 1366 McPhee Road
Vankleek Hill, ON
K0B 1R0
Work Phone: (613) 790-5459
Other Phone: (613) 678-7675
Email 1: tara.barton-maclaren@canada.ca
Email 2: tbartonmaclaren@gmail.com

EMPLOYMENT

Health Canada, Healthy Environments and Consumer Safety Branch (**11/2007 – present)**

- **Sr Research Manager, Emerging Approaches Unit, 2017 - present**
- **Manager – Hazard Methodology Division, 08/2012 – 2017**
  (Parental Leave – 08/2011 – 08/2012)
- **Acting Manager – Hazard Methodology Division, 06/2011 – 08/2012**
  - Responsibilities: lead multidisciplinary scientific team in the development and application of risk assessment methodologies for human health risk assessment, including novel assessment approaches and tools such as cheminformatics, predictive toxicity tools ((Q)SAR) and toxicogenomics; liaise with the research community and provide guidance on research projects to support risk assessment activities; provide support for the development of learning opportunities (courses/workshops) in specialized areas of hazard assessment; represent Department / Program at OECD workshops; manage financial resources.

- **Acting Manager - Assessment Division 4, 01/2010 – 06/2011**
  - Responsibilities: lead multidisciplinary team in strategic and innovative thinking for the exposure and human health effects assessment of complex mixtures; participate in stakeholder engagement activities both internally and externally; lead and coordinate assessment activities and information sharing with partners; contract development; preparation of technical documents, briefing notes and communications materials for Senior Management; responsible for the management of division financial resources.

- ***Evaluator / Toxicologist***, **Existing Substances Risk Assessment Bureau (08/2007 – 12/2009)**
  - Responsibilities include: the evaluation of information relevant to the hazard assessment of exposure of the general public to chemicals in the environment; preparation of critical scientific toxicology reviews of chemical substances and complex mixtures; provide technical guidance for policy implementation.

EDUCATION

Ph.D., Pharmacology (**2000 – 2007, Area of expertise: Pharmacology and Toxicology)**
McGill University, Department of Pharmacology and Therapeutics, Montreal, Canada.

- Thesis studies the impact of the anticancer agent cyclophosphamide on male germ cell quality and the consequences on early embryonic development.
- Supervisors: Barbara F. Hales and Bernard Robaire
- Project focuses on several different fields of research including: Toxicology, Germ cell development, Male germ cell numerical chromosomal anomalies, Epigenetics, Chromatin remodeling, DNA damage recognition and repair during zygotic development.

B.Sc.(Honours, **1996 – 2000**), Specialized Honours Bio-medical Science
University of Guelph, College of Biological Sciences, Guelph, Canada.

- Graduated with honours

EXPERIENCE AND SKILLS

Strengths:

- Excellent interpersonal and communication skills (oral and written).
- Versatile and skilled at multi-tasking.
- A dedicated and motivated team player comfortable working in collaborations.
- Focused, efficient and accurate with a demonstrated ability to set priorities and work well under pressure to meet tight deadlines.
- Results oriented with well developed administrative and problem-solving skills.
- Methodological and detail oriented.
- A flexible, organized leader with an interactive approach and demonstrated ability to engage others.
- Goal-oriented and motivational management style.

Scientific Skills and Experience:

- Extensive experience in the review and critical analysis of scientific data and reports.
- Extensive experience in conducting and reviewing scientific assessments of risks to human health from complex mixtures including the evaluation and review of exposure and mammalian toxicology data.
- Knowledge of the principles and federal legislation relevant for the assessment and management of risks to human health in the context of existing substances and complex mixtures.
- Considerable experience in leading multidisciplinary scientific teams in the conducting of risk assessments under Canada's Chemicals Management Plan (CMP) and coordinating assessment, peer review, information sharing and approvals activities of various assessment reports.
- Experience in contributing to complex decision-making, communicating and defending recommendations.
- Considerable experience in consultation and liaison with internal and external stakeholders in the preparation of risk assessments and related hazard methodology approach documents.
- Significant experience in developing and preparing concise reports, technical documents, briefing notes and communications materials for senior management.
- Experience in the preparation of responses to media enquiries, Question Period Notes, Memos to Minister, Petitions.
- Extensive experience in preparing and giving oral presentations to local and international audiences. Key scientific communications highlighted in respective section below.
- Advanced knowledge of toxicology.
- Knowledge of principles of epidemiology, human relevance of modes of action in animals and statistics for scientific risk assessment.
- Risk assessment lead on various research initiatives both within the Bureau and in collaboration with others related to the transition from using only the existing *in vivo*

toxicity data into an increasingly dynamic integrated testing and assessment approach to regulatory toxicology.
- Internal reviewer of research proposals submitted in response to the Safe Environments Programme Request for Proposals under the Chemicals Management Plan.
- Experience in managing financial resources related to the activities of the Hazard Methodology Division.

- Supervision and mentorship of scientific staff and co-op students in the Existing Substances Risk Assessment Bureau (05/2008 – 09/2008; 01/2010 - present).
- Supervision and mentorship of undergraduate and graduate students in lab techniques and specific knowledge relevant to project development and implementation (2002-2006).

Partnerships and Advisory Memberships:
- Research Partnership - Dre Géraldine Delbès (INRS- Institut Armand Frappier) and Drs Tara Barton Maclaren and Mike Wade (Health Canada)**:** Cumulative effects of reproductive endocrine disruptors – Adverse Outcome Pathways as a means to assess risks of chemical mixtures – RQR compétition 2019 pour de nouvelles collaborations avec un partenaire non-académique
- HESI RISK21 – Ad-hoc Science Advisor
- Health Canada Modern Approach to Risk Sciences (formerly Toxicogenomics) Working Group
- CMP Research Network – Existing Substances Risk Assessment Bureau representative
- Center for Alternatives to Animal Testing (CAAT) Board Member
- CIHR Signature Initiative - Advisory Board Member on project in the research area of chronic diseases related to reproduction, fetal and/or early childhood development. (Funded December 2016). Title: Endocrine Disrupting Chemicals: Towards Responsible Replacements

International Activities and Alliances:
- Co-lead with US Environmental Protection Agency and European Chemicals Agency (ECHA) for the international initiative Accelerating the Pace of Chemical Risk Assessment. The goal of which is to advance acceptance and application of new approach methodologies in risk assessment. (2016 – current)
- Health Canada lead in collaboration with Environment and Climate Change Canada for data sharing initiatives and agreements with European Chemicals Agency (ECHA), ECHA, March 2016 – present.
- Represented the Department on the organizing committee for and at the US Environmental Protection Agency (EPA) Workshop on Accelerating the Pace of Chemical Risk Assessment with a focus of integrating new approach methodologies. Led the pre-workshop analysis of international chemical inventories to support case study selection of chemicals of international interest. September, 2016.
- Member of international organizing committee, ECHA Topical Scientific Workshop – New Approach Methodologies in Regulatory Science, April 2016.
- Collaborative research and risk assessment initiatives with Health Canada scientists and EPA research and regulatory scientists under the Materials Transfer Agreement (Health Canada – USEPA). The focus is on the integration of emerging technologies to identify the potential for toxicity of compounds and to examine the utility of these methodologies and data to inform chemical hazard and risk.
- International collaborations in the area of QSAR model development and validation; various co-authored manuscripts as evidence of successful collaborations.
- Represent the Program / Department on high priority initiatives under the revised mandate of the OECD Cooperative Chemicals Assessment Programme with a focus on methodology development. Including the development and application of Integrated Approaches to Testing and Assessment (IATA) and the assessment of risks from the combined exposure to multiple chemicals. November 2014 – present.

Information Technology:

- Knowledge of QSAR/SAR models (e.g. OECD QSAR Toolbox, TOPKAT®, CASETOX, DEREK) as tools for predicting inherent toxicity to humans and applications in risk assessment of chemicals.
- Knowledge of exposure models (e.g. ChemCAN, ConsExpo, IHMOD, SCREEN3) and the application in risk assessment.
- Proficient use of various databases and literature search enginesfor the identification of information relevant for scientific risk assessment.
- Advanced knowledge with word processing (Word, Word Perfect), spreadsheet (Excel), presentation (PowerPoint), database, graphics (Adobe Photoshop, Corel Photo paint, Corel Draw) and statistics (Sigma Stat, Sigma Plot) software.

SPECIAL HONORS AND RECOGNITION

- 2019 HPFB ADM Award of Excellence - Science
- 2018 HECSB ADM Award of Excellence – Science
- 2017 Safe Environments Above and Beyond Award - Science
- Government of Canada Workplace Charitable Campaign (GCWCC) Collaboration Award from the DM, ADM and GCWCC Champion for sharing the highest level of collaborative spirit throughout the 2015 GCWCC for HECSB (GCWCC Safe Environments Directorate Coordinator, 09/2015 – 12/2015).
- 2013 HECSB Above and Beyond Awards - Honorable Mention for dedicated work and significant contribution in the categories of Excellence and Team Work
- 2008 HECSB ADM Award of Excellence in the category of New Public Servant, 06/2008
- Health Canada Instant Award from A/Director General, Safe Environments Programme, HECSB, for Outstanding Contribution to the work on bisphenol A risk assessment 06/2008.

PUBLICATIONS

Maureen Gwinn, Russell Thomas, Robert Kavlock, Mike Rasenberg, **Tara Barton-Maclaren.** APCRA Report 4: Expert Focus: Advancing new approach methodologies for chemical risk assessment. Four years on from the launch of APCRA - an international project to accelerate the use of NAM for chemical risk assessment - participants report on progress to-date and next steps. Chemical Watch 11 June 2020 https://chemicalwatch.com/123913/expert-focus-advancing-new-approach-methodologies-for-chemical-risk-assessment

Costanza Rovida, **Tara Barton-Maclaren** et al. Internationalization of read-across as a validated new approach method (NAM) for regulatory toxicology. ALTEX. 2020; 37(4) :579-606. DOI: 10.14573/altex.1912181

Krewski D, Andersen ME, Tyshenko MG, Krishnan K, Hartung T, Boekelheide K, Wambaugh JF, Jones D, Whelan M, Thomas R, Yauk C, **Barton-Maclaren** T, Cote I. (2020) Toxicity testing in the 21st century: progress in the past decade and future perspectives. Arch Toxicol. 2020 Jan;94(1):1-5817. doi: 10.1007/s00204-019-02613-4.

Katie Paul Friedman, Matthew Gagne, Lit-Hsin Loo, Panagiotis Karamertzanis, Tatiana Netzeva, Tomasz Sobanski, Jill Franzosa, Ann Richard, Ryan Lougee, Andrea Gissi, Jia-Ying Joey Lee, Michelle Angrish, Jean-Lou Dorne, Stiven Foster, Kathleen Raffaele, Tina Bahadori, Maureen Gwinn, Jason Lambert, Maurice Whelan, Mike Rasenberg, **Tara Barton-Maclaren**, Russell S. Thomas (2020) Examining the Utility of In Vitro Bioactivity as a Conservative Point of Departure: A Case Study. Toxicol Sci. 2020 Jan 1;173(1):202-225.

Anne Marie Gannon, Marjory Moreau, Reza Farmahin, Russell S. Thomas, **Tara S Barton-Maclaren**, Andy Nong, Ivan Curran and Carole L. Yauk (2019) Hexabromocyclododecane (HBCD): A case study applying tiered testing for human health risk assessment**.** Food Chem Toxicol. Sep;131:110581.

Hasselgren C, Ahlberg E, Akahori Y, Amberg A, Anger LT, Atienzar F, Auerbach S, Beilke L, Bellion P, Benigni R, Bercu J, Booth ED, Bower D, Brigo A, Cammerer Z, Cronin MTD, Crooks I, Cross KP, Custer L, Dobo K, Doktorova T, Faulkner D, Ford KA, Fortin MC, Frericks M, Gad-McDonald SE, Gellatly N, Gerets H, Gervais V, Glowienke S, Van Gompel J, Harvey JS, Hillegass J, Honma M, Hsieh JH, Hsu CW, **Barton-Maclaren TS**, Johnson C, Jolly R, Jones D, Kemper R, Kenyon MO, Kruhlak NL, Kulkarni SA, Kümmerer K, Leavitt P, Masten S, Miller S, Moudgal C, Muster W, Paulino A, Lo Piparo E, Powley M, Quigley DP, Reddy MV, Richarz AN, Schilter B, Snyder RD, Stavitskaya L, Stidl R, Szabo DT, Teasdale A, Tice RR, Trejo-Martin A, Vuorinen A, Wall BA, Watts P, White AT, Wichard J, Witt KL, Woolley A, Woolley D, Zwickl C, Myatt GJ. (2019) Genetic toxicology in silico protocol. Regul Toxicol Pharmacol. Oct;107:104403.

Francina Webster, Matthew Gagné, Grace Patlewicz, Prachi Pradeep, Nicholas Trefiak, Richard Judson, **Tara S. Barton-Maclaren** (2019) Predicting Estrogenicity of a Group of Substituted Phenols: An Integrated Approach to Testing and Assessment Case Study. Reg Tox Pharm Aug;106:278-291.

Yauk C, Cheung C, **Barton-Maclaren T**, Boucher S, Bourdon-Lacombe J, Chauhan V, Gagne M, Gillespie Z, Halappanavar S, HoneymN m, Jones SR, Jones-McLean E, Labib S, MacAulay J, Moore J, Paquette M, Petronella N, Semalulu S, Slot A, Vespa A, Woodland C. (2019) Evaluation of the use of toxicogenomics in risk assessment at Health Canada. Current Opinion in Toxicology. Volume 18, Pages 34-45.

Barton-Maclaren TS, Maureen R. Gwinn, Russell S. Thomas, Mike Rasenberg, Robert J. Kavlock (2019) Insights: New Approaches to Chemical Assessment- A progress Report. Bloomberg Environment.

Slikker W Jr, de Souza Lima TA, Archella D, de Silva JB Junior, **Barton-Maclaren T**, Bo L, Buvinich D, Chaudhry Q, Chuan P, Deluyker H, Domselaar G, Freitas M, Hardy B, Eichler HG, Hugas M, Lee K, Liao CD, Loo LH, Okuda H, Orisakwe OE, Patri A, Sactitono C, Shi L, Silva P, Sistare F, Thakkar S, Tong W, Valdez ML, Whelan M, Zhao-Wong A. (2018) Emerging technologies for food and drug safety. Regul Toxicol Pharmacol. Oct;98:115-128.

Kavlock RJ, Bahadori T, **Barton-Maclaren TS**, Gwinn MR, Rasenberg M, Thomas RS. Accelerating the Pace of Chemical Risk Assessment (2018) Chem Res Toxicol. 21;31(5):287-290.

Myatt…….Kulkarni S…… **Barton-Maclaren TS**….. et al (2018) In silico toxicology protocols. Reg Tox Pharm. 96:1-17.

Robert J. Kavlock, Tina Bahadori, **Tara S. Barton-Maclaren**, Maureen R. Gwinn, Mike Rasenberg, Russell S. Thomas. Accelerating the Pace of Chemical Risk Assessment (2018) Chemical Research in Toxicology. May 21;31(5):287-290.

Petkov P, Kulkarni S et al. (2017) Procedure for toxicological predictions based on mechanistic weight of evidences: Application to Ames mutagenicity, Computational Toxicology, 1-49.

Barton-Maclaren TS, Westphal M, Sarwar E, Mattison D, Chiu W, Dix D, Kavlock B, Krewski D. (2017) Challenges in the Risk Assessment of Existing Substances. International Journal of Risk Assessment and Management. 20(1/2/3):261-283.

Farmahin R, Williams A, Kuo B, Chepelev NL, Thomas RS, **Barton-Maclaren TS**, Curran IH, Nong A, Wade MG, and Carole L. Yauk CL (2017). Recommended Approaches in the application of toxicogenomics to derive points of departure for chemical risk assessment. Arch. Tox. May;91(5):2045-2065.

Kulkarni SA, Benfenati E, **Barton-Maclaren TS** (2016) Improving the confidence in (Q)SAR predictions under the Canada's Chemicals Management Plan - A chemical space approach. SAR QSAR Environ Res. Vol 27 (10): 851-863.

Marzo M, Kulkarni SA, Wu S, Manganaro A, Roncaglioni A, **Barton-Maclaren T**, Lester C, Benfenati E (2016) Integrating in silico models to enhance predictivity for developmental toxicity. Toxicology, 370, 127-137.

Manganelli S, Benfenati E, Manganaro A, Kulkarni S, **Barton-Maclaren TS**, Honma M. (2016) New quantitative structure–activity relationship models improve predictability of Ames mutagenicity for aromatic azo compounds. Toxicol. Sci. 153 (2): 316-326.

Marzo M, Roncaglion A, Kulkarni S, **Barton-Maclaren TS**, Benfenati E. (2016). In Silico Model for Developmental Toxicity: How to Use QSAR Models and Interpret Their Results. In Silico Methods for Predicting Drug Toxicity. Methods Mol Biol. 1425:139-61.

Becker RA, Ankley GT, Edwards SW, Kennedy S, Linkov I, Meek B, Sachana M, Segner H, Van Der Burg B, Villeneuve DL, Watanabe H, **Barton-Maclaren TS**.(2015) Increasing Scientific Confidence in Adverse Outcome Pathways: Application of Tailored Bradford-Hill Considerations for Evaluating Weight of Evidence. Regul. Toxicol. Pharmacol. 72(3): 514-37.
Paper tied for the 1st place award with another Health Canada co-authored paper, SOT March 2016 Risk Assessment Specialty Section (RASS) in the category *Outstanding Paper Published in 2015 Advancing the Science of Risk Assessment*.

Kulkarni SA, **Barton-Maclaren TS**.(2014) Performance of (Q)SAR models for predicting Ames mutagenicity of aryl azo and benzidine based compounds. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 32(1):46-82.

Barton TS, Robaire B, Hales BF. (2007) DNA damage recognition in the rat zygote following chronic paternal cyclophosphamide exposure. Toxicol Sci. 100(2):495-503.

Barton TS, Robaire B, Hales BF. (2005) Epigenetic programming in the preimplantation rat embryo is disrupted by chronic paternal cyclophosphamide exposure. Proc Natl Acad Sci U S A. 102(22):7865-70.

Hales BF, **Barton TS**, Robaire B. (2005) Impact of paternal exposure to chemotherapy on offspring. Journal of the National Cancer Institute. J Natl Cancer Inst Monogr. (34):28-31.

Barton TS, Wyrobek AJ, Hill FS, Robaire B, Hales BF. (2003) Numerical chromosomal abnormalities in rat epididymal spermatozoa following chronic cyclophosphamide exposure. Biol Reprod. 69(4):1150-7.

SCIENTIFIC COMMUNICATIONS

Exploring Transcriptomic and In Vitro Genotoxicity Data to Estimate a Point of Departure (POD) for Human Health Risk Assessment. Assessing Carcinogenicity: Hazard Classification, and Risk Assessment. A Toxicology Forum State-of-the-Science Workshop. December 7-10, 2020, Virtual Workshop (Presentation Advance recorded, October 2020)

Bisphenols IATA Case Study Update. Organization for Economic Cooperation and Development (OECD) Integrated Approach to Testing and Assessment (IATA) Case Studies Project, November 16-17, 2020, Virtual.

Embracing the Challenge: Exploring New Approach Methods (NAM) to Advance Risk Science for Chemicals Management in Canada. American Scoity for Cellular and Computational Toxicology (ASCCT), October 21, Virtual.

Using the RISK21 Approach for prioritization of chemicals in drinking water. HESI Risk Assessment Summit 2020: Challenges and Applications, February 18-19, 2020, Washington, DC, USA.

Application of NAMs for quantitative screening level risk decisions. Invited presentation - EPA State of the Science on Development and Use of NAMs for Chemical Safety Testing. December 2019, Washington, DC. https://www.epa.gov/chemical-research/first-annual-conference-state-science-development-and-use-new-approach-methods-0

Translating from Case Studies to Implementation of NAMs for Priority Setting and Risk Assessment Modernization in Canada. Accelerating the Pace of Chemical Risk Assessment (APCRA)-4. EPA, Raleigh, North Carolina. October 2019.

Modern Approaches for Risk Assessment under Canada's Chemicals Management Plan: Building Confidence through Collaboration. HESI 30th Anniversary Annual Meeting. Alexandria, Virginia. June 11-12, 2019.

Integrating Emerging Science for Prioritization and Assessment of Chemicals under the Canadian Environment Protection Act (CEPA) 1999. Symposium session - New Approach Methods: The Brave New World in Toxicology & Risk Assessment. GlobalChem. Washington, DC. March 2019.

Application of Data from New Approach Methodologies to Prioritization Activities under Canada's Chemicals Management Plan. Symposium Session – Application of Data from New Approaches in Regulatory and Product Safety Decisions. SOT 57th Annual Meeting and ToxExpo, San Antonio, Texas. March 12, 2018.

Alternatives Assessment: Current Status under the CMP. CIHR Team Grant Annual Meeting, Towards Responsible Replacements (Aim 3: Promotion). McGill Faculty Club, Montreal, QC. November 3, 2017.

Canadian Perspectives Using New Approach Methodologies. 2nd Accelerating the Pace for Chemical Risk Assessment Working Meeting. ECHA, Helsinki, Finland. October 11, 2017.

The integration of emerging data and novel methodologies to support risk assessment under Canada's Chemicals Management Plan. Global Summit on Regulatory Science, Emerging Technologies for Drug and Food Safety, Brasilia, Brazil. September 18-20, 2017.

Integrating New Approach Methodologies within the CMP: Identifying Priorities for Risk Assessment. Trilateral Meeting on Priority Setting, USEPA/ECHA/Canada. Ottawa. August 28-2017.

OECD 56th Joint Meeting Focus Session on Reconciling Integrated Approaches to Testing and Assessment with the OECD System of Mutual Acceptance of Data. Presentation – Canadian Experiences Using Alternative Testing Methods (prepared by Barton-Maclaren TS; presented by Norman C.), Paris, France. May 30, 2017.

Regulatory Applications of Toxicogenomics Data in Human Health Risk Assessment: Perspectives from Chemicals Assessment. Workshop on Advances and Roadblocks for Use of Genomics Data in Cancer Risk Assessment for Drugs and Chemicals. Montreal, QC. May 25-26, 2017.

New Approach Methodologies to Support Priority Setting and Risk Assessment under Canada's Chemicals Management Plan: A Substituted Phenol Case Study. EPA Workshop Accelerating the Pace of Chemical Risk Assessment, Washington, DC. September 14-15, 2016.

Integration of High-Throughput Technologies in a Margin of Exposure Approach to Support Risk Assessment Activities under Canada's Chemicals Management Plan. Society of Toxicology Annual Meeting, New Orleans, LA. March 15, 2016.

Actualizing the OECD revised guidance on grouping of Chemicals with Practical examples: considerations from read-across case studies. Barton-Maclaren TS (on behalf of OECD). Society of Toxicology Annual Meeting, New Orleans, LA. March 15, 2016.

Integrating New Approaches to Support Risk Assessment under Canada's Chemicals Management Plan. Society of Toxicology of Canada, Ottawa, Ontario, Canada. December 9, 2015.

Regulatory perspective on the selection of *in vitro* points of departure to inform the assessment of existing substances under the Chemicals Management Plan. Workshop on Determining Adverse Responses Using *In Vitro* Assays. Brown University. June 25-26, 2015

Integrating New Approaches under Canada's Chemicals Management Plan. ICCA-LRI & US EPA Workshop. Application of New Approaches for Chemical Safety Assessment. New Orleans, LA. June 16-17, 2015

Trefiak N, Gagné M, Doane A, and Kulkarni S, and Barton-Maclaren TS.
Applying a Big Data Approach to Data Curation, Data-Gap Filling and Assessment Prioritization. Poster and Platform Presentation (by Trefiak N.), Health Canada Science Forum 2015.

Nong A, Barton-Maclaren TS. Evaluating the potential of ToxCast™ to inform the assessment of existing substances under the Chemicals Management Plan: phthalates as a case study. Invited Speakers (collaborative presentation), EPA Data Summit, September 29-30, 2015.

Moving Forward with the Chemicals Management Plan: Integrating Emerging Science to Support Decision-Making. Presentation to Health Canada Science Advisory Board, November 13, 2014. Subsequently presented to Environmental Health Industry Coordinating Group (EHICG), Ottawa, November 21, 2014.

Gagné M, Kulkarni S, Barton-Maclaren TS. Best Practices for Deriving a Rationale for Read-Across in Screening Assessment Reports under the Chemicals Management Plan. CMP Science Committee, Ottawa, November 4-5, 2014.

Barton-Maclaren TS, Yauk CL. Genomics: Integrating New Technologies into Risk Assessment. Invited collaborative presentation to CMP Workshop - Strengthening the Bridge between Research Regulatory Communities. April 16, 2014.

Approaches for Risk Assessment of Existing Substances under Canada's Chemicals Management Plan. Invited Speaker, Drug Development Training Program Symposium, McGill University, April 26, 2013.

Endocrine Modulating Substances: Global Overview and Assessment, Research and International Engagement under Canada's Chemicals Management Plan. Invited Speaker, Seminar Series Presentation November 11, 2013
Department of Pharmacology and Therapeutics, McGill University

Health component of the draft screening assessment of bisphenol A under the Chemicals Management Plan. Ontario Public Health and Medical Officers of Health. Oral presentation via teleconference. Health Canada, June 2008.

Weihsueh A. Chiu, PhD

Curriculum Vitae
October 2020

CONTACT INFORMATION

Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences
Texas A&M University
4458 TAMU
College Station, TX 77843-4458, USA
Tel: +1 979-845-4106
Fax: +1 979-847-8981
Cell: +1 703-541-8833
wchiu@cvm.tamu.edu

EDUCATION

Princeton University, Princeton, NJ

Ph.D., Physics **1998**
Dissertation: "From X-ray Clusters to Galactic Spheroids: Semi-analytic Modeling of the Origin of Structure in the Universe"

Certificate in Science, Technology, and Environmental Policy **1998**

M.A., Physics **1995**
Williams Fellow, Spring 1994

Harvard University, Cambridge, MA

A.B., Physics **1993**
Summa cum laude with highest honors

PROFESSIONAL EXPERIENCE

Professor, Department of Veterinary Integrative Biosciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University

2015–present

Additional academic appointments

- Member, Interdisciplinary Faculty of Toxicology, Texas A&M University, 2015-present
- Research Fellow, Institute for Science, Technology, and Public Policy, Bush School of Government and Public Service, Texas A&M University, 2016-present
- Fellow, Institute for Sustainable Communities, Texas A&M University, 2017-present
- Director, Health Assessment Track, and Externship Coordinator, Regulatory Science in Environmental Health and Toxicology Training Program (T32 ES026568), Texas A&M University, 2016-present

Outside appointments

- Councilor, Society for Risk Analysis, 2019-present
- Trustee-at-large, Society for Risk Analysis, Dose-response Specialty Group, 2014-2016.
- Chair-elect, Society for Risk Analysis, Dose-response Specialty Group, 2016-2017
- Chair, Society for Risk Analysis, Dose-response Specialty Group, 2017-2018
- Member, Society of Toxicology, Committee on Contemporary Concepts in Toxicology, March 2017-present

Research Funding

Ongoing Research Support

- STAR RD-84004601, U.S. Environmental Protection Agency Chiu, W (PI) 08/01/20 – 07/31/23. Engaging the Galena Park Community to Build Resilience to Excess Industrial Pollutant Releases after Hurricanes and Floods in Greater Houston. Role: PI
- STAR RD-84003201, U.S. Environmental Protection Agency, Rusyn, I (PI) 08/01/20 – 07/30/23. Integrating tissue chips, rapid untargeted analytical methods and molecular modeling for toxicokinetic screening of chemicals, their metabolites and mixtures. Role: Co-Investigator
- T32 ESMG135748, National Institute of Environmental Health Sciences, Butler-Pury, K (PI) 02/01/2020-01/31/2025. Initiative for Maximizing Student Diversity in Biomedical Sciences. Role: Externship coordinator.
- Contract, PSA 50076, Centers for Disease Control and Prevention, subcontract through Abt and Associates, Chiu W (PI). Mission Support for Preparation of Toxicological Profiles. Role: PI.
- P30ES029067, National Institute of Environmental Health Sciences, Threadgill, D (PI). 05/01/2019- 03/31/2024. Texas A&M Center for Environmental Health Research. Role: PI, Data Science Core Facility.
- U24TR002633, National Center for Advancing Translational Sciences, Rusyn, I (PI) 09/19/18-07/31/2021. TEX-VAL: Texas A&M Tissue Chip Validation Consortium. Role: Co-Investigator
- National Academies Gulf Research Program, Chiu, W (PI). 12/15/2017-12/14/2020. Prioritizing Risks from Oil Spills: Supporting Decisions with Read-Across Using 21st Century Exposure and Toxicological Sciences
- P42 ES027704, National Institute of Environmental Health Sciences, Rusyn, I (PI) 04/01/17-03/31/22. Comprehensive tools and models for addressing exposure to mixtures during environmental emergency-related contamination events. Role: PI, Decision Sciences Core, Co-I, Research Translation Core, Exposure Core.
- T32 ES026568, National Institute of Environmental Health Sciences, Rusyn, I (PI) 04/01/2016-03/31/2021. Regulatory Science in Environmental Health and Toxicology. Role: Director, Health Assessment Track, Mentor
- STAR RD-83580201, U.S. Environmental Protection Agency, Rusyn, I (PI) 06/01/15 – 05/31/21. Cardiotoxicity Adverse Outcome Pathway Center – Project 1. Role: Co-Investigator

Completed Research Support

- Contract 1112-000000-11050-110-00, Environmental Defense Fund, Chiu, W (PI). 09/01/18-09/30/20. Data Visualization of Environmental Pollution and Associated Risks in Houston.
- U01 FD005838, Food and Drug Administration, Reisfeld, B (PI) 09/01/2016 - 01/31/2020. Enhancing the reliability, efficiency, and usability of Bayesian population PBPK modeling. Role: Co-Investigator (PI, TAMU Subcontract)
- Contract M1702165, California Environmental Protection Agency, Chiu, W (PI) 06/06/2017-06/30/2019. Risk assessment training and technical advice. Role: PI.
- U24 TR001950 National Center for Advancing Translational Sciences, Rusyn, I (PI) 09/23/16-08/31/2018. TEX-VAL: Texas A&M Tissue Chip Validation Center. Role: Co-Investigator
- STAR RD-83561201, U.S. Environmental Protection Agency, Rusyn, I (PI) 06/01/14-05/31/17 Toxicogenetics of tetrachloroethylene metabolism and toxicity: Using Collaborative Cross mouse population approach to address remaining gaps in human health assessments. Role: Co-Investigator
- STAR RD-83516601, U.S. Environmental Protection Agency, Rusyn, I (PI) 07/01/12-06/30/16 Carolina Center for Computational Toxicology: Experimental and computational tools for NexGen safety assessments. Role: Co-Investigator

- P42 ES-005948, National Institute of Environmental Health Sciences, Swenberg, J (PI) 04/01/11-03/31/16. Elucidating Risks: From Exposure and Mechanism to Outcome – Project 2. Role: Co-Investigator

Consulting

- Consultant to U.S. EPA through subcontract from ICF to provide advice on dose-response modeling of inorganic arsenic, as part of EPA Contract #EP-C-14-001. Aug 2015.
- Consultant to Organisation for Economic Co-operation and Development (OECD) to develop Working Paper on how information in chemical risk assessments translate to socio-economic analyses, under contract SRM #500044635. Feb-Nov 2016.
- Consultant to Risk Sciences International to provide technical and communication support for the development of harmonized methods between Life Cycle Impact Assessment (LCIA) and Risk Assessment approaches to establishing the impacts of chemical emissions, under personal services contract PSC-1255 (Apr-May 2017).
- Consultant to Risk Sciences International to provide technical and communication support for the development of probabilistic risk assessment approaches for LCIA and FDA iRisk applications, as well as for feedback on Bayesian weight of evidence approaches, under personal services contract PSC-1265 (Sep 2017-Jan 2018).
- Consultant to Centers for Disease Control, through subcontract with Abt Associates, to provide technical support to pharmacokinetic modeling of PFOA, PFAS, PFHxS, and PFNA. Consultant Agreement 50788 (Sep 2019-Mar 2020).

Supervisory Physical Scientist, National Center for Environmental Assessment (NCEA), Office of Research and Development, U.S. Environmental Protection Agency (USEPA) ***2012–2015***

Chief, Toxicity Pathways Branch, Integrated Risk Information System Division 2012–2015

- Supervising the development of multiple human health assessments for the Integrated Risk Information System, including
  - Vanadium pentoxide
  - Inorganic arsenic
  - Hexavalent chromium
  - Naphthalene
  - Tert-butyl alcohol
  - Ethyl tert-butyl ether
- Supervising development of a physiologically-based pharmacokinetic modeling and dose-response analyses for tert-butyl alcohol and ethyl tert-butyl ether.

Management Liaison, Toxicity Pathways and Genotoxicity Workgroup 2013–2015

- Guiding a workgroup of 14 scientists on the identification, evaluation, application of mechanistic data (including genotoxic and non-genotoxic mechanisms) to assess human health risk of environmental chemicals, including:
  - Hexavalent chromium
  - Hexabromocyclododecane
  - Diisononyl phthalate
  - Formaldehyde
  - Libby asbestos
  - Tert-butyl alcohol
  - Ethyl tert-butyl ether
  - Ethylene oxide
  - Vanadium pentoxide

Task Lead for multiple tasks under "Advancing and Transforming Risk Assessment Methods" Project in the Human Health Risk Assessment Research Area 2013–2015

- ***Noncancer Economic Valuation***
  - Developed a summary report from an internal EPA workshop on economic valuation for noncancer outcomes (served as co-lead of workshop).
  - Coordinating Agency activities on noncancer economic valuation as part of a Health Benefits Workgroup.
- ***Dose-response analysis methods***
  Coordinating development of dose-response modeling and extrapolation approaches to
  - Improve model fit,
  - Better characterize uncertainty/variability,
  - Facilitate greater integration of dose-response information with exposure or economic valuation analysis.

Environmental Health Scientist, National Center for Environmental Assessment (NCEA), U.S. Environmental Protection Agency (USEPA) ***2002–2012***

Project Area Lead for "Advancing Dose Response Analysis" in the Human Health Risk Assessment Research Area **2011–2013**

- Lead a team of 30+ scientists in the development of detailed project activities, milestones, outputs, and products.
- Coordinated tracking of schedule for milestones/deliverables.

Chemical manager for health risk assessment of trichloroethylene **2003–present**

- Completed Toxicological Review of Trichloroethylene was posted to the IRIS website on 9/28/2011, leading a team of 15+ scientists to comprehensively review the toxicological and epidemiologic data on the health effects of trichloroethylene (TCE).
- Led development of physiologically-based pharmacokinetic (PBPK) models of mice, rats, and humans for TCE and its metabolites, integrating data from over 40 studies (comprising over 800 time-courses) using a hierarchical Bayesian population approach.
- Contributed to analyses of toxicity, carcinogenicity, and mode/mechanism-of-action for the effects of TCE in the liver, lung, and kidney.
- Developed methods for quantitative uncertainty analysis of dose-response modeling in the presence of pharmacokinetic uncertainty and variability in internal dosimetry.
- Presented TCE health risk assessment issues and results to various scientific and technical audiences, including the National Research Council (NRC) and Science Advisory Board (SAB) panels.
- Draft report released November, 2009 was favorably reviewed by the SAB.
- Continuing to provide technical assistance and advice on implementation of assessment conclusions to EPA programs and regions, and state agencies.

Physiologically-based pharmacokinetic modeling lead for health risk assessment of tetrachloroethylene **2009–present**

- Led development of physiologically-based pharmacokinetic (PBPK) models of mice, rats, and humans for tetrachloroethylene and its metabolites, integrating data from over 25 studies (comprising over 200 time-courses) using a simplified Bayesian approach.
- Contributed to analyses of dose-response for non-cancer and cancer endpoints.
- Facilitated closure as to decisions on major scientific issues.
- Provided technical input to preparation of final Toxicological Review of Tetrachloroethylene, which was posted to the IRIS website 2/10/2012.
- Continuing to provide technical assistance and advice on implementation of assessment conclusions to EPA programs and regions, and state agencies.

NCEA Pharmacokinetics Work Group **2005–present**

- Inaugural co-chair of workgroup, 2005-2006.
- Led reviews of pharmacokinetics and PBPK modeling of styrene, 1,4-dioxane, and di-*n*-butyl-phthalate.

- Developed approach to use steady-state solutions for PBPK models for risk assessment applications (see Chiu and White, 2006 publication).
- Developed statistical methods for extracting information on inter-individual pharmacokinetic variability from aggregated data (see Chiu and Bois, 2007 publication).
- Using dichloromethane (methylene chloride) as a case study, investigated approaches to account for serial correlation in toxicokinetic data when calibrating PBPK models (see Klein et al. 2013 publication).

Other Biological/Statistical Modeling Research Projects 2002–present

- Investigation of the *in vitro* basis for allometric scaling relationships for xenobiotic metabolism.
- Analysis of the effect of age-of-exposure in multi-stage cancer models.

Lead/Contributor to multiple Office or Agency-wide workgroups/committees/panels

- Co-chair of Risk Assessment Forum *Dose-Response Technical Panel,* leading a diverse panel to the develop scope and plan dose-response state-of-the-science reviews related to human variability, susceptibility, and dose-response analysis approaches. 2013-present
- Co-chair of Risk Assessment Forum *Dose-Response Matrix Technical Panel,* leading a diverse panel to develop a decision support tool for scoping and planning dose-response analyses to best meet decision-maker needs. 2011-2013
- Co-lead for Risk Assessment Colloquium Breakout Group for Unified Dose-Response and Defaults, leading a diverse breakout group to develop an action plan for responding to recent National Research Council recommendations for risk assessment 2010
- Co-chair of Risk Assessment Forum *Unified Dose Response Assessment & Defaults Technical Panel*, leading a diverse panel to development of a consensus report on responding to recent National Research Council recommendations for risk assessment 2010
- Member of Risk Assessment Forum, Human Health Oversight Committee, contributing to planning and review of projects sponsored by the Forum 2009-present
- Member of Assessment Factors Workgroup, contributing to development of the Science Policy Council document *A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information* 2001-2003

Environmental Scientist, Office of Radiation and Indoor Air (ORIA),
U.S. Environmental Protection Agency (USEPA) 2000–2002

Exposure/dose assessment for radionuclides in sewage sludge and ash 2000–2002

- Performed statistical analyses of radioactivity sample data.
- Developed methodology for probabilistic dose modeling under various exposure scenarios.

Analyst/Evaluator, National Security and International Affairs Division (NSIAD),
U.S. General Accounting Office [henceforth renamed "U.S. Governmental Accountability Office"] 1998–2000

Evaluator-in-Charge, Review of Air Force "Ranch Hand" (Epidemiologic) Study

- Analyzed study statistical power to detect increased cancer incidence from Agent Orange exposure.
- Formulated recommendations to improve communication and dissemination of study results.

Team member, Review of Chemical/Biological Agent Defense Research

- Compiled R&D funding trends and analyzed program planning documents.

AWARDS AND HONORS

Society of Toxicology 2018 Best Overall Risk Assessment-related Abstract
Chiu WA, Ouyang Q, Dalaijamts C, Axelrad D, Dockins C, Paoli G. 2018. "Broad application of a probabilistic dose-response framework to improve chemical risk assessments"

Society of Toxicology Occupational and Public Health Specialty Section: 2013 Paper of the Year

Zeise L, Bois FY, **Chiu WA**, Hattis D, Rusyn I, Guyton KZ. 2013. "Addressing human variability in next-generation human health risk assessments of environmental chemicals." *Environ Health Perspect.* 121(1):23-31.

Society of Toxicology Risk Assessment Specialty Section: One of 2006's top ten papers "Advancing the Science of Risk Assessment

Chiu WA, White P. 2006, "Steady-state solutions to PBPK models and their applications to risk assessment I: Route-to-route extrapolation of volatile chemicals", *Risk Analysis*, 26:3, 769-780.

U.S. EPA Scientific and Technical Achievement Awards

2014 Level III: "Developing an Approach and Case Study Template for Evaluating and Utilizing Toxicogenomic Data in Risk Assessment"

2010 Level III: "Research Critical to Understanding the Metabolism and Mode of Action of the Environmental Contaminant Trichloroethylene"

Chiu WA, Okino MS, Evans MV. 2009, "Characterizing uncertainty and population variability in the toxicokinetics of trichloroethylene and metabolites in mice, rats, and humans using an updated database, physiologically based pharmacokinetic (PBPK) model, and Bayesian approach", *Toxicol Appl Pharmacol.* 241:1, 36-60.

Evans MV, **Chiu WA**, Okino MS, Caldwell JC. 2009, "Development of an updated PBPK model for trichloroethylene and metabolites in mice, and its application to discern the role of oxidative metabolism in TCE-induced hepatomegaly", *Toxicol Appl Pharmacol.* 236:3, 329-40.

2010 Level III: "A Multidisciplinary Review of PPARalpha Activation Science Motivating an Update of Cancer Mechanisms Analysis Methods"

Guyton KZ, **Chiu WA**, Bateson TF, Jinot J, Scott CS, Brown RC, Caldwell JC. 2009, "A reexamination of the PPAR-alpha activation mode of action as a basis for assessing human cancer risks of environmental contaminants", *Environ Health Perspect.* 117:11, 1664-72.

2007 Level II: "An Update and Perspective on Some of the More Critical and Contentious Scientific Issues in the Risk Assessment of TCE"

Chiu WA, Caldwell JC, Keshava N, Scott CS. 2006, "Key scientific issues in the health risk assessment of trichloroethylene", *Environmental Health Perspectives*, 114:9, 1445-1449.

Chiu WA, Okino MS, Lipscomb JC, Evans MV. 2006, "Issues in the pharmacokinetics of trichloroethylene and its metabolites", *Environmental Health Perspectives*, 114:9, 1450-1456.

Caldwell JC, Keshava N. 2006, "Key Issues in the Modes of Action and Effects of Trichloroethylene Metabolites for Liver and Kidney Tumorigenesis", *Environmental Health Perspectives*, 114:9, 1457-1463.

Keshava N, Caldwell JC. 2006, "Key Issues in the Role of Peroxisome Proliferator–Activated Receptor Agonism and Cell Signaling in Trichloroethylene Toxicity", *Environmental Health Perspectives*, 114:9, 1464–1470.

Scott CS, **Chiu WA**. 2006, "Trichloroethylene cancer epidemiology: A consideration of select issues", *Environmental Health Perspectives*, 114:9, 1471-1478.

U.S. EPA Gold Metal

2012 Trichloroethylene *and Tetrachloroethylene Toxicological Review Teams*

U.S. EPA. 2011. *Toxicological review of Trichloroethylene (CASRN 79-01-6) in support of summary information on the Integrated Risk Information System (IRIS).* U.S. EPA, Washington, DC, EPA/635/R-09/011F.

U.S. EPA. 2012. *Toxicological review of Tetrachloroethylene (Perchloroethylene) (CASRN 127-18-4) in support of summary information on the Integrated Risk Information System (IRIS).* U.S. EPA, Washington, DC, EPA/635/R-08/011F.

U.S. EPA Bronze Medals for Commendable Service

2014 Workplan Chemicals Assessme nt Teams for TCE, DCM/NMP, ATO and HHCB
U.S. EPA. 2014. *TSCA Work Plan Chemical Risk Assessment - Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Uses (CASRN: 79-01-6)*. U.S. EPA, Washington, DC, EPA/740-R1-4002

2014 Forging International Partnerships for Advancing EPA's Mission of Protecting Human Health and the Environment
WHO/IPCS. 2014. *Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization.* World Health Organization, Geneva, IPCS Harmonization Project Document No. 11.

2009 Toxicogenomics in Risk Assessment DBP Case Study Group
U.S. EPA. 2009. *An Approach to Using Toxicogenomic Data in U.S. EPA Human Health Risk Assessments: A Dibutyl Phthalate Case Study*. U.S. EPA, Washington, DC, EPA/600/R-09/028F.

2005 Physiologically-based pharmacokinetic Modeling Team
U.S. EPA. 2006. *Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment.* U.S. EPA, Washington, DC, EPA/600/R-05/043F.

2004 Trichloroethylene Risk Assessment Team
TCE Issue Paper 1: Issues in Trichloroethylene Pharmacokinetics - EPA/600/R-05/022, 2005.
TCE Issue Paper 2: Interactions of Trichloroethylene, Its Metabolites, and Other Chemical Exposures - EPA/600/R-05/023, 2005.
TCE Issue Paper 3: Role of Peroxisome Proliferator-Activated Receptor Agonism and Cell Signaling in Trichloroethylene Toxicity - EPA/600/R-05/024, 2005.
TCE Issue Paper 4: Issues in Trichloroethylene Cancer Epidemiology - EPA/600/R-05/025, 2005.

2002 Assessment Factors Workgroup:
U.S. EPA. 2003. *A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information*. Science Policy Council, Washington, DC, EPA/100/B-03/001.

U.S. EPA Monetary Awards/Promotions for Outstanding Performance of Scientific Work

9/1/2011 - $3500 (Individual)
9/21/2010 - $3000 (Individual)
8/25/2010 - $400 (Individual)
6/3/2010 - $300 (Group)
9/8/2009 - $4000 (Group)
9/4/2008 - $3500 (Individual)
7/11/2008 - $750 (Individual)
8/22/2007 - $2000 (Individual)
11/26/2006 – Quality Step Increase
11/28/2004 – Promotion (GS-13 to GS-14)
6/16/2002 – Quality Step Increase

U.S. EPA Time-off Awards

2006 Recognition of Organizing and Leading the International Workshop on Uncertainty and Variability in Physiologically-based Pharmacokinetic Models

2005 Recognition of Review and Analysis of Dibutyl Phthalate Pharmacokinetics

COMPUTER SKILLS

- Able to develop original mathematical computer models and perform original complex data and statistical analysis using C, Mathematica, IDL, FORTRAN, Microsoft Excel, MCSIM, MatLab, and R.
- Proficient with Microsoft Word, Excel, Powerpoint, Outlook, and Access; Corel Wordperfect; and Lotus Notes.

LANGUAGES

English: *mother tongue*
French: *basic reading, writing, and speaking ability*
Mandarin Chinese: *rudimentary speaking, reading, and writing ability*

TEACHING/TRAINING/MENTORING

Academic Courses taught

VIBS 641: Principles of Human Health Risk Assessment of Chemicals (Fall 2017, 2017, 2019 – 3 credit hours). Lead instructor.

VIBS 645: Practice of Human Health Risk Assessment of Chemicals (Spring 2019, 2020 – 2 credit hours). Co-lead instructor.

VIBS 689: Special Topics – Principles of Human Health Risk Assessment of Chemicals (Fall 2015 and Fall 2016 – 3 credit hours). Lead instructor.

VIBS 689: Special Topics – Practice of Human Health Risk Assessment of Chemicals (Spring 2016, 2017, 2018 – 2 credit hours). Co-lead instructor.

VIBS 670: Environmental Toxicology (Spring 2016, 2017, 2018, 2019, 2020 – 3 credit hours). Instructor for 1 unit.

Invited lecturer/speaker

SRA 2017 Continuing Education Workshop (Arlington, VA)

Probabilistic Dose-Response Assessment: New Guidance from the World Health Organization: Primary Instructor: "Principles underlying the WHO-IPCS Approach," Derivation of adjustment factor distributions from data," "Future Directions in Dose-Response Harmonization," December, 2017.

SOT 2016 Continuing Education Course (New Orleans, LA)

Genetics and Population Variability in Chemical Toxicity: The What, the How, and So What?: Instructor, "Advancing Risk Assessment with Genetic and Population Variability Data," March 2016.

Eurotox 2015 Continuing Education Course (Porto, Portugal)

Evaluating and Expressing Uncertainty in Hazard Characterization: New Guidance from the World Health Organization: Invited speaker, "Deriving generic distributions from historical data for interspecies, intraspecies, and subchronic-chronic extrapolation, and how to deal with other uncertainties," and Case Study instructor, September, 2015.

SOT FDA Colloquia on Emerging Toxicological Science Challenges in Food and Ingredient Safety (College Park, MD):

Contemporary Issues in Risk Assessment: Invited speaker, "Opportunities and Challenges for Using IVIVE to Improve Decision Making," December, 2016.

Contemporary Issues in Risk Assessment: Invited speaker, "Harmonizing Dose-Response Assessment for Cancer and Non-cancer Endpoints in Human Health Assessments," June, 2015.

Complexities in Evaluating Human Clinical and Observational Data for Ingredient Safety Assessment: Partially Hydrogenated Oils As a Case Study: Invited speaker, "Dose-Response

Assessment Approaches to the Analysis of Noncancer Health Effects: Current Practices, Advice from the National Academies, and 2014 WHO/IPCS Guidance," November, 2014.

SRA 2016 Continuing Education Workshop (San Diego, CA)

Probabilistic Dose-Response Assessment: New Guidance from the World Health Organization: Primary Instructor: "Principles underlying the WHO-IPCS Approach," Derivation of adjustment factor distributions from data," "Future Directions in Dose-Response Harmonization," December, 2016.

Public Health Risk Science and Management Course (George Washington University, Washington, DC): Invited lecturer, "Dose-Response Assessment: Current Approaches, Key Challenges, and New Opportunities," September, 2014.

Training Seminar on Risk Science in the 21st Century (University of Ottawa, Canada): Invited speaker for Discussion on Risk Assessment Implications of Toxicity Testing in the 21st Century, March 2013.

UNC ENVR 742: Theory and practice of evaluating human health risks of chemicals (University of North Carolina [UNC], Chapel Hill, NC): Invited lecturer, "Challenges and Opportunities from National Research Council Recommendations for Risk Assessment: Review of EPA's Draft IRIS Assessment of Formaldehyde and Science and Decisions," December, 2012.

Academic Mentoring

Suji Jang, PhD Student at TAMU (2019-)

- Role: Chair of dissertation committee.

Alan Valdiviezo, PhD Student at TAMU (2019-)

- Role: Member of dissertation committee.

Alina Roman-Hubers, PhD Student at TAMU (2019-)

- Role: Member of dissertation committee.

Pierre Ferrer, PhD Student at TAMU (2019-)

- Role: Member of dissertation committee.

Brittni Ming-Whitfield, PhD Student at TAMU (2019-)

- Role: Member of dissertation committee.

Alexander Blanchette, PhD Student at TAMU (2018-)

- Role: Chair of dissertation committee.

Sarah Burnett, PhD Student at TAMU (2017-)

- Role: Member of dissertation committee.

Gaston Casillas, PhD Student at TAMU (2017-)

- Role: Member of dissertation committee.

Krisa Camargo, PhD Student at TAMU (2017-)

- Role: Co-chair of dissertation committee.

Zun-wei Chen, PhD Student at TAMU (2017-)

- Role: Member of dissertation committee.

Natalie Olson, BS student in Biomedical Sciences (2017-2019)

- Role: Undergraduate research mentor (systematic review of air pollution and birth weight).

Angelica Fuentes, BS student in Biomedical Sciences (2017-2019)

- Role: Undergraduate research mentor (systematic review of air pollution and birth weight).

Kyle Ferguson, MS in Toxicology Student at TAMU (2016-2018)

- Role: Chair of masters committee.

Yu-Syuan Luo, PhD Student at TAMU (graduated 2018)

- Role: Member of dissertation committee. Provide guidance on statistical and computational methods.

Elizabeth Barney, PhD Student at TAMU (graduated 2017)

- Role: Chair of dissertation committee. Provide guidance on project related to risk assessment methods.

Megan Moriarty, Masters of Public Health Student, TAMU (2015-2017)

- Role: Supervisor of Student Research Assistant. Provide guidance on project related to systematic review methods.

Qianwen Ouyang, Masters of Biotechnology Student, TAMU (2015-2016)

- Role: Supervisor for Research Credit. Provide guidance on projected related to probabilistic dose-response assessment.

Abhishek Venkatratnam, PhD Student at UNC (graduated 2017)

- Role: Serve on dissertation committee. Provide guidance on statistical and computational methods.
- Outputs: Co-author journal article (Yoo et al., 2015).

Jessica Wignall, Masters Student at UNC (graduated 2014)

- Role: Guidance on application of benchmark dose modeling of toxicological data and statistical modeling of toxicity values based on chemical structure.
- Outputs: Multiple poster and oral presentations at professional meetings; one published journal article (Wignall et al., 2014); additional article in preparation.

Andrew Shapiro, Masters Student at UNC (graduated 2014)

- Role: Guidance on application of benchmark dose modeling and development of web-based workspace for searching, reviewing, and modeling scientific literature.
- Outputs: Multiple poster and oral presentations at professional meetings; one published journal article (Wignall et al., 2014); working web-based prototype platform for conducting human health assessments.

Mary Kushman, Masters Student at UNC (graduated 2014)

- Role: Guidance on developing a systematic review methodology for mechanistic data.
- Outputs: Multiple poster and oral presentations at professional meetings; one published journal article (Kushman et al., 2014).

Hong-Sik Yoo, PhD Student at UNC

- Role: Guidance on trichloroethylene metabolism.
- Outputs: Poster presentation at professional meeting.

Martin Klein, PhD Student at University of Maryland at Baltimore County (graduated 2009)

- Role: Guidance on statistical issues in physiologically-based pharmacokinetic modeling.
- Outputs: One published journal article (Klein et al., 2013).

Tracey Woodruff, Professor at UCSF and Oak Ridge Institute for Science and Education Faculty Fellow

- Role: Guidance on application of benchmark dose modeling of toxicological data and statistical modeling of toxicity values based on chemical structure.
- Outputs: Multiple poster and oral presentations at professional meetings; one published journal article (Wignall et al., 2014); additional article in preparation.

Kenny Crump, Research Professor at Louisiana Technical College and Oak Ridge Institute for Science and Education Faculty Fellow

- Role: Guidance on probabilistic and statistical dose-response issues relevant to risk assessment.
- Outputs: Three published journal articles (Chiu and Crump, 2012; Crump et al., 2010a; Crump et al., 2010b).

PEER REVIEW EXPERIENCE

Study Sections

National Institute for Environmental Health Sciences

- R24 Special Emphasis Panel. March, 2018. Role: Member.

- PRIME R01 Special Emphasis Panel. July, 2017. Role: Member.

Panel reviews

National Toxicology Program

- NTP Report on Carcinogens (RoC) Monograph on Haloacetic Acids Found as Water Disinfection By-products. July, 2017. Role: Chair.
- NTP Monograph on Immunotoxicity Associated with Exposure to Perfluorooctanoic Acid (PFOA) or Perfluorooctane Sulfonate (PFOS). July, 2016. Role: Chair.

Letter reviews

Food and Drug Administration

- iRISK software. September, 2016.

Agency for Toxic Substances and Disease Registry

- Public Health Assessment, Camp Lejeune Drinking Water Public Health Assessment. October, 2015.

State of California Department of Pesticide Regulation, California Environmental Protection Agency

- 1,3- Dichloropropene Risk Characterization Document: Inhalation Exposure to Workers, Bystanders and the General Public. November, 2015.

Academic journals

Associate editor:

- Environmental Health Perspectives, July 2016-present
- Journal of Exposure Science and Environmental Epidemiology, March 2017-present

Manuscript reviewer:

- Risk Analysis
- Environmental Health Perspectives
- Toxicological Sciences
- Regulatory Toxicology and Pharmacology
- Critical Reviews in Toxicology
- Journal of Regulatory Science

CONFERENCES, WORKSHOPS, SYMPOSIA, WORKGROUPS, and ADVISORY COMMITTEES

Organized

Understanding and Applying Read-Across for Human Health Risk Assessment, Oakland, CA May, 2019

- Co-chair of Organizing Committee
- Moderator

International Workshop on Uncertainty and Variability in PBPK Models, Research Triangle Park, NC October-November 2006

- Chair of Organizing Committee
- Rapporteur, Breakout Group on Model Prediction
- Speaker, Plenary Session

Symposium on Recent Scientific Research Related to the Health Effects of Trichloroethylene, Washington, DC February 2004

Representative at International Workshops or Workgroups

- **World Health Organization/International Agency for Research on Cancer (WHO/IARC) Advisory Group to Recommend an Update to the Preamble:**
  - Invited Advisory Group member, November 2018.
  - Chair, Mechanisms Subgroup
- **World Health Organization/International Agency for Research on Cancer (WHO/IARC) Monograph 120:**
  - Invited Working Group member for Monograph 120 "Benzene," October 2017.
  - Chair, Mechanisms Subgroup
- **World Health Organization/International Agency for Research on Cancer (WHO/IARC) Monograph 117:**
  - Invited Working Group member for Monograph 117 "Pentachlorophenol and related compounds," October 2016.
  - Overall Chair
- **World Health Organization/International Agency for Research on Cancer (WHO/IARC) Monograph 113:**
  - Invited Working Group member for Monograph 113 "DDT, lindane, and 2,4-D," June 2015.
  - Chair, Mechanisms Subgroup
- **World Health Organization/International Agency for Research on Cancer (WHO/IARC) Monograph 110:**
  - Invited Working Group member for Monograph 110 "Perfluoro-octanoic acid, Tetrafluoroethylene, Dichloromethane, 1,2-Dichloropropane, and 1,3-Propane sultone," June 2014.
  - Chair, Mechanisms Subgroup
- **WHO/International Program on Chemical Safety (IPCS) Project on Uncertainty in Hazard Characterization:**
  - Original project workgroup member.
  - Co-author of draft working papers, September 2010
  - Co-author of draft guidance document, November 2011
  - Co-author of revised draft guidance document, November 2013.
  - Lead author of final guidance document, September 2014.
- **WHO/IARC Monograph 106:**
  - Invited Working Group member for International Agency for Research on Cancer Monograph 106 "Trichloroethylene and other chlorinated agents," October 2012.
  - Member, Mechanisms Subgroup
- **WHO/IPCS Project on PBPK Modeling in Risk Assessment:**
  - Invited representative at Workshop on PBPK Modeling in Risk Assessment, July 2009.
  - Rapporteur for multiple breakout sessions, formulating and facilitating consensus recommendations for a variety of topics.

Representative on National-level Committees or Workgroups

- **National Toxicology Program Board of Scientific Counselors:**
  - Member, May 2019-present.
- **Health Canada Chemicals Management Plan Science Committee:**
  - Member, January 2018-present.
- **National Academy of Sciences/National Research Council Committee to Review the Dietary Reference Intakes of Sodium and Potassium:**
  - Member, December 2017-March 2018.
- **National Academy of Sciences/National Research Council Committee on Development of Guiding Principles for the Inclusion of Chronic Disease Endpoints in Future Dietary Reference Intakes:**

  - Consultant, October 2016-August 2017.
- **National Academy of Sciences/National Research Council Standing Committee on Use of Emerging Science for Environmental Health Decisions:**
  - Member, September 2016-present.
- **National Academy of Sciences/National Research Council Committee on Unraveling Low Dose Toxicity: Case Studies of Systematic Review of Evidence:**
  - Committee member, June 2015-July 2017.
- **National Academy of Sciences/National Research Council Committee on Predictive-Toxicology Approaches for Military Assessments of Acute Exposures:**
  - Committee member, September 2014-July 2015.

Additional Advisory Committees

- **Oregon State University Superfund Research Program External Advisory Committee:**
  - Member, March 2018-present.

Invited Speaker/Panel Member

University of Ottawa on the Best Practices in Evidence Integration: Invited panelist "Meta-analysis and other approaches for pooling data from multiple outcomes," December 2019

Harvard Center for Risk Analysis Risk Assessment, Economic Evaluation, and Decisions Workshop: Invited speaker "Recent advances in probabilistic dose-response assessment to inform socioeconomic benefits analysis," September 2019.

University of Ottawa Workshop on the Development of an Evidence Based Risk Assessment Framework: Invited speaker "New approaches to characterizing uncertainty in risk assessment," December 2018

Food and Drug Administration, Cardiac Journal Club: Invited speaker at weekly journal club (title: Thorough QT/QTc in a Dish: An In Vitro Human Model That Accurately Predicts Clinical Concentration-QTc Relationships), March 2019.

Laboratory Animal Sciences 2019 Conference: Invited speaker, "Accurate clinical concentration-response predictions for cardiac arrhythmias using a population-based in vitro/in silico model," February 2019

University of Ottawa Workshop on the Development of an Evidence Based Risk Assessment Framework: Invited speaker "New approaches to characterizing uncertainty in risk assessment," December 2018

National Academies of Sciences, Engineering, and Medicine: Invited speaker at Strategies and Tools for Conducting Systematic Reviews of Mechanistic Data to Support Chemical Assessments. (title: Development and Use of Quantitative Adverse Outcome Pathways: Lessons Learned from Application to Cardiotoxicity), December 2018.

UCSF PRHE Webinar: Invited speaker at monthly webinar, "Beyond the RfD: Broad Application of a Probabilistic Approach to Improve Chemical Dose-Response Assessments for Non-Cancer Effects," November, 2018.

ASCCT Webinar: Invited speaker at monthly webinar, "Thorough QT/QTc in a Dish: An In Vitro Human Model That Accurately Predicts Clinical Concentration-QTc Relationships," November, 2018.

Cancer and Environmental Mixtures Meeting, Berkeley, CA: Invited speaker (title: Using ToxCast Data in Support of the Key Characteristics of Carcinogens: Opportunities and Challenges), August 2018.

National Academy of Sciences: Invited speaker at meeting of the *Committee on Army Test Subjects* (title: Overview of Approaches to Hazard Identification), November 2017.

U.S. Department of Agriculture: Invited speaker at *Office of Risk Assessment and Cost-Benefit Analysis, Science, Policy, and Risk Forum* (title: WHO/IPCS Guidance on Probabilistic Dose-Response Assessment: Basic principles and general approach), July 2017.

National Academy of Sciences: Invited speaker at meeting *Workshop on the Development of Guiding Principles for the Inclusion of Chronic Disease Endpoints in Future Dietary Reference Intake* (title: A Probabilistic Hazard Characterization Framework for Addressing Uncertainty and Variability), January 2017.

Food and Drug Administration: Invited speaker at *Risk Assessment of Tobacco Products: A Public Workshop.* (title: Addressing Population Variability and Susceptibility in Risk Assessment), November 2016.

OECD Workshop on Socioeconomic impact assessment of chemicals management (Helsinki, Finland)
Invited speaker: "Chemical Risk Assessment and Translation to Socio-Economic Assessments," July 2016.

U.S. EPA Aggregate Exposure Pathway meeting. Member of new initiative on "Aggregate Exposure Pathway" that better takes into account aggregate exposures. May 2016.

Society of Toxicology, Occupational and Public Health Specialty Section: Luncheon speaker. Addressing Uncertainty, Variability, Susceptibility and Risk in the 21st Century: The Union of Two NAS Reports? March 2016.

Brown University Superfund Research Program: Invited speaker and workgroup member for *Determining Adverse Responses Using In Vitro Assays* (title: Perspectives on "Determining Adverse Response Using In Vitro Assays"), June 2015.

National Institute of Environmental Health Sciences: Invited speaker for *Population-Based Rodent Resources for Environmental Health Sciences Meeting* (title: Advancing Risk Assessment with Population-Based Rodent Resources), March 2015.

Society for Risk Analysis Annual Meeting: Invited speaker for Symposium *Understanding and Communicating Hazard Assessment* (title: Evaluating and expressing uncertainty in hazard characterization: a new WHO/IPCS guidance incorporating probabilistic approaches), December 2014.

Society of Toxicology/Food and Drug Administration: Invited speaker and panel member for Colloquium *Complexities in Evaluating Human Clinical and Observational Data for Ingredient Safety Assessment: Partially Hydrogenated Oils As a Case Study* (title: Dose-Response Assessment Approaches to the Analysis of Non-cancer Health Effects: Current Practices, Advice from the National Academies, and 2014 WHO/IPCS Guidance), November 2014.

Society of Toxicology: Invited presentation to Occupational and Public Health Specialty Section (title: Addressing Human Variability in Next-Generation Human Health Risk Assessments of Environmental Chemicals), October 2014.

George Washington University: Invited lecturer for *Public Health Risk Science and Management Course* (title: Dose-Response Assessment: Current Approaches, Key Challenges, and New Opportunities), September 2014.

National Academy of Sciences: Invited speaker and panel member National Research Council meeting *Emerging Science for Environmental Health Decisions: The Potential of the Tissue Chip for Environmental Health Studies* (title: Key challenges in environmental health and the risk assessment of chemicals: opportunities for tissue chips?), July 2014.

Texas A&M University: Invited speaker for *Toxicology Seminar Series* (title: Advancing chemical risk assessment with new experimental, computational, and conceptual approaches), May 2014.

Society of Toxicology/FutureTox II: Invited speaker for FutureTox II Contemporary Concepts in Toxicology Conference, *Pathways to Prediction: In Vitro Data and In Silico Models for Predictive Toxicology* (title: Opportunities and challenges in the use of *in vitro* data and *in silico* models in risk assessment of chemicals), January 2014.

Toxicology Forum: Invited speaker for session on The Use of Population Based Mouse Models in Toxicology (title: Opportunities and Challenges to Incorporating Genetic Variability Data in Risk Assessment), July 2013.

Society of Toxicology: Invited speaker for Symposium on Modeling human genetic variability and susceptibility in the laboratory (title: Opportunities and Challenges to Incorporating Genetic Variability Data in Risk Assessment), March 2013.

U.S. EPA Inorganic Arsenic Public Stakeholder Meeting: Co-chair of Session on Dose-Response, January 2013.

International Conference on Environmental Health (Korea): Invited speaker for Session on Mechanistic Basis for Risk Assessment (title: *Use of mechanistic data in risk assessment - examples from EPA's IRIS assessment of Trichloroethylene*), May-June 2012

National Academy of Sciences: Invited speaker for Workshop on Biological Factors that Underlie Individual Susceptibility to Environmental Stressors, and Their Implications for Decision-Making (title: *Biological Variability and Improving Environmental Decision Making*), April 2012

Federal-State Toxicology Risk Assessment Committee Webinar: Invited presentation on EPA's Trichloroethylene Risk Assessment (title: *Key Aspects of U.S. EPA's Toxicological Review of Trichloroethylene*), April 2012

Toxicology Forum: Invited co-speaker for Session on Advancing Risk Assessment Approaches in the 21st Century (title: *U.S. EPA Risk Assessment Forum Action Plan for Advancing Human Health Risk Assessment*), January 2012

American Public Health Association Annual Meeting: Invited panel member for Session on the Next Generation of Human Health Risk Assessment and the Protection of Public Health, November 2011

Society for Risk Analysis Teleseminar: Invited presentation to dose-response specialty group (title: *NexGen Risk Assessments: Challenges and Opportunities for Dose-Response Assessment*), April 2011

Federal-State Toxicology Risk Assessment Committee Meeting: Invited presentation (title: *Key Aspects of U.S. EPA's External Review Draft Toxicological Review of Trichloroethylene*), October 2010

Society for Risk Analysis Annual Meeting: Invited speaker for Symposium on Evolution of Response to the NRC (title: *Science and Decisions Recommendations for Dose-Response Assessment: Issues and Challenges*), December 2009

Midwestern States Risk Assessment Symposium: Invited presentation on EPA's TCE Human Health Risk Assessment (title: *Key Aspects of U.S. EPA's External Review Draft Toxicological Review of Trichloroethylene*), November 2009

Society for Risk Analysis Teleseminar: Invited presentation to dose-response specialty group (title: *Dose-Response Analysis in Environmental Risk Assessment: Where are we, and where are we going?*), June 2008

National Academy of Sciences: Invited panel member for Workshop on Mouse Liver Tumors, November 2007

Resources for the Future: Invited panel member for Workshop on Dealing With Simple Bioassay Data: Where Do We Go From Here? October 2007

Society for Risk Analysis Annual Meeting: Invited speaker for Symposium on Issues from Recent Chemical Risk Assessments of Ethylene Oxide, Perchloroethylene, and Trichloroethylene (title: *Issues in the Application of PBPK Models in Risk Assessment: Examples from Trichloroethylene and Perchloroethylene*), December 2005

National Academy of Sciences: Invited speaker at Committee Meetings on Key Issues in TCE Health Risks (titles: *TCE Pharmacokinetics - Recent and Ongoing PBPK Modeling Efforts* and *What are the Key Difficult Scientific Issues in the Assessment of TCE Health Risks?*), March and June 2005

Toxicology Forum: Invited speaker at Session on Issues in Trichloroethylene Risk Assessment (title: *Issues in Trichloroethylene Risk Assessment*), July 2003

American Geophysical Union Spring Meeting: Invited poster for Session on Uncertainty & Variability (title: *A Framework for Uncertainty & Parameter Estimation in Exposure Assessment*), May 2002

Other Professional training/workshops

- "Beyond Point Estimates: Risk Assessment Using Interval, Fuzzy and Probabilistic Arithmetic," December 2, 2001, sponsored by Society for Risk Analysis.
- "Uncertainty Assessment Methodology for Dose Assessment Modeling: Lessons Learned from Test Case Studies," October 29, 2001, sponsored by U.S. Nuclear Regulatory Commission.
- "A Comprehensive Strategy for Hydrogeological Modeling and Uncertainty Analysis for Nuclear Facilities and Sites," August 14-15, 2001, sponsored by U.S. Nuclear Regulatory Commission.
- "Ground Water Pollution and Hydrology," July 9-13, 2001 sponsored by Princeton Groundwater.
- "Advanced Methods for Dose-Response Assessment: Bayesian Approaches," September 18-20, 2000, sponsored by Resources for the Future, U.S. EPA, the Society for Risk Analysis, and the Electric Power Research Institute.

PUBLICATIONS

Journal Articles (peer-reviewed)

1. **Chiu WA**, Fischer R, Ndeffo-Mbah, ML State-level needs for social distancing and contact tracing to contain COVID-19 in the United States. Nat Hum Behav (2020). https://doi.org/10.1038/s41562-020-00969-7
2. Brozek JL, Canelo-Aybar C, Akl EA, Bowen JM, Bucher J, **Chiu WA**, Cronin M, Djulbegovic B, Falavigna M, Guyatt GH, Gordon AA, Boon MH, Hutubessy RCW, Joore MA, Katikireddi V, LaKind J, Langendam M, Manja V, Magnuson K, Mathioudakis AG, Meerpohl J, Mertz D, Mezencev R, Morgan R, Morgano GP, Mustafa R, O'Flaherty M, Patlewicz G, Riva JJ, Posso M, Rooney A, Schlosser PM, Schwartz L, Shemilt I, Tarride JE, Thayer KA, Tsaioun K, Vale L, Wambaugh J, Wignall J, Williams A, Xie F, Zhang Y, Schünemann HJ; GRADE Working Group. GRADE Guidelines 30: The GRADE Approach to Assessing the Certainty of Modelled Evidence - an Overview in the Context of Health Decision-making. J Clin Epidemiol. 2020 Sep 24:S0895-4356(20)31103-3. doi: 10.1016/j.jclinepi.2020.09.018. Online ahead of print. PMID: 32980429
3. Chiu WA, Paoli GM. Recent Advances in Probabilistic Dose-Response Assessment to Inform Risk-Based Decision Making. Risk Anal. 2020 Sep 23. doi: 10.1111/risa.13595. Online ahead of print. PMID: 32966629
4. Grimm FA, Klaren WD, Li X, Lehmler HJ, Karmakar M, Robertson LW, **Chiu WA**, Rusyn I. Cardiovascular Effects of Polychlorinated Biphenyls and Their Major Metabolites. Environ Health Perspect. 2020 Jul;128(7):77008. doi: 10.1289/EHP7030. Epub 2020 Jul 23. PMID: 32701041; PMCID: PMC7377239.
5. Bois FY, Hsieh NH, Gao W, **Chiu WA**, Reisfeld B. Well-tempered MCMC simulations for population pharmacokinetic models. J Pharmacokinet Pharmacodyn. 2020 Jul 31. doi: 10.1007/s10928-020-09705-0. Epub ahead of print. PMID: 32737765.
6. Blessinger T, Davis A, **Chiu WA**, Stanek J, Woodall GM, Gift J, Thayer KA, Bussard D. Application of a unified probabilistic framework to the dose-response assessment of acrolein. Environ Int. 2020 Aug 5;143:105953. doi: 10.1016/j.envint.2020.105953. Epub ahead of print. PMID: 32768806.
7. Aly NA, Luo YS, Liu Y, Casillas G, McDonald TJ, Kaihatu JM, Jun M, Ellis N, Gossett S, Dodds JN, Baker ES, Bhandari S, **Chiu WA**, Rusyn I. 2020 Temporal and spatial analysis of per and polyfluoroalkyl substances in surface waters of Houston ship channel following a large-scale industrial fire incident.Environ Pollut. 2020 Oct;265(Pt B):115009. doi: 10.1016/j.envpol.2020.115009. Epub 2020 Jun 12.PMID: 32574947
8. Chen Z, Liu Y, Wright FA, **Chiu WA**, Rusyn I. 2020. Rapid hazard characterization of environmental chemicals using a compendium of human cell lines from different organs. ALTEX. 2020 Jun 8. doi: 10.14573/altex.2002291. Online ahead of print. PMID: 32521033

9. Dalaijamts C, Cichocki JA, Luo YS, Rusyn I, **Chiu WA**. 2020. PBPK modeling of impact of nonalcoholic fatty liver disease on toxicokinetics of perchloroethylene in mice. Toxicol Appl Pharmacol. 2020 Aug 1;400:115069. doi: 10.1016/j.taap.2020.115069. Epub 2020 May 21. PMID: 32445755
10. Smith MT, Guyton KZ, Kleinstreuer N, Borrel A, Cardenas A, **Chiu WA**, Felsher DW, Gibbons CF, Goodson WH, Houck KA, Kane A, La Merrill MA, Lebrec H, Lowe L, McHale CM, Minocherhomji S, Rieswijk L, Sandy MS, Sone H, Wang A, Zhang L, Zeise L, Fielden M. The Key Characteristics of Carcinogens: Relationship to the Hallmarks of Cancer, Relevant Biomarkers, and Assays to Measure Them. Cancer Epidemiol Biomarkers Prev. 2020 Mar 9. pii: cebp.1346.2019. doi: 10.1158/1055-9965.EPI-19-1346. [Epub ahead of print] PubMed PMID: 32152214.
11. Bhandari S, Lewis PGT, Craft E, Marvel SW, Reif DM, **Chiu WA**. HGBEnviroScreen: Enabling Community Action through Data Integration in the Houston-Galveston-Brazoria Region. Int J Environ Res Public Health. 2020 Feb 11;17(4). pii: E1130. doi: 10.3390/ijerph17041130. PubMed PMID: 32053902; PubMed Central PMCID: PMC7068489.
12. Luo YS, Ferguson KC, Rusyn I, **Chiu WA**. In Vitro Bioavailability of the Hydrocarbon Fractions of Dimethyl Sulfoxide Extracts of Petroleum Substances. Toxicol Sci. 2020 Apr 1;174(2):168-177. doi: 10.1093/toxsci/kfaa007. PubMed PMID: 32040194; PubMed Central PMCID: PMC7098373.
13. Sakolish C, Chen Z, Dalaijamts C, Mitra K, Liu Y, Fulton T, Wade TL, Kelly EJ, Rusyn I, **Chiu WA**. Predicting tubular reabsorption with a human kidney proximal tubule tissue-on-a-chip and physiologically-based modeling. Toxicol In Vitro. 2020 Mar;63:104752. doi: 10.1016/j.tiv.2019.104752. Epub 2019 Dec 17. PubMed PMID: 31857146; PubMed Central PMCID: PMC7053805.
14. Kvasnicka J, Stylianou KS, Nguyen VK, Huang L, **Chiu WA**, Burton GA Jr, Semrau J, Jolliet O. Human Health Benefits from Fish Consumption vs. Risks from Inhalation Exposures Associated with Contaminated Sediment Remediation: Dredging of the Hudson River. Environ Health Perspect. 2019 Dec;127(12):127004. doi:10.1289/EHP5034. Epub 2019 Dec 13. PubMed PMID: 31834828; PubMed Central PMCID: PMC6957280.
15. Bera G, Camargo K, Sericano JL, Liu Y, Sweet ST, Horney J, Jun M, **Chiu W**, Rusyn I, Wade TL, Knap AH. Baseline data for distribution of contaminants by natural disasters: results from a residential Houston neighborhood during Hurricane Harvey flooding. Heliyon. 2019 Nov 16;5(11):e02860. doi: 10.1016/j.heliyon.2019.e02860. eCollection 2019 Nov. PubMed PMID: 31763489; PubMed Central PMCID: PMC6861583.
16. Danforth C, **Chiu WA**, Rusyn I, Schultz K, Bolden A, Kwiatkowski C, Craft E. An integrative method for identification and prioritization of constituents of concern in produced water from onshore oil and gas extraction. Environ Int. 2020 Jan;134:105280. doi: 10.1016/j.envint.2019.105280. Epub 2019 Nov 6. PubMed PMID: 31704566.
17. Wang M, Orr AA, He S, Dalaijamts C, **Chiu WA**, Tamamis P, Phillips TD. Montmorillonites Can Tightly Bind Glyphosate and Paraquat Reducing Toxin Exposures and Toxicity. ACS Omega. 2019 Oct 17;4(18):17702-17713. doi: 10.1021/acsomega.9b02051. eCollection 2019 Oct 29. PubMed PMID: 31681876; PubMed Central PMCID: PMC6822125.
18. Onel M, Beykal B, Ferguson K, **Chiu WA**, McDonald TJ, Zhou L, House JS, Wright FA, Sheen DA, Rusyn I, Pistikopoulos EN. Grouping of complex substances using analytical chemistry data: A framework for quantitative evaluation and visualization. PLoS One. 2019 Oct 10;14(10):e0223517. doi: 10.1371/journal.pone.0223517. eCollection 2019. PubMed PMID: 31600275; PubMed Central PMCID: PMC6786635.
19. Samet JM, **Chiu WA**, Cogliano V, Jinot J, Kriebel D, Lunn RM, Beland FA, Bero L, Browne P, Fritschi L, Kanno J, Lachenmeier DW, Lan Q, Lasfargues G, Curieux FL, Peters S, Shubat P, Sone H, White MC, Williamson J, Yakubovskaya M, Siemiatycki J, White PA, Guyton KZ, Schubauer-Berigan MK, Hall AL, Grosse Y, Bouvard V, Benbrahim-Tallaa L, Ghissassi FE, Lauby-Secretan B, Armstrong B, Saracci R, Zavadil J, Straif K, Wild CP. The IARC Monographs: Updated procedures

for modern and transparent evidence synthesis in cancer hazard identification. J Natl Cancer Inst. 2019 Sep 9. pii: djz169. doi: 10.1093/jnci/djz169. PMID: 31498409

20. Burnett SD, Blanchette AD, Grimm FA, House JS, Reif DM, Wright FA, **Chiu WA,** Rusyn I. Population-based toxicity screening in human induced pluripotent stem cell-derived cardiomyocytes. Toxicol Appl Pharmacol. 2019 Oct 15;381:114711. doi: 10.1016/j.taap.2019.114711. Epub 2019 Aug 16. PMID: 31425687
21. Luo YS, Cichocki JA, Hsieh NH, Lewis L, Wright FA, Threadgill DW, **Chiu WA**, Rusyn I. Using Collaborative Cross Mouse Population to Fill Data Gaps in Risk Assessment: A Case Study of Population-Based Analysis of Toxicokinetics and Kidney Toxicodynamics of Tetrachloroethylene. Environ Health Perspect. 2019 Jun;127(6):67011. doi: 10.1289/EHP5105. Epub 2019 Jun 27. PMID: 31246107
22. Ferguson KC, Luo YS, Rusyn I, **Chiu WA.** Comparative analysis of Rapid Equilibrium Dialysis (RED) and solid phase micro-extraction (SPME) methods for In Vitro-In Vivo extrapolation of environmental chemicals. Toxicol In Vitro. 2019 Oct;60:245-251. doi: 10.1016/j.tiv.2019.06.006. Epub 2019 Jun 10. PMID: 31195086
23. Lewis L, Borowa-Mazgaj B, de Conti A, Chappell GA, Luo YS, Bodnar W, Konganti K, Wright FA, Threadgill DW, **Chiu WA**, Pogribny IP, Rusyn I. Population-Based Analysis of DNA Damage and Epigenetic Effects of 1,3-Butadiene in the Mouse. Chem Res Toxicol. 2019 Apr 25. doi: 10.1021/acs.chemrestox.9b00035. [Epub ahead of print] PubMed PMID: 30990016.
24. Stermer AR, Klein D, Wilson SK, Dalaijamts C, Bai CY, Hall SJ, Madnick S, Bianchi E, **Chiu WA**, Boekelheide K. Differential toxicity of water versus gavage exposure to trichloroethylene in rats. Environmental Toxicology and Pharmacology, 68, 1-3.
25. Englehardt JD, **Chiu WA.** A general dose-response relationship for chronic chemical and other health stressors and mixtures based on an emergent illness severity model. PLoS One. 2019 Feb 15;14(2):e0211780. doi: 10.1371/journal.pone.0211780. eCollection 2019. PubMed PMID: 30768598.
26. Cichocki JA, Luo YS, Furuya S, Venkatratnam A, Konganti K, **Chiu WA**, Threadgill DW, Pogribny IP, Rusyn I. Modulation of Tetrachloroethylene-Associated Kidney Effects by Nonalcoholic Fatty Liver or Steatohepatitis in Male C57BL/6J Mice. Toxicol Sci. 2019 Jan 1;167(1):126-137. doi: 10.1093/toxsci/kfy223. PubMed PMID: 30202895; PubMed Central PMCID: PMC6317418.
27. Guyton KZ, Rieswijk L, Wang A, **Chiu WA**, Smith MT. Key Characteristics Approach to Carcinogenic Hazard Identification. Chem Res Toxicol. 2018 Dec 6. doi: 10.1021/acs.chemrestox.8b00321. [Epub ahead of print] PubMed PMID: 30521319.
28. Fantke P, Aylward L, Bare J, **Chiu WA**, Dodson R, Dwyer R, Ernstoff A, Howard B, Jantunen M, Jolliet O, Judson R, Kirchhübel N, Li D, Miller A, Paoli G, Price P, Rhomberg L, Shen B, Shin HM, Teeguarden J, Vallero D, Wambaugh J, Wetmore BA, Zaleski R, McKone TE. Advancements in Life Cycle Human Exposure and Toxicity Characterization. Environ Health Perspect. 2018 Dec;126(12):125001. doi: 10.1289/EHP3871. PubMed PMID: 30540492.
29. Luo YS, Hsieh NH, Soldatow VY, **Chiu WA**, Rusyn I. Comparative analysis of metabolism of trichloroethylene and tetrachloroethylene among mouse tissues and strains. Toxicology. 2018 Jul 24;409:33-43. doi: 10.1016/j.tox.2018.07.012. [Epubahead of print] PubMed PMID: 30053492.
30. Dorman DC, **Chiu W**, Hales BF, Hauser R, Johnson KJ, Mantus E, Martel S, Robinson KA, Rooney AA, Rudel R, Sathyanarayana S, Schantz SL, Waters KM. Polybrominated diphenyl ether (PBDE) neurotoxicity: a systematic review and meta-analysis of animal evidence. J Toxicol Environ Health B Crit Rev. 2018;21(4):269-289. doi: 10.1080/10937404.2018.1514829. Epub 2018 Oct 23. PubMed PMID: 30352012.
31. Blanchette AD, Grimm FA, Dalaijamts C, Hsieh NH, Ferguson K, Luo YS, Rusyn I, **Chiu WA**. Thorough QT/QTc in a Dish: An In Vitro Human Model That Accurately Predicts Clinical Concentration-QTc Relationships. Clin Pharmacol Ther. 2018 Oct 22. doi: 10.1002/cpt.1259. [Epub ahead of print] PubMed PMID: 30346629.

32. Sakolish C, Weber EJ, Kelly EJ, Himmelfarb J, Mouneimne R, Grimm FA, House JS, Wade T, Han A, **Chiu WA**, Rusyn I. Technology Transfer of the Microphysiological Systems: A Case Study of the Human Proximal Tubule Tissue Chip. Sci Rep. 2018 Oct 5;8(1):14882. doi: 10.1038/s41598-018-33099-2. PubMed PMID: 30291268; PubMed Central PMCID: PMC6173737.
33. Dorman DC, **Chiu W**, Hales BF, Hauser R, Johnson KJ, Mantus E, Martel S, Robinson KA, Rooney AA, Rudel R, Sathyanarayana S, Schantz SL, Waters KM. Systematic reviews and meta-analyses of human and animal evidence of prenatal diethylhexyl phthalate exposure and changes in male anogenital distance. J Toxicol Environ Health B Crit Rev. 2018;21(4):207-226. doi: 10.1080/10937404.2018.1505354. Epub 2018 Sep 10. PubMed PMID: 30199328.
34. Grimm FA, Blanchette A, House JS, Ferguson K, Hsieh NH, Dalaijamts C, Wright AA, Anson B, Wright FA, **Chiu WA**, Rusyn I. A human population-based organotypic in vitro model for cardiotoxicity screening. ALTEX. 2018 Jul 8. doi: 10.14573/altex.1805301. [Epub ahead of print] PubMed PMID: 29999168.
35. **Chiu WA**, Axelrad DA, Dalaijamts C, Dockins C, Shao K, Shapiro AJ, Paoli G. Beyond the RfD: Broad Application of a Probabilistic Approach to Improve Chemical Dose-Response Assessments for Noncancer Effects. Environ Health Perspect. 2018 Jun 28;126(6):067009. doi: 10.1289/EHP3368. eCollection 2018 Jun. PubMed PMID: 29968566; PubMed Central PMCID: PMC6084844.
36. Hsieh NH, Reisfeld B, Bois FY, **Chiu WA**. Applying a Global Sensitivity Analysis Workflow to Improve the Computational Efficiencies in Physiologically-Based Pharmacokinetic Modeling. Front Pharmacol. 2018 Jun 8;9:588. doi: 10.3389/fphar.2018.00588. eCollection 2018. PubMed PMID: 29937730; PubMed Central PMCID: PMC6002508.
37. Dalaijamts C, Cichocki JA, Luo YS, Rusyn I, **Chiu WA**. Incorporation of the glutathione conjugation pathway in an updated physiologically-based pharmacokinetic model for perchloroethylene in mice. Toxicol Appl Pharmacol. 2018 Aug 1;352:142-152. doi: 10.1016/j.taap.2018.05.033. Epub 2018 May 29. PubMed PMID: 29857080; PubMed Central PMCID: PMC6051410.
38. Wignall JA, Muratov E, Sedykh A, Guyton KZ, Tropsha A, Rusyn I, **Chiu WA**. Conditional Toxicity Value (CTV) Predictor: An In Silico Approach for Generating Quantitative Risk Estimates for Chemicals. Environ Health Perspect. 2018 May 29;126(5):057008. doi: 10.1289/EHP2998. eCollection 2018 May. PubMed PMID: 29847084; PubMed Central PMCID: PMC6071978.
39. Guyton KZ, Rusyn I, **Chiu WA**, Corpet DE, van den Berg M, Ross MK, Christiani DC, Beland FA, Smith MT. Application of the key characteristics of carcinogens in cancer hazard identification. Carcinogenesis. 2018 Apr 5;39(4):614-622. doi: 10.1093/carcin/bgy031. PubMed PMID: 29562322; PubMed Central PMCID: PMC5888955.
40. Venkatratnam A, House JS, Konganti K, McKenney C, Threadgill DW, **Chiu WA**, Aylor DL, Wright FA, Rusyn I. Population-based dose-response analysis of liver transcriptional response to trichloroethylene in mouse. Mamm Genome. 2018 Jan 20. doi: 10.1007/s00335-018-9734-y. [Epub ahead of print] PubMed PMID: 29353386.
41. **Chiu WA**, Rusyn I. Advancing chemical risk assessment decision-making with population variability data: challenges and opportunities. Mamm Genome. 2018 Jan 3. doi: 10.1007/s00335-017-9731-6. [Epub ahead of print] PubMed PMID: 29299621.
42. Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Vilahur N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of benzene. Lancet Oncol. 2017 Dec;18(12):1574-1575. doi: 10.1016/S1470-2045(17)30832-X. Epub 2017 Oct 26. No abstract available. PMID: 29107678
43. Zhou YH, Cichocki JA, Soldatow VY, Scholl E, Gallins P, Jima D, Yoo HS, **Chiu WA**, Wright FA, Rusyn I. 2017. Comparative dose-response analysis of liver and kidney transcriptomic effects of trichloroethylene and tetrachloroethylene in B6C3F1 mouse. Toxicol Sci. doi: 10.1093/toxsci/kfx165.
44. Bokkers BGH, Mengelers MJ, Bakker MI, **Chiu WA,** Slob W. APROBA-Plus: A probabilistic tool to evaluate and express uncertainty in hazard characterization and exposure assessment of substances. Food Chem Toxicol. 2017 Oct 23. pii: S0278-6915(17)30636-1. doi: 10.1016/j.fct.2017.10.038.

45. Cichocki JA, Furuya S, Luo YS, Iwata Y, Konganti K, **Chiu WA**, Threadgill DW, Pogribny IP, Rusyn I. Nonalcoholic Fatty Liver Disease Is a Susceptibility Factor for Perchloroethylene-Induced Liver Effects in Mice. Toxicol Sci. 2017 Sep 1;159(1):102-113. doi: 10.1093/toxsci/kfx120.
46. **Chiu WA**, Guyton KZ, Martin MT, Reif DM, Rusyn I. 2017. Use of high-throughput in vitro toxicity screening data in cancer hazard evaluations by IARC Monograph Working Groups. ALTEX. doi: 10.14573/altex.1703231.
47. Grimm FA, Russell WK, Luo YS, Iwata Y, **Chiu WA**, Roy T, Boogaard PJ, Ketelslegers HB, Rusyn I. .2018. Grouping of Petroleum Substances as Example UVCBs by Ion Mobility-Mass Spectrometry to Enable Chemical Composition-Based Read-Across. Environ Sci Technol. 51(12):7197-7207. doi: 10.1021/acs.est.6b06413.
48. Cichocki JA, Furuya S, Venkatratnam A, McDonald TJ, Knap AH, Wade T, Sweet S, **Chiu WA**, Threadgill DW, Rusyn I. Characterization of Variability in Toxicokinetics and Toxicodynamics of Tetrachloroethylene Using the Collaborative Cross Mouse Population. 2017. Environ Health Perspect. 125(5):057006. doi: 10.1289/EHP788
49. Venkatratnam A, Furuya S, Kosyk O, Gold A, Bodnar W, Konganti K, Threadgill DW, Gillespie KM, Aylor DL, Wright FA, **Chiu WA**, Rusyn I. Collaborative Cross mouse population enables refinements to characterization of the variability in toxicokinetics of trichloroethylene and provides genetic evidence for the role of PPAR pathway in its oxidative metabolism. Toxicol Sci. 2017 Mar 27;PubMed PMID: 28369613.
50. Sirenko O, Grimm FA, Ryan KR, Iwata Y, **Chiu WA**, Parham F, Wignall JA, Anson B, Cromwell EF, Behl M, Rusyn I, Tice RR. (2017) In vitro cardiotoxicity assessment of environmental chemicals using an organotypic human induced pluripotent stem cell-derived model. Toxicol Appl Pharmacol. 2017 Mar 1;322:60-74. doi: 10.1016/j.taap.2017.02.020.
51. Cichocki JA, Furuya S, Konganti K, Luo YS, McDonald TJ, Iwata Y, **Chiu WA**, Threadgill DW, Pogribny IP, Rusyn I. 2017. Impact of nonalcoholic fatty liver disease on toxicokinetics of tetrachloroethylene. J Pharmacol Exp Ther. 2017 Feb 1. pii: jpet.116.238790. doi: 10.1124/jpet.116.238790. [Epub ahead of print] PMID: 28148637
52. **Chiu WA,** Wright FA, Rusyn I. 2017. A tiered, Bayesian approach to estimating of population variability for regulatory decision-making. ALTEX.34(3):377-388. doi: 10.14573/altex.1608251. PMID: 27960008
53. Barton-Maclaren, T.S., Westphal, M., Sarwar, E., Mattison, D., **Chiu, W.A.**, Dix, D., Kavlock, R. and Krewski, D. 2017. Challenges and opportunities in the risk assessment of existing substances in Canada: lessons learned from the international community, Int. J. Risk Assessment and Management, 20: 1/2/3, 2017.
54. Guyton K, Loomis D, Grosse Y, El Ghissasi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group, IARC, Lyon, France. 2016. "Carcinogenicity of pentachlorophenol and some related compounds." Lancet Oncol. 17(12):1637-8. doi: 10.1016/S1470-2045(16)30513-7.
55. Cichocki JA, Guyton KZ, Guha N, **Chiu WA**, Rusyn I, Lash LH. 2016. Target Organ Metabolism, Toxicity, and Mechanisms of Trichloroethylene and Perchloroethylene: Key Similarities, Differences, and Data Gaps. J Pharmacol Exp Ther. 2016 Aug 10. pii: jpet.116.232629
56. Cote I, Andersen ME, Ankley GT, Barone S, Birnbaum LS, Boekelheide K, Bois FY, Burgoon LD, **Chiu WA**, Crawford-Brown D, Crofton KM, DeVito M, Devlin RB, Edwards SW, Guyton KZ, Hattis D, Judson RS, Knight D, Krewski D, Lambert J, Maull EA, Mendrick D, Paoli GM, Patel CJ, Perkins EJ, Poje G, Portier CJ, Rusyn I, Schulte PA, Simeonov A, Smith MT, Thayer KA, Thomas RS, Thomas R, Tice RR, Vandenberg JJ, Villeneuve DL, Wesselkamper S, Whelan M, Whittaker C, White R, Xia M, Yauk C, Zeise L, Zhao J, DeWoskin RS. "The Next Generation of Risk Assessment Multiyear Study- Highlights of Findings, Applications to Risk Assessment and Future Directions." Environ Health Perspect. 2016 Apr 19. E-pub ahead of print.

57. Salazar KD, Brinkerhoff CJ, Lee JS, **Chiu WA**. 2015. "Development and application of a rat PBPK model to elucidate kidney and liver effects induced by ETBE and tert-butanol," *Toxicol Appl Pharmacol*. 288(3):439-52. doi: 10.1016/j.taap.2015.08.015.
58. Yoo HS, Cichocki JA, Kim S, Venkatratnam A, Iwata Y, Kosyk O, Bodnar W, Sweet S, Knap A, Wade T, Campbell J, Clewell HJ, Melnyk SB, **Chiu WA**, Rusyn I. 2015. "The Contribution of Peroxisome Proliferator-Activated Receptor Alpha to the Relationship Between Toxicokinetics and Toxicodynamics of Trichloroethylene." *Toxicol Sci.* 147(2):339-49. doi: 10.1093/toxsci/kfv134.
59. **Chiu WA**, Slob W. 2015. "A unified probabilistic framework for dose-response assessment of human health effects." *Environ Health Perspect.* 123(12):1241. doi:10.1289/ehp.1409385.
60. Woo HD, **Chiu WA,** Jo S, Kim J. 2015. "Benchmark Dose for Urinary Cadmium based on a Marker of Renal Dysfunction: A Meta-Analysis." PLoS One. 10(5):e0126680. doi:10.1371/journal.pone.0126680.
61. Loomis D, Guyton K, Grosse Y, El Ghissasi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group, IARC, Lyon, France. 2015. "Carcinogenicity of lindane, DDT, and 2,4-dichlorophenoxyacetic acid." Lancet Oncol. 16(8):891-2. doi: 10.1016/S1470-2045(15)00081-9.
62. Abdo N, Xia M, Brown CC, Kosyk O, Huang R, Sakamuru S, Zhou YH, Jack J, Gallins P, Xia K, Li Y, **Chiu WA**, Motsinger-Reif A, Austin CP, Tice RR, Rusyn I, Wright FA. 2015. "Population-Based In Vitro Hazard and Concentration-Response Assessment of Chemicals: The 1000 Genomes High Throughput Screening Study." *Environ Health Perspect.* 123(5):458-66. doi:10.1289/ehp.1408775.
63. Lash LH, **Chiu WA,** Guyton KZ, Rusyn I. 2014. "Trichloroethylene biotransformation and its role in mutagenicity, carcinogenicity and target organ toxicity." *Mutation Research/Reviews in Mutation Research.* 762:22-36. doi:10.1016/j.mrrev.2014.04.003.
64. Krewski D, Westphal M, Andersen ME, Paoli GM, **Chiu WA**, Al-Zoughool M, Croteau MC, Burgoon LD, Cote I. 2014. "A Framework for the Next Generation of Risk Science." *Environ Health Perspect.* 122(8):796-805. doi: 10.1289/ehp.1307260.
65. Wignall JA, Shapiro AJ, Wright FA, Woodruff TJ, **Chiu WA**, Guyton KZ, Rusyn I. 2014. "Standardized Benchmark Dose Calculation: Opportunities to Inform Science-Based Decisions in Human Health Assessments." *Environ Health Perspect.* 122(5):499-505. doi: 10.1289/ehp.1307539.
66. **Chiu WA**, Campbell JL, Clewell HJ, Zhou Y-H, Wright FA, Guyton KZ, Rusyn I. 2014. "Physiologically-Based Pharmacokinetic (PBPK) Modeling of Inter-strain Variability in Trichloroethylene Metabolism in the Mouse." *Environ Health Perspect.* 122(5):456-63. doi: 10.1289/ehp.1307623.
67. Guyton KZ, Hogan K, Scott CS, Cooper G, Bale AS, Kopylev L, Barone S Jr, Makris SL, Glenn B, Subramaniam R, Gwinn MR, Dzubow RC, **Chiu WA**. 2014. "Human health effects of tetrachloroethylene: key findings and scientific issues." *Environ Health Perspect.* 122(4):325-34. doi: 10.1289/ehp.1307359.
68. Benbrahim-Tallaa L, Lauby-Secretan B, Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Bouvard V, Guha N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group. 2014. "Carcinogenicity of perfluorooctanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone." Lancet Oncol. 15(9):924-5.
69. Rusyn I, **Chiu WA**, Lash LH, Kromhout H, Hansen J, Guyton KZ. 2014. "Trichloroethylene: Mechanistic, epidemiologic and other supporting evidence of carcinogenic hazard." *Pharmacol Ther.* 141(1):55-68. doi: 10.1016/j.pharmthera.2013.08.004.
70. Kushman ME, Kraft AD, Guyton KZ, **Chiu WA**, Makris SL, Rusyn I. 2013. "A systematic approach for identifying and presenting mechanistic evidence in human health assessments." *Regul Toxicol Pharmacol.* 67(2):266-77. doi: 10.1016/j.yrtph.2013.08.005.
71. Wilson VS, Keshava N, Hester S, Segal D, **Chiu W**, Thompson CM, Euling SY. 2013. "Utilizing toxicogenomic data to understand chemical mechanism of action in risk assessment." *Toxicol Appl Pharmacol.* 271(3):299-308.

72. **Chiu WA**, Euling SY, Scott CS, Subramaniam RP. 2013a. "Approaches to advancing quantitative human health risk assessment of environmental chemicals in the post-genomic era." *Toxicol Appl Pharmacol.* 271(3):309-23.
73. Euling SY, Thompson CM, **Chiu WA**, Benson R. 2013. "An approach for integrating toxicogenomic data in risk assessment: The dibutyl phthalate case study." *Toxicol Appl Pharmacol.* 271(3):324-35.
74. Klein M, Jeerchal N, Sinha B, **Chiu W**, White P. 2013. "Statistical inferences from serially correlated methylene chloride data." *Sankhya B,* 74(2), 211-237.
75. **Chiu WA**, Jinot J, Scott CS, Makris SL, Cooper GS, Dzubow RC, Bale AS, Evans MV, Guyton KZ, Keshava N, Lipscomb JC, Barone S Jr, Fox JF, Gwinn MR, Schaum J, Caldwell JC. 2013b. "Human health effects of trichloroethylene: key findings and scientific issues." *Environ Health Perspect.* 121(3):303-11.
76. Zeise L, Bois FY, **Chiu WA**, Hattis D, Rusyn I, Guyton KZ. 2013. "Addressing human variability in next-generation human health risk assessments of environmental chemicals." *Environ Health Perspect.* 121(1):23-31.
77. **Chiu WA**, Crump, KS. 2012. "Using Copulas to Introduce Dependence in Dose-Response Modeling of Multiple Binary Endpoints", *Journal of Agricultural Biological and Environmental Statistics*, 17:1, 107-127.
78. Guha N, Loomis D, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Baan R, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group. 2012. "Carcinogenicity of trichloroethylene, tetrachloroethylene, some other chlorinated solvents, and their metabolites." Lancet Oncol. 13(12):1192-3.
79. **Chiu WA**. 2011, "Trichloroacetic acid: Updated estimates of its bioavailability and its contribution to trichloroethylene-induced mouse hepatomegaly", *Toxicology*, 285:114-25.
80. **Chiu WA**, Ginsberg GL. 2011, "Development and evaluation of a harmonized physiologically based pharmacokinetic (PBPK) model for perchloroethylene toxicokinetics in mice, rats, and humans", *Toxicol Appl Pharmacol.*, 253:203-34.
81. Crump KS, Chen C, **Chiu WA**, Louis TA, Portier CJ, Subramaniam RP, White PD. 2010a, "What role for biologically based dose-response models in estimating low-dose risk?", *Environ Health Perspect.* 118:5, 585-8.
82. Crump KS, **Chiu WA**, Subramaniam RP. 2010b, "Issues in using human variability distributions to estimate low-dose risk", *Environ Health Perspect.* 118:3, 387-93.
83. Guyton KZ, **Chiu WA**, Bateson TF, Jinot J, Scott CS, Brown RC, Caldwell JC. 2009, "A reexamination of the PPAR-alpha activation mode of action as a basis for assessing human cancer risks of environmental contaminants", *Environ Health Perspect.* 117:11, 1664-72.
84. **Chiu WA**, Okino MS, Evans MV. 2009, "Characterizing uncertainty and population variability in the toxicokinetics of trichloroethylene and metabolites in mice, rats, and humans using an updated database, physiologically based pharmacokinetic (PBPK) model, and Bayesian approach", *Toxicol Appl Pharmacol.* 241:1, 36-60.
85. Evans MV, **Chiu WA**, Okino MS, Caldwell JC. 2009, "Development of an updated PBPK model for trichloroethylene and metabolites in mice, and its application to discern the role of oxidative metabolism in TCE-induced hepatomegaly", *Toxicol Appl Pharmacol.* 236:3, 329-40.
86. Thompson CM, Sonawane B, Barton HA, DeWoskin RS, Lipscomb JC, Schlosser P, **Chiu WA**, Krishnan K. 2008, "Approaches for applications of physiologically based pharmacokinetic models in risk assessment", *J Toxicol Environ Health B Crit Rev.* 11:7, pp.519-47.
87. Barton HA, **Chiu WA**, Setzer RW, Andersen ME, Bailer AJ, Bois FY, Dewoskin RS, Hays S, Johanson G, Jones N, Loizou G, MacPhail RC, Portier CJ, Spendiff M, Tan YM. 2007. "Characterizing uncertainty and variability in physiologically based pharmacokinetic models: State of the science and needs for research and implementation", *Toxicological Sciences*, 99:2, 395-402.
88. **Chiu WA**, Bois FY. 2007, "An approximate method for population toxicokinetic analysis with aggregated data", *Journal of Agricultural Biological and Environmental Statistics*, 12:3, 346-363.

89. **Chiu WA**, Barton HA, Dewoskin RS, Schlosser P, Thompson CM, Sonawane B, Lipscomb JC, Krishnan K. 2007, "Evaluation of physiologically based pharmacokinetic models for use in risk assessment", *Journal of Applied Toxicology*, 27:3, 218-237.
90. **Chiu WA**, Micallef S, Monster AC, Bois FY. 2007, "Toxicokinetics of inhaled trichloroethylene and tetrachloroethylene in humans at 1 ppm: Empirical results and comparisons with previous studies", *Toxicological Sciences*, 95:1, 23-36.
91. Hack CE, **Chiu WA**, Zhao QJ, Clewell HJ. 2006, "Bayesian population analysis of a harmonized physiologically based pharmacokinetic model of trichloroethylene and its metabolites", *Regulatory Toxicology and Pharmacology*, 46:1, 63-83.
92. **Chiu WA**, Caldwell JC, Keshava N, Scott CS. 2006, "Key scientific issues in the health risk assessment of trichloroethylene", *Environmental Health Perspectives*, 114:9, 1445-1449.
93. **Chiu WA**, Okino MS, Lipscomb JC, Evans MV. 2006, "Issues in the pharmacokinetics of trichloroethylene and its metabolites", *Environmental Health Perspectives*, 114:9, 1450-1456.
94. Scott CS, **Chiu WA**. 2006, "Trichloroethylene cancer epidemiology: A consideration of select issues", *Environmental Health Perspectives*, 114:9, 1471-1478.
95. **Chiu WA**, White P. 2006, "Steady-state solutions to PBPK models and their applications to risk assessment I: Route-to-route extrapolation of volatile chemicals", *Risk Analysis*, 26:3, 769-780.
96. **Chiu WA**, Bois FY. 2006, "Revisiting the population toxicokinetics of tetrachloroethylene", *Archives of Toxicology*, 80:6, 382-385.
97. Wolbarst AB, **Chiu WA**, Yu C, Aiello K, Bachmaier JT, Bastian RK, Cheng JJ, Goodman J, Hogan R, Jones AR, Kamboj S, Lenhartt T, Ott WR, Rubin A, Salomon SN, Schmidt DW, Setlow LW. 2006, "Radioactive materials in biosolids: Dose modeling", *Health Physics*, 90:1, 16-30.
98. Bastian RK, Bachmaier JT, Schmidt DW, Salomon SN, Jones A, **Chiu WA**, Setlow LW, Wolbarst AB, Yu C, Goodman J, Lenhart T. 2005, "Radioactive materials in biosolids: National survey, dose modeling, and publicly owned treatment works (POTW) guidance", *Journal of Environmental Quality*, 34:1, 64-74.
99. **Chiu WA**, Fan XH, Ostriker JP. 2003, "Combining Wilkinson Microwave Anisotropy Probe and Sloan Digital Sky Survey quasar data on reionization constrains cosmological parameters and star formation efficiency", *Astrophysical Journal*, 599:2, 759-772.
100. **Chiu WA**, Gnedin NY, Ostriker JP. 2001, "The expected mass function for low-mass galaxies in a cold dark matter cosmology: Is there a problem?", *Astrophysical Journal*, 563:1, 21-27.
101. **Chiu WA**, Ostriker JP. 2000, "A semianalytic model for cosmological reheating and reionization due to the gravitational collapse of structure", *Astrophysical Journal*, 534:2, 507-532.
102. **Chiu WA**, Hassenzahl DM, Kammen DM. 1999, "A comparison of regulatory implications of traditional and exact two-stage dose-response models", *Risk Analysis*, 19:1, 15-22.
103. **Chiu WA**, Ostriker JP, Strauss, MA. 1998, "Using cluster abundances and peculiar velocities to test the Gaussianity of the cosmological density field", *Astrophysical Journal*, 494:2, 479-490.
104. Grady CA, Bruhweiler FC, Cheng KP, **Chiu WA**, Kondo Y. 1991, "The Circumstellar Disks of Beta-Pictoris Analogs", *Astrophysical Journal*, 367:1, 296-301.
105. Bruhweiler FC, Grady CA, **Chiu WA**. 1989, "Highly Ionized Species and Circumstellar Shells in B8-A1 Stars", *Astrophysical Journal*, 340:2, 1038-1048.

Book Chapters

1. Krishnan K, McPhail, B, **Chiu W,** White P. Modeling of Sensitive Subpopulations and Interindividual Variability in Pharmacokinetics for Health Risk Assessments, in *Computational Toxicology: Methods and Applications for Risk Assessment,* ed. B.A. Fowler, New York: Elsevier. 2013.
2. **Chiu WA**. Statistical Issues in Physiologically Based Pharmacokinetic Modeling, in *Toxicokinetics and Risk Assessment,* ed. J. C. Lipscomb and E. V. Ohanian, New York: Informa Healthcare, Inc. 2006.

3. **Chiu WA**, Wolbarst AB. Radiation Uses and Protection, in *Environmental Engineering and Sanitation*, 5th edition, ed. J. Salvato, N. Nemerow, and F. Agardy, New York: John Wiley & Sons, Inc. 2003.

U.S. Government Reports

1. U.S. EPA. 2014. *Toxicological review of Vanadium Pentoxide (V2O5) (CASRN 1314-62-1) in support of summary information on the Integrated Risk Information System (IRIS): Final Agency Review/Interagency Science Discussion draft.* U.S. EPA, Washington, DC, EPA/635/R-11/004D.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
2. U.S. EPA. 2014. *Scoping and Problem Formulation for the Identification of Potential Health Hazards for the Integrated Risk Information System (IRIS) Toxicological Review of Naphthalene (CASRN 91-20-3).* U.S. EPA, Washington, DC, EPA/635/R-14/199.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
3. U.S. EPA. 2014. *Preliminary Materials for the Integrated Risk Information System (IRIS) Toxicological Review of Hexavalent Chromium Part 1: Experimental Animal Studies (CASRN 18540-29-9).* U.S. EPA, Washington, DC, EPA/635/R-14/094.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
4. U.S. EPA. 2014. *Draft Development Materials for the Integrated Risk Information System (IRIS) Toxicological Review of Inorganic Arsenic [CASRN 7440-38-2].* U.S. EPA, Washington, DC, EPA/635/R-14/101.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
5. U.S. EPA. 2013. *Preliminary Materials for the Integrated Risk Information System (IRIS) Toxicological Review of Ethyl tert-Butyl Ether (ETBE) (CASRN 637-92-3).* U.S. EPA, Washington, DC, EPA/635/R-13/108.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
6. U.S. EPA. 2013. *Preliminary Materials for the Integrated Risk Information System (IRIS) Toxicological Review of tert-Butyl Alcohol (tert-Butanol) (CASRN 75-65-0).* U.S. EPA, Washington, DC, EPA/635/R-13/107.
    - Supervisor, providing mentorship, direction, and training to staff scientists.
7. U.S. EPA. 2012. *Toxicological review of Tetrachloroethylene (Perchloroethylene) (CASRN 127-18-4) in support of summary information on the Integrated Risk Information System (IRIS).* U.S. EPA, Washington, DC, EPA/635/R-08/011F.
    - Lead scientist, toxicokinetics and physiologically-based pharmacokinetic modeling.
    - Contributing scientist, dose-response modeling.
8. U.S. EPA. 2011. *Toxicological review of Trichloroethylene (CASRN 79-01-6) in support of summary information on the Integrated Risk Information System (IRIS).* U.S. EPA, Washington, DC, EPA/635/R-09/011F.
    - Overall project lead (2003-completion).
    - Lead scientist, physiologically-based pharmacokinetic modeling.
    - Lead scientist, quantitative uncertainty analysis.
    - Contributing scientist, carcinogenicity, liver toxicity, kidney toxicity, and mode/mechanism-of-action, dose-response modeling.
9. U.S. EPA. 2009. *An Approach to Using Toxicogenomic Data in U.S. EPA Human Health Risk Assessments: A Dibutyl Phthalate Case Study.* U.S. EPA, Washington, DC, EPA/600/R-09/028F.
    - Contributing scientist, toxicokinetics.
10. U.S. EPA. 2006. *Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment.* U.S. EPA, Washington, DC, EPA/600/R-05/043F.
    - Lead scientist, uncertainty and variability analysis.
    - Lead scientist, model evaluation.
11. U.S. EPA. 2005. TCE Issue Paper 1: Issues in Trichloroethylene Pharmacokinetics. U.S. EPA, Washington, DC, EPA/600/R-05/022.

- Team leader
- Lead scientist.

12. U.S. EPA. 2005. TCE Issue Paper 2: Interactions of Trichloroethylene, Its Metabolites, and Other Chemical Exposures. U.S. EPA, Washington, DC, EPA/600/R-05/023.
    - Team leader.
13. U.S. EPA. 2005. TCE Issue Paper 3: Role of Peroxisome Proliferator-Activated Receptor Agonism and Cell Signaling in Trichloroethylene Toxicity. U.S. EPA, Washington, DC, EPA/600/R-05/024.
    - Team leader.
14. U.S. EPA. 2005. TCE Issue Paper 4: Issues in Trichloroethylene Cancer Epidemiology. U.S. EPA, Washington, DC, EPA/600/R-05/025.
    - Team leader.
15. U.S. EPA. 2003. *A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information*. Science Policy Council, Washington, DC, EPA/100/B-03/001.
    - Contributing scientist.
16. Interagency Steering Committee on Radiation Standards. 2005. *Assessment of Radioactivity in Sewage Sludge: Recommendations on Management of Radioactive Materials in Sewage Sludge and Ash at Publicly Owned Treatment Works.* U.S. Department of Energy, Washington DC, DOE/EH-0668; EPA 832-R-03-002B.
    - Lead scientist, uncertainty analysis.
    - Contributing scientist, dose-modeling.
17. Interagency Steering Committee on Radiation Standards. 2004. *Assessment of Radioactivity in Sewage Sludge: Modeling to Assess Radiation Doses.* Nuclear Regulatory Commission, Washington DC, NUREG-1783; EPA 832-R-03-002A; DOE/EH-0670EPA-832/R-03/002A.
    - Lead scientist, uncertainty analysis.
    - Contributing scientist, dose-modeling.

International Agency Publications and Reports

1. Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Vilahur N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of benzene. Lancet Oncol. 2017 Dec;18(12):1574-1575. doi: 10.1016/S1470-2045(17)30832-X. Epub 2017 Oct 26. PubMed PMID: 29107678.
    - Member of Working Group.
    - Chair of subgroup on Mechanisms of Carcinogenicity.
2. Chiu WA. Chemical risk assessment and translation to socio-economic assessments. OECD Environment Working Papers. 2017 March 14; (117). http://dx.doi.org/10.1787/a930054b-en
3. Guyton K, Loomis D, Grosse Y, El Ghissasi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group, IARC, Lyon, France. 2016. "Carcinogenicity of pentachlorophenol and some related compounds." Lancet Oncol. 17(12):1637-8. doi: 10.1016/S1470-2045(16)30513-7.
    - Overall Chair of Working Group.
    - Member of subgroup on Mechanisms of Carcinogenicity.
4. Loomis D, Guyton K, Grosse Y, El Ghissasi F, Bouvard V, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K; International Agency for Research on Cancer Monograph Working Group. 2015. Carcinogenicity of lindane, DDT, and 2,4-dichlorophenoxyacetic acid. Lancet Oncol. 16(8):891-2. doi: 10.1016/S1470-2045(15)00081-9.
    - Member of Working Group.
    - Chair of subgroup on Mechanisms of Carcinogenicity.
5. WHO/IPCS. 2014. Guidance Document on Evaluating and Expressing Uncertainty in Hazard Characterization. World Health Organization, Geneva, IPCS Harmonization Project Document No. 11.
    - Lead author.

6. Benbrahim-Tallaa L, Lauby-Secretan B, Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Bouvard V, Guha N, Mattock H, Straif K, on behalf of the International Agency for Research on Cancer Monograph Working Group. 2014. Carcinogenicity of perfluorooctanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone. The Lancet Oncology, 15(9): 924-925. DOI: 10.1016/S1470-2045(14)70316-X
    - Member of Working Group.
    - Chair of subgroup on Mechanisms of Carcinogenicity.
7. WHO/IARC. 2014. Trichloroethylene, Tetrachloroethylene, and Some Other Chlorinated Agents. IARC Monogr Eval Carcinog Risk Chem Hum, 106: 1-514.
    - Member of Working Group.
8. Guha N, Loomis D, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Benbrahim-Tallaa L, Baan R, Mattock H, Straif K, on behalf of the International Agency for Research on Cancer Monograph Working Group. 2012. Carcinogenicity of trichloroethylene, tetrachloroethylene, some other chlorinated solvents, and their metabolites. The Lancet Oncology, 13(12): 1192-1193. DOI: 10.1016/S1470-2045(12)70485-0
    - Member of Working Group.
9. WHO/IPCS. 2010. Characterization and application of physiologically based pharmacokinetic models in risk assessment. World Health Organization, Geneva, IPCS Harmonization Project Document No. 9.
    - Workshop participant.

Other Published Articles (e.g., non-peer-reviewed letters)

1. Rusyn I, **Chiu WA**, Wright FA. Questioning existing cancer hazard evaluation standards in the name of statistics. Toxicol Sci. 2020 May 27:kfaa077. doi: 10.1093/toxsci/kfaa077. Online ahead of print. PMID: 32462183
2. **Chiu WA**; Chen C; Hogan K; Lipscomb JC; Scott CS; Subramaniam R, 2007, "High-to-low dose extrapolation: Issues and approaches," *Human and Ecological Risk Assessment,* 13:1, 46-51.
3. **Chiu WA**, White P. 2006, "Steady-state solutions to PBPK models and their applications to risk assessment I: Route-to-route extrapolation of volatile chemicals - Authors' response to letter by Dr. Kenneth Bogen", *Risk Analysis*, 26:6, 1417-1418.
4. Cox LA, **Chiu WA**, Kammen DM. 2000, "Low dose responses - Response", *Risk Analysis*, 20:3, 298-299.
5. Caldwell JC, Evans MV, Marcus AH, Scott CS, **Chiu WA**, Okino MS, Preuss PW. 2006, "Comments on article "Applying mode-of-action and pharmacokinetic considerations in contemporary cancer risk assessments: An example with trichloroethylene" by Clewell and Andersen", *Critical Reviews in Toxicology*, 36:3, 291-294.

Other Abstracts, Posters, and Presentations (representative examples)

Chiu WA, Ouyang O, Dalaijamts C, Axelrad DA, Dockins C, Paoli G. Broad Application Of A Probabilistic Dose-response Framework To Improve Chemical Risk Assessment. Society of Toxicology annual meeting, March 2018.

Dalaijamts C, Cichocki JA, Luo YS, Rusyn I, Chiu WA. Physiologically Based Pharmacokinetic (PBPK) Modeling of Interstrain Variability In Perchloroethylene Metabolism In Mice Society for Risk Analysis annual meeting, December 2017.

Hsieh NH, Reisfeld B, Bois FY, Chiu WA. Applying A Global Sensitivity Analysis Workflow to Improve Computational Efficiency in Physiologically-Based Pharmacokinetic Model. Society for Risk Analysis annual meeting, December 2017.

Cichocki JA,. Furuya S, Pogribny I, **Chiu W**, Threadgill W, Rusyn I. 2017. Non-Alcoholic Fatty Liver Disease as a Modifier of Perchloroethylene-Induced Toxicity. Society of Toxicology annual meeting, March 2017.

Grimm FA, **Chiu W**, Hsieh NH, Dalaijamts C, Burnett S, Anson B, Wright A, Wright F, Rusyn I. 2017.. Organotypic Human In Vitro Model for Cardiotoxicity Testing. Society of Toxicology annual meeting, March 2017.

Chiu WA. 2016. Next Generation Human Health Decision-Making Incorporating Population and Inter-individual Variability. Society for Risk Analysis meeting, December 2016.

Chiu WA, Guyton KZ, Martin MT, Reif DM, Rusyn, I. 2016. Use of high throughput screening data in IARC monograph evaluations. International Agency for Research on Cancer, 50th Anniversary meeting, June 2016.

Chiu WA. 2016. Probabilistic dose-response assessment: Basic principles and general approach developed by the WHO/IPCS. Society of Toxicology meeting, March 2016.

Rusyn I, **Chiu WA**, Guyton KZ, Martin M, Reif D. 2016. Use of high throughput screening data in International Agency for Research on Cancer (IARC) monograph evaluations. Society of Toxicology meeting, March 2016.

Cichocki JA, Furuya S, Chappell G, Venkatratnam A, Sweet S, Wade T, Knap A, McDonald T, **Chiu WA**, Threadgill D, Rusyn I. 2016. Inter-individual variability in the relationship between toxicokinetics and toxicodynamics of tetrachloroethylene. Society of Toxicology meeting, March 2016.

Venkatrtnam A, Furuya S, Kosyl O., Soldatow V, Sweet S, Wade T, Knap A, Gold A, Bodnar W, **Chiu WA**, Rusyn I. Using the Collaborative Cross mouse model to investigate population-level variability in trichloroethylene toxicity. Society of Toxicology meeting, March 2016.

Herzler M, **Chiu WA**, Slob W. 2016. New WHO Guidance on Uncertainty in Hazard Characterization: A Unified Tiered Approach Integrating Deterministic and Probabilistic Methods. German Pharm-Tox Summit (3/1-3/2/2016).

Chiu WA. 2015. Probabilistic dose-response assessment: Basic principles and general approach developed by the WHO/IPCS. Society for Risk Analysis Annual Meeting.

Chiu WA. 2015. Practical integration of old and new evidence streams with a harmonized dose-response assessment tool developed by WHO/IPCS. Society for Risk Analysis Annual Meeting.

Chiu WA. 2015. Evaluating and Expressing Uncertainty in Dose-Response Assessment: A New WHO/IPCS Guidance Incorporating Probabilistic Approaches. Society of Toxicology Annual Meeting.

Salazar K, Lee J, **Chiu WA**, Brinkerhoff C. 2015. Application of a rat PBPK model to elucidate kidney effects induced by ETBE and tert-butanol. Society of Toxicology Annual Meeting.

Cichocki J, Yoo HS, Benkatratunam A, **Chiu WA**, Rusyn I, Kim S, Kosyk O, Bodnar W, Sweet S, Wade T, Knapp A, Campbell J, Clewell H, Melnyk S. 2015. The Role of Peroxisome Proliferator-Activated Receptor-Alpha in the Relationship between Trichloroethylene toxicokinetics and toxicodynamics. Society of Toxicology Annual Meeting.

Flowers L, Cogliano V, **Chiu WA,** Hogan K, Bussard D, Birchfield N. 2015. Characterizing Uncertainty in Human Health Risk Assessment: An Agency Perspective. Society of Toxicology Annual Meeting.

Shao K, Allen BC, Farrar D, **Chiu WA,** Cowden J, Gift JS. 2014. Bayesian probabilistic dose-response analysis using epidemiologic data. Society for Risk Analysis Annual Meeting.

Zeise L, Bois FY, **Chiu WA,** Hattis D, Rusyn I, Guyton KZ. 2014. Addressing human variability in human health risk assessments of environmental chemicals using emerging data streams. Society for Risk Analysis Annual Meeting.

Gibbons CF, Caldwell JC, **Chiu WA**, DeMarini D, Fritz J. 2014. A Systematic Approach to Organizing Mechanistic Data for Risk Assessment by Linking Endpoints With Informative Mechanistic Characteristics of Carcinogenesis. Environmental Mutagenesis and Genomics Society Annual Meeting.

Wignall JA, Shapiro AJ, Wright FA, Woodruff TJ, **Chiu WA**, Guyton KZ, Rusyn I. 2014. "Standardized Benchmark Dose Calculation: Opportunities to Inform Science-Based Decisions in Human Health Assessments." Society of Toxicology Annual Meeting.

Keshava C, Zaccaria K, Adams J, Carlson-Lynch H, McClure P, Melia J, **Chiu WA**. 2014. "Development of a database tool to track the study selection for hazard identification: Naphthalene case study." Society of Toxicology Annual Meeting.

Hattis D, **Chiu WA**. 2012. Maternal cigarette smoking and human birth weight: patterns of change, risks of associated outcomes, and implications for environmental chemicals. American Public Health Association Annual Meeting.

Crump KS, **Chiu WA**, Subramaniam RP, 2010. Issues in Using Human Variability Distributions to Estimate Low-dose Risk. Society of Toxicology Annual Meeting.

Chiu WA, Bale AS, Barone, Jr. S, Brown RC, Caldwell JC, Cooper GS, Evans MV, Fox J, Guyton KZ, Gwinn M, Jinot J, Keshava N, Lipscomb J, Makris S, Schaum J, Scott CS. 2009. Key Aspects of U.S. EPA's External Review Draft Toxicological Review of Trichloroethylene. Society for Risk Analysis Annual Meeting.

Crump KS, Chen C, **Chiu WA**, Louis TA, Portier CJ, Subramaniam RP, White P. 2009. Major Challenges to Biologically-Based Dose-Response Modeling for Estimating Low-Dose Human Risk using Molecular Toxicology Data. National Research Council Symposium on Toxicity Pathway-based Risk Assessment: Preparing for Paradigm Change.

Crump KS, **Chiu WA**, Subramaniam RP. 2009. Issues in Using Human Variability Distributions to Estimate Low Dose Risk. National Research Council Symposium on Toxicity Pathway-based Risk Assessment: Preparing for Paradigm Change.

Chiu WA, Crump KS. 2009. Issues in Using Human Variability Distributions to Estimate Low Dose Risk. Society of Toxicology Annual Meeting.

White P, **Chiu WA**, Bale AS, Barone, Jr. S, Brown RC, Caldwell JC, Cooper GS, Evans MV, Fox J, Guyton KZ, Gwinn M, Jinot J, Keshava N, Lipscomb J, Makris S, Schaum J, Scott CS. 2009. Key Aspects of U.S. EPA's External Review Draft Toxicological Review of Trichloroethylene (TCE). Society of Toxicology Annual Meeting.

Curriculum Vitae

Helen M Goeden, Ph.D.
Health Risk Assessment Unit
Minnesota Department of Health
625 Robert Street N, PO Box 64975
Saint Paul, MN 55164-0975

Phone: 651-201-4904
helen.goeden@state.mn.us

WORK EXPERIENCE:

Principal Toxicologist – Minnesota Department of Health (MDH)
(Epidemiologist-Principal – Toxicology, 4/2011 to present)
(Research Scientist 3, 12/2001 to 4/2011)

Senior toxicologist and human health risk researcher for the Health Risk Assessment Unit. Lead MDH's effort to update and promulgate methods for deriving human health-based drinking water guidance. Assisted in creation of MDH's Drinking Water Contaminants of Emerging Concern program. Responsibilities include: leadership role in the development, improvement and integration of risk assessment methods and policies that are protective of sensitive or more highly exposed populations (e.g., infants and children); toxicological assessment of a wide range of environmental contaminants (e.g., industrial, agricultural, pharmaceutical, consumer product); development of state-wide health-based criteria for contaminants in groundwater and drinking water; and case-by-case health risk assessments or research projects specific to emerging environmental health threats (e.g., perfluorochemicals, alternative methods for providing risk context for chemicals with little or no toxicity data).

Toxicologist/Research Scientist 3 - Minnesota Pollution Control Agency
10/1992 to 12/2001

Senior toxicologist and risk assessor for environmental remediation and waste programs. Responsibilities included: development and implementation of multi-media, multi-duration human health risk assessment methodology, including development of procedures and guidance documents; mentoring of project staff to facilitate the utilization of risk assessment methods in site investigations and decisions; reviewing and evaluating scientific data on toxicity associated with toxicants; and coordinating health risk assessment activities within the remediation and waste programs as well as acting as liaison with interagency programs (e.g., Minnesota Department of Health).

Toxicologist/Manager - Health Risk Associate, Inc.
12/1986 to 10/1992

Managed, directed and coordinated staff in preparation of risk assessment reports. Directly supervised three staff and coordinated activities of student and contract researchers. Managed contracts with clients for risk assessment and toxicology services. Co-authored risk assessment

reports for clients. Specific responsibilities included assessment of potential environmental exposure to human populations; assessment of environmental fate of contaminants; and co-authored and presented scientific papers.

Specialist - University of California at Berkeley
2/1988 to 10/1992

Co-authored health assessment and criteria documents for the State of California Environmental Protection Agency (Cal-EPA). Critically reviewed and compiled scientific data, specifically dose-response and quantitative risk assessment. Additional responsibilities included management and coordination of staff in preparation and production of assessment documents and lectures to graduate students on the use of toxicological data in risk assessment.

Post-doctoral fellow - University of Calgary, Dept of Pharmacology
9/1985 to 11/1986

Initiated research within the Department of Pharmacology in the area of environmental toxicology. Obtained, managed and served as co-principal investigator for two major grants (totaling $204,000) to assess the health effects of low-level exposure to hydrogen sulfide. Specific responsibilities also included supervision of research technicians and design of inhalation exposure system.

Research Assistant - University of Cincinnati
1/1984 to 5/1985

Assisted in conducting general male reproductive screening tests for the Cincinnati U.S. Environmental Protection Agency. Supervised and coordinated human semen analyses for the University of Cincinnati occupational health clinic (as part of an occupational study), the infertility clinic, and the in vitro fertilization clinic. Supervised research lab with two staff and several student researchers.

EDUCATION:
University of Cincinnati, Cincinnati, Ohio
Ph.D., Environmental Health/Toxicology
June 1985

College of St. Scholastica, Duluth, MN
B.S., Biology
May 1980
Minor: Chemistry

PROFESSIONAL MEMBERSHIPS:

- Society of Toxicology
    - National member since 1986. Member of the National Risk Assessment Specialty Section.
    - Northland Regional Chapter member. Founding member of the Regional Chapter Education Committee. Councilor (May 1, 2010 to May 1, 2011), President (May 1, 2005 to May 2006) and President-Elect (May 1, 2004 to May 1, 2005). Significant accomplishments as President include:
        - Initiated feed-back survey of membership;
        - Facilitated effective drive to increase both local membership and membership participation in the activities of the Chapter; and
        - Coordinated effort to revise Chapter By-laws.
- Society for Risk Analysis - Member since 1986. Founding member of the National Dose-Response Specialty Section.

PROFESSIONAL COMMITTEES:

- EPA Chemical Assessment Advisory Committee (Dec 2012 to Dec 2015)
    - Trimethylbenzene SAB
    - Benzo[a]pyrene SAB
- NSF International Health Advisory Board (member 2011 to 2020, vice-chair 2018-2020)
- Federal State Toxicology and Risk Assessment Committee (FSTRAC) (2001 to present) Member of annual meeting planning subcommittee (2003 to 2019)
- Water Quality Association Toxicological Review Committee (2007 to 2011)

VOLUNTEER EXPERIENCE:

- Nativity Episcopal Church Community Outreach Team co-lead (2014 – 2020)
- Second Harvest Heartland Volunteer. (2013-present)
- Read Aloud Literacy Volunteer. (1994 to present)
- Dakota County Wetland Health Evaluation Program Volunteer. (2000 to 2016)
- Open Your Heart to the Hungry and Homeless (2002 – 2004): served as an Executive Board Member as well as a member of the Education and Grant Auditing Committees.

SCIENTIFIC MEETING PRESENTATIONS:

"Derivation of Health-Protective Water Guidance for Bioaccumulative PFAS Chemicals Requires Incorporation of Placental and Breast Milk Exposure Pathways." (Invited presentation). Society of Toxicology Symposium - Developmental Toxicity of Per- and Polyfluoroalkyl Substances (PFAS): Current In Vivo Approaches and Application to Human Health Risk Assessment. March 2020.

"Embracing the elephant in the room: the critical role of breastmilk transfer as a major driver of PFOA, PFOS, and PFHxS water guidance." Society of Risk Analysis Annual Meeting, 2019. Also co-organizer of the Symposium – Derivation of Human Health Based Water Guidance for Noncarcinogens: Is it time to Change the Standard Default Approach?

"Novel methodology for deriving water screening values for pharmaceuticals and application for contextualizing potential human health risk of ambient detections." Society of Risk Analysis Annual Meeting, 2019. Also co-organizer of the Symposium – Derivation of Human Health Based Water Guidance: Challenges of Assessing Emerging Contaminants and Mixtures.

"The Persistent Challenge of PFAS: Minnesota's 17 Year Journey". (Invited presentation) Texas A&M University Interdisciplinary Faculty of Toxicology Training Program 2019 Annual Regulatory Science Symposium. The Sticky Subject of Non-Stick: Regulatory Science Challenges of Per- and Poly-Fluorinated Compounds (PFAS). August 2019.

"Recent updates to Minnesota drinking water guidelines for PFOS and PFOA – Incorporation of an Excel-based Model to Address Indirect Exposure Pathways". (Invited presentation) Toxicology and Risk Assessment Conference, April 2018.

"Application of an Excel-based Toxicokinetic Model for Deriving Health-based Water Guidance for PFOS and PFOA". (Poster presentation) Society for Risk Analysis Annual Meeting, December 2017.

"Screening level benchmarks – providing risk-based prioritization for environmental contaminants with minimal toxicity data". (Platform presentation and session co-chair). Society of Environmental Toxicology and Chemistry, November 2017.

"Incorporating Indirect Exposure Pathways – Derivation of Health-based Water Guidance for PFOA and PFOS Using an Excel-based Toxicokinetic Model". (Platform presentation and session co-chair). Society of Environmental Toxicology and Chemistry, November 2017.

"Incorporation of Early-Life Exposure Using a Simplified Toxicokinetic Model in the Derivation of Health-Based Water Guidance for PFOA and PFOS". (Poster presentation) Society of Toxicology Annual Meeting, March 2017.

"Providing Risk Context for Environmental Contaminants with Minimal Toxicity Data". (Poster presentation) Society of Toxicology Annual Meeting, March 2017.

"Chronically underestimated: The impact of high early life water intake rates and short-term effects for deriving health-protective drinking water criteria". Invited speaker. US EPA Temporal Exposure Issues for Environmental Pollutants: Health Effects and Methodologies for Estimating Risk Workshop. January 27-29, 2016.

"Evaluating and Providing Risk Context for Water Contaminants with Minimal or No Toxicity Data". (Poster presentation) Society of Toxicology Annual Meeting, March 22-26, 2015.

"Incorporating Multiple Duration Assessments into Derivation of Drinking Water Guidance". (Poster presentation) Society of Toxicology Annual Meeting, March 14, 2012.

"Implementing Body Weight Scaling as a Default Approach for Deriving Oral Reference Doses". (Poster presentation) Society of Toxicology Annual Meeting, March 14, 2012.

Session organizer, facilitator and presenter for "Advancing Risk Assessment: New Toxicity Evaluation Methods". Federal State Toxicology and Risk Assessment Committee (FSTRAC) Annual Meeting, Helena, MT. Oct. 3-5, 2011.

"Incorporating Multiple Duration and Human Equivalent Dose Methodology – Derivation of Drinking Water Guidance". Federal State Toxicology and Risk Assessment Committee (FSTRAC) Annual Meeting, Helena, MT. Oct. 3-5, 2011.

"Insufficient Data? Assessment of Alternative Risk-based Methods". Federal State Toxicology and Risk Assessment Committee (FSTRAC) Annual Meeting, Helena, MT. Oct. 3-5, 2011.

"Advancing the Next Generation (NexGen) of Risk Assessment: The Prototypes." Invited commenter and workshop participant. Research Triangle Park, NC. November 1-3, 2010.

Session organizer and facilitator for "NRC Recommendations on Advancing Risk Assessment and New Challenges Ahead" and "Interpreting Dose Response Data for Hormonally Active Chemicals". FSTRAC Annual Meeting, Arlington, VA. Oct. 13-15, 2010.

"Overview and Current Activities of Minnesota's Contaminants of Emerging Concern Program". FSTRAC invited speaker. Arlington, VA. Oct. 13-15, 2010.

"Derivation of Health Based Criteria for Perfluorobutyric Acid (PFBA), Perfluoroctanoic Acid (PFOA), Perfluorobutane Sulfonate (PFBS), and Perfluorooctanoic Acid (PFOA)". EPA PFAA Days III Workshop (poster presentation). June 8-10, 2010.

"Use of Early-Life Stage Cancer Potency Adjustments in Minnesota Groundwater Rules." Invited speaker for: "Life-Stage Adjustment Five Years Later; Experiences from the Cancer Risk Assessment Field" session. Annual Society of Toxicology Meeting. Salt Lake City, UT. March 2010.

"Governmental Risk Assessment – Regulatory Perspective. How to implement this new thinking?" Invited panelist for Moving Upstream: Thyroid meeting. Oakland, CA. Nov 16 - 17, 2009.

"Health-based Guidance for PFBA, PFOA, PFBS, PFHxS and PFOS". Invited speaker for Federal State Toxicology and Risk Assessment Committee (FSTRAC). Princeton, NJ. Oct. 21-23, 2009.

"Issues and Needs for PFAA Exposure and Health Research: A State Perspective". Invited speaker for EPA PFAA Days II Workshop. June 3 – 4, 2008.

"Derivation of Health Based Criteria for Perfluorobutyric Acid (PFBA) and Perfluorooctanoic Acid (PFOA)". EPA PFAA Days II Workshop (poster presentation). June 3-4, 2008.

"Integration of Life-stage and Exposure Duration Assessments into Derivation of Standards". Society of Toxicology Annual Meeting (poster presentation), March 18, 2008.

"Perfluorochemicals in Minnesota - Derivation of Health Protective Criteria". Federal-State Toxicology Risk Analysis Committee (FSTRAC) Annual Fall Meeting, October 18, 2007. Session moderator and invited speaker.

"Use of Multiple Intake Rates in the Derivation of Groundwater Standards". International Society of Exposure Analysis (ISEA) Annual Meeting. October 17, 2007. Invited speaker.

"Minnesota's Proposed Approach for Addressing Children's Risks in Setting Drinking Water Criteria". Invited Speaker, Society of Risk Analysis – Northeast Regional Chapter. June 19, 2007.

"Perfluorochemicals in Minnesota - Environmental Occurrence and Exposure". FSTRAC Annual Fall Meeting, Dec 2006. Session moderator and invited speaker.

"Incorporation of a Multi-duration RfD Matrix into Drinking Water Criteria Development". FSTRAC Annual Fall Meeting, Dec 2006. Session moderator and invited speaker.

"Minnesota's Health Risk Limits for Groundwater Rule Revision Effort". Society for Risk Analysis Annual Meeting (poster presentation). Dec 3-6, 2006.

"Minnesota's Proposed Approach for Addressing Children's Risks in Setting Drinking Water Criteria". Association of State and Territorial Health Officials (ASTHO) Web cast Seminar. April 25, 2006.

"Are Chronic RfDs Really Chronic?" Society of Toxicology Annual Meeting (poster presentation). March 5-9, 2006.

"What is Chronic?" FSTRAC Annual Fall Meeting, October 19-21, 2005

"Minimum Data Requirement for Derivation of RfDs for Pesticide Degradates". FSTRAC Fall Meeting, October 2004. Session moderator and invited speaker.

"Development of Groundwater Criteria – Addressing Children's Cancer Risk". FSTRAC Fall Meeting, October 2002

"Is The Chronic Exposure Default Approach Protective of Short-term Exposure?" FSTRAC Spring Biannual Meeting May 2000,

"Public Health Risk Assessment: A New Tool for Risk Management of Hazardous Chemicals". Society for Risk Analysis Annual Meeting, 1992.

"Risk of Lung Cancer Due to Airborne Nickel Exposure". Society of Toxicology Annual Meeting 1992.

"Screening Method for Estimation of Potential Fish and Shellfish Contamination from Metals". Society of Toxicology Annual Meeting 1991

"Use of Background Levels in Estimating Potential Fish and Shellfish Contamination from Metal Emissions". Society for Risk Analysis Annual Meeting 1989.

"A Method for Estimation of Fish Contamination from Dioxins and Furans Emitted by Resource Recovery Facilities". Society for Risk Analysis Annual Meeting 1987.

PUBLICATIONS:

Government Reports –

Principal author. Minnesota Department of Health, Background Document: Toxicokinetic Model for Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) and Its Use in the Derivation of Human Health-Based Water Guidance Values. May 2017.

Principal author. Minnesota Department of Health, the Use of Human Equivalent Dose (HED) Calculations to Derive Oral Reference Doses. May 2011.
https://www.health.state.mn.us/communities/environment/risk/docs/guidance/hedrefguide.pdf

Principal author. Minnesota Department of Health, Risk Assessment Advice for Incorporating Early-Life Sensitivity into Cancer Risk Assessments for Linear Carcinogens. July 2010.
https://www.health.state.mn.us/communities/environment/risk/docs/guidance/adafrecmd.pdf

Co-author. Minnesota Department of Health Statement of Need and Reasonableness (technical support document) for the Health Risk Limit Rule for Groundwater (2008).
https://www.health.state.mn.us/communities/environment/risk/docs/rules/hrlsonar08.pdf

Co-author. Minnesota Department of Health, Health Risk Limits for Perfluorochemicals: Report to the Minnesota Legislature (2008).
http://www.health.state.mn.us/divs/eh/hazardous/topics/pfcs/finalreport011508.pdf

Principal author. Minnesota Department of Health, Facts about Dioxins (updated Oct. 2006, https://www.health.state.mn.us/communities/environment/risk/docs/guidance/adafrecmd.pdf), Development of an Inhalation Benchmark for Dioxin-like Compounds (March 2004, https://www.health.state.mn.us/communities/environment/risk/docs/guidance/air/dioxins.pdf) and Methods for Estimating the Carcinogenic Health Risks from Dioxin-like Compounds (update June 2009, https://www.health.state.mn.us/communities/environment/risk/docs/guidance/dioxinmemo1.pdf)

Co-author. Minnesota Pollution Control Agency Remediation Program Risk-based Site Evaluation Fact Sheets and Guidance Documents (1998).

Author. Minnesota Pollution Control Agency Remediation Program Risk-based Site Evaluation Guidance for Soil – Human Health Pathway and Technical Support Document for the Development of Soil Reference Values (SRVs) (1998).

Numerous screening and limited site-specific baseline risk assessments.

Journal and Book Publications –

1. Scher D, Goeden H, and Klos, K. Potential for manganese-induced neurologic harm to formula-fed infants: A risk assessment of total oral exposure. Submitted and under review at Environmental Health Perspectives.

2. Goeden, H. M., Greene, C. W., & Jacobus, J. A. (2019). A transgenerational toxicokinetic model and its use in derivation of Minnesota PFOA water guidance. Journal of Exposure Science & Environmental Epidemiology. https://doi.org/10.1038/s41370-018-0110-5

3. Suchomel A, Goeden H, and Dady J. A Method for Developing Rapid Screening Values for Active Pharmaceutical Ingredients (APIs) in Water and Results of Initial Application for 119 APIs. International Journal of Environmental Research and Public Health. 15(3) 1308; doi:10.3390/ijerph15071308, 2018. Open Access Available at: http://www.mdpi.com/1660-4601/15/7/1308

4. Goeden, H. Focus on Chronic Exposure for Deriving Drinking Water Guidance Underestimates Potential Risk to Infants. International Journal of Environmental Research and Public Health. 15(3) 512; doi:10.3390/ijerph15030512, 2018. Open Access Available at: http://www.mdpi.com/1660-4601/15/3/512

5. Smith AH, Sciortino S, Goeden H, and Wright CC. Consideration of Background Exposures in the Management of Hazardous Waste Sites: A New Approach to Risk Assessment. Risk Anal Oct; 16(5)619-625, 1996.

6. Hopenhayn-Rich C, Smith AH, and Goeden H. Human Studies Do Not Support the Methylation Threshold Hypothesis for the Toxicity of Inorganic Arsenic. Environ Res 60:161-177, 1993.

7. Smith AH, Hopenhayn-Rich C, Bates MN, Goeden H, Hertz-Picciotto I, Duggan HM, Wood R, Smith MT, and Kosnett MJ. Cancer Risks from Arsenic in Drinking Water. Environ Health Perspect 97:259-267, 1992.

8. Smith AH and Goeden HM. Health Risk Assessment of Incinerator Air Emissions Incorporating Background Ambient Air Data. J Combust Science and Tech 74:51-61, 1990.

9. Hayden LJ, Goeden H, and Roth SH. Exposure to low levels of hydrogen sulfide elevates circulating glucose in maternal rats. J Toxicol Indust Hlth 31:27-34, 1990

10. Hayden LJ, Goeden H, and Roth SH. Growth and development in the rat during sub-chronic exposure to low levels of hydrogen sulfide. J Toxicol Indust Hlth 6(3-4): 389-401, 1990.

11. Goeden HM and Smith AH. A method for estimation of fish contamination from dioxins and furans emitted by resource recovery facilities. In: Advances in Risk Analysis Series Vol. 7. Risk Assessment in Setting National Priorities. Eds: JJ Bonin and DE Stevenson. Plenum Press, New York, 1989.

12. Smith AH, Goeden H, and Frisch J. The importance of the hazard identification phase of health risk assessments illustrated with antimony emissions from waste incineration facilities. In: Advances in Risk Analysis Series Vol. 7 - Risk Assessment in Setting National Priorities. Eds: JJ Bonin and DE Stevenson. Plenum Press, New York, 1989.

13. Goeden HM and Smith H. Estimation of Human Exposure from Fish Contaminated with Dioxins and Furans Emitted by a Resource Recovery Facility. Risk Analysis 9(3)377-383, 1989.

14. Hayden LJ, Goeden H, and Roth SH. Effects of exposure to low levels of hydrogen sulfide during gestation in developing and maternal rats. Proc. Can. Fed. Biol. Soc. 30:128, 1987.

15. Zenick H and Goeden H. Chapter 8 Evaluation of copulatory behavior and sperm in rats. Role in reproductive toxicity assessment. In: Physiology and Toxicology of Male Reproduction. Eds: JC Lamb IV and PMD Foster, pp 178-201, 1987.

16. Goeden H and Zenick H. Disposition of ethanol in blood and uterine fluid of estrous rats. Annual Meeting 1985, Society of Toxicology, Toxicologist 5(1): 186.

17. Goeden H and Zenick H. Influence of the uterine environment on rat sperm motility and swimming speed. J. Exp. Zool. 233:247-251, 1985.

18. Zenick H, Blackburn K, Hope E, Oudiz D and Goeden H. Evaluating male reproductive toxicity in rodents: a new animal model. Teratogen. Carcinogen. Mutagen. 4:109-128, 1984.

19. McKim JM and Goeden HM. A direct measure of the uptake efficiency of a xenobiotic chemical across the gills of brook trout (*Salvelinus fontinalis*) under normoxic and hypoxic conditions. Comp. Biochem. Physiol. 72 (Part C): 65-74, 1982.

Industry Health Assessment Documents and Reports –

1. Goeden H. Final Report - Evaluation of the Uptake/Biokinetic Model (Lead 4) and Its Application at the Marjol Battery Site. May 1992. HRA, 2030 Addison Street, Berkeley, CA 94704

2. Smith AH, Goeden H, and Bates M. Final Draft Health Risk Assessment for Diesel Exhaust Emissions. September 1991. Department of Biomedical & Environmental Health, University of California at Berkeley, Berkeley, CA 94720. Submitted to California EPA, Office of Environmental Health Hazard Assessment.

3. Goeden H amd Smith AH. Pre-remediation Exposure Assessment of the Former Plessey Microscience Site, 2274-2296 Mora Drive, Mountain View, CA. Volume II, Appendices A, J, and M. June 1991. HRA, 2030 Addison Street, Berkeley, CA 94704.

4. Smith AH, Goeden H, Wood R, Shearn V. Mann J, Frisch J, Allen H, and Hertz-Picciotto I. Health Risk Assessment for Nickel (Final). April 1991. Department of Biomedical & Environmental Health, University of California at Berkeley, Berkeley, CA 94720. Submitted to California Department of Health Services.

5. Smith AH and Goeden H. Responses to Public Comments on the Draft Health Risk Assessment for Nickel 1988. April 1991. Department of Biomedical & Environmental Health, University of California at Berkeley, Berkeley, CA 94720. Submitted to California Department of Health Services.

6. Smith AH, Goeden H, Wood R. Draft Health Risk Assessment for the Epping Recycling/Trash-to-Energy Facility July 1990. HRA, 2030 Addison Street, Berkeley, CA 94704.

7. Smith AH, Goeden H, Wood R. Draft Health Risk Assessment for the Babylon Resource Recovery Facility. April 1989. HRA, 2030 Addison Street, Berkeley, CA 94704.

8. Smith AH, Goeden H, Shearn V, Bates M, Allen H. Health Risk Assessment for Arsenic Ingestion. December 30, 1988. HRA, 2030 Addison Street, Berkeley, CA 94704.

9. Smith AH, Smith MT, Wood R, Goeden H. Health Risk Assessment for the Brooklyn Navy Yard Resource Recovery Facility. November 1988. HRA, 2030 Addison Street, Berkeley, CA 94704.

10. Smith AH, Goeden H, Wood R, Shearn V, Mann J, Frisch J. Health Risk Assessment for Nickel. July 24 1988. HRA, 2030 Addison Street, Berkeley, CA 94704.

11. Smith AH, Smith MT, Goeden H, Lopipero P. Health Risk Assessment concerning Airborne PCBs at the MGM Brakes Site. January 19, 1988. HRA, 2030 Addison Street, Berkeley, CA 94704.

12. Smith AH, Smith MT, Wood R, Goeden H, Coyle P, Chambers T, Wei ET. Health Risk Assessment of the Los Angeles City Energy Recovery (LANCER) Project. April 17, 1987. HRA, 2030 Addison Street, Berkeley, CA 94704.

AWARDS

Minnesota Public Health Association 2020 Harvey G. Rogers Environmental Health Leadership award.

Society of Risk Analysis 2019 Outstanding Practitioner award.

GRANTS

Occupational Health and Safety Heritage Grant Program. Co-principal investigator. A Multi-Disciplinary Assessment of the Effect of Chronic Low Doses of Hydrogen Sulfide.
6/86 - 5/87: $150,000.

Alberta Heritage Foundation for Medical Research Award. The Effects of Environmental Pollutants on the Developing Central Nervous System. 9/85-8/86: $26,000: renewal 9/86-8/87: $28,000.

March of Dimes Grant 15-59. Co-principal investigator: The Effects of Xenobiotics in Uterine Fluid on Sperm Integrity.
12/83-11/85: $6,000.

Dr Kerry W. Nugent

154 Forest Rd
Gymea Bay NSW 2227 Australia **+614 78 401 209 (Mob)**
kerry.nugent@industriachemicals.gov.au **+612 8577 8861 (W)**
kerry.nugent@iinet.net.au **+612 9526 5284 (H)**

Date Of Birth **29-7-59**
Sex **Male**
Nationality **Australian**

CAREER PROFILE

Qualified (PhD) in chemistry. Career change in 1998 turned focus to toxicology, and particularly to the role of chemistry in exposure pathways and toxicological responses. This led directly to the career highlight of development and scientific management of the NICNAS IMAP program, and involvement in international activities to increase the availability of risk based information on chemicals.

CAREER SUMMARY

Australian Industrial Chemicals Introduction Scheme (AICIS) (formerly National Industrial Chemicals Notification and Assessment Scheme (NICNAS)) 1998 - present

Principal Scientist (since 2011)

I am one of three Principal Scientists in AICIS. My area of responsibility has been the NICNAS Inventory Multitiered Assessment and Prioritisation (IMAP) program which was largely of my design, and its successor program under AICIS. When NICNAS was established in 1990, 38000 chemicals were designated "existing chemicals" without any assessment. In the next 20 years, around 200 of these were assessed. Under IMAP, 15000 have been assessed for human health risks in 7 years. I personally signed off on all these assessments, plus many more assessments of environmental risks.

IMAP achievements have twice been honoured with the Department of Health Australia Day Award.

Leader, Exposure Team

This involved improvement of NICNAS capacity to estimate exposure to industrial chemicals. During this time, I developed the framework to rapidly integrate hazard and exposure which became the key to IMAP.

Existing Chemicals Assessor

Focus was on a number of key groups of chemicals, including brominated flame retardants, and perfluorinated chemicals,

New Chemicals Assessor

During the period prior to being made permanent EL2 as a Principal Scientist, I aggregated several years Acting as team leader across New Chemicals, Compliance and Existing Chemicals.

University of Melbourne **1993 - 1998**

Senior Research Fellow, School of Physics
Research Fellow, School of Physics

University of Sydney **1986 - 1993**

Senior Professional Officer (School of Chemistry/Optical Fibre Technology Centre)
Research Fellow (School of Chemistry)
Half Time Tutor (School of Chemistry)

QUALIFICATIONS

BSc (Hons I)) Griffith (1981)

PhD Sydney (1988) in Inorganic Chemistry
My Ph.D. work involved handling a very toxic, air sensitive organometallic compound. This required extreme care, and the design of some specialised equipment and safety procedures.

REPRESENTATIONAL EXPERIENCE

Commonwealth Representative on TGA Advisory Committee on Chemical Scheduling (ACCS) (since 2016)
NICNAS standing observer to ACCS (2012-2016)

Member of organizing committee for the 2020 Annual Scientific Meeting of the Australian College of Toxicology and Risk Assessment (ACTRA), since postponed to 2021

Member of an international invited expert group on "Accelerating the Pace of Chemical Risk Assessment" since 2016

Invited expert at Helsinki Chemicals Forum 2019
Invited presentation to Health Canada 2016
Invited to expert group on "New Approach Methodologies in Chemical Risk Assessment" by European Chemicals Agency

Represented NICNAS at a number of international meetings under the Organisation for Economic Cooperation and Development, World Health Organisation and United Nations Environment Program.

SCIENTIFIC PUBLICATIONS

I have contributed as an author on 47 publications in the scientific literature, mostly in Inorganic Chemistry and Materials Science. My publications have also included other areas including environmental science, biological chemistry, marine biology and art history. Please see the list appended at the end of this document. This list is not indicative of my current work, however.

My regulatory toxicology work is published by NICNAS/AICIS, rather than individually. This has included assessment of around 200 New Chemicals and one major existing chemicals publication on polybrominated diphenyl ethers (PBDEs).

More recently, I have scientifically supervised and peer reviewed a very large number of both human health (around 900 assessments covering 4685 chemicals) and environment (70 reports with around 600 chemicals) summary risk assessments under the NICNAS IMAP program. A number of additional explanatory scientific papers on specific approaches to assessment were produced for publication on the NICNAS website.

List of Published Scientific Papers

"A Precise Low Temperature Crystal Structure of Bis(cyclopentadienyl)beryllium." K. W. Nugent, J. K. Beattie, T. W. Hambley and M. R. Snow. Aust. J. Chem. 1984, 37, 1601.

"Dynamics of Beryllocene (Bis(cyclopentadienyl)beryllium) Inversion by 13C nmr Spectroscopy." K. W. Nugent and J. K. Beattie. J. Chem. Soc., Chem. Commun. 1986, 186.

"Vapor-Phase Infrared Spectrum of Bis(cyclopentadienyl)beryllium." K. W. Nugent and J. K. Beattie. Inorg. Chem. 1988, 27, 4269.

"Molecular Inversion Dynamics of Bis(cyclopentadienyl)beryllium Inferred from Partially Relaxed Spin-Spin Coupling between Carbon-13 and Beryllium-9." K. W. Nugent, J. K. Beattie and L. D. Field. J. Phys. Chem. 1989, 93, 5371.

"Assignment of the Electronic Spectrum of Tris(μ-halo)bis(triammineruthenium(2+) ions Using Resonance Raman Spectroscopy." R. S. Armstrong, W. A. Horsfield and K. W. Nugent. Inorg. Chem. 1990, 29, 4551.

"Infrared and Raman Spectra of (η6-mesitylene)M(CO)3 complexes (M = Cr, Mo or W): an Insight into Metal-Arene Bonding." R. S. Armstrong, M. J. Aroney, C. M. Barnes and K. W. Nugent. Applied Organometallic Chemistry 1990, 29, 569.

"Beryllocene and Related Slip-Sandwich Structures" J. K. Beattie and K. W. Nugent, Inorg. Chim. Acta, 1992, 200, 309.

"Infrared and Raman Spectra of (6-C6H6-nXn)Cr(CO)3 Complexes Where X=Me, n=0-6 or X=OMe, n=0-2. A Study of Metal Ligand Interactions" R. S. Armstrong, M. J. Aroney,C. M. Barnes and K. W. Nugent, J. Mol. Struct, 1994, 323 15.

"Polarized Raman Spectroscopy Of Chemically Vapour Deposited Diamond Films" S. Prawer, K. W. Nugent and P. S. Weiser Appl. Phys. Lett., 1994 65 (18).

"Synthesis of Carbo-Nitride Films Using High-Energy Shock Plasma Deposition"V. N. Gurarie, A. V. Orlov, K. W. Nugent, P. S. Weiser and S. Prawer, Mat. Res. Soc. Symp. Proc. (1994), 349 37.

"Ion Beam Modification of Buckminsterfullerene" S. Prawer, K. W. Nugent, S. Biggs, D. McCulloch, W. H. Leong, A. Hoffmann and R. Kalish, Phys. Rev. B, (1995) 65 841.

"Confocal Raman Microscope Studies of Keratin Fibres" L. Jurdana, K. H. Ghiggino, K. W. Nugent and I. P. Leaver Textile Res. J. (1995) 65(10) 593

"Cross Sectional Raman Microscopy of MeV Ion Implanted Diamond" D. N. Jamieson, S. Prawer, K. W. Nugent and S. P. Dooley, Nucl. Instrum. Methods B (1995) 106, p641

"Realization of Si1-x-yGexCy Heterostructures by Pulsed Laser Induced Epitaxy of C+ Implanted Pseudomorphic SiGe Films and of a-SiGeC:H Films Deposited on Si(100)"J. Boulmer, A. Desmur-Larr□, C. Guedj, D. D□barre, P. Boucaud, F. H. Julien, E. Finkman, K. Nugent, R. Laval, J.-B. Ozenne, H. Yang, D. Bouchier, C. Godet, P. Roca I Cabarrocas, G. G. Calvarin and C. Clerc, SPIE Proceedings 2403, (1995) p362

"Realization of Si1-x-yGexCy Heterostructures by Pulsed Laser Induced Epitaxy of C+ Implanted Pseudomorphic SiGe Films and of a-SiGeC:H Films Deposited on Si(100)"J. Boulmer, P. Boucaud, C. Guedj, D. D□barre, D. Bouchier, E. Finkman, S. Prawer, K. Nugent, A. Desmur-Larr□, C. Godet and P. Roca I Cabarrocas, J. Cryst. Growth, 157 (1995), p436.

"Raman Spectroscopy of Si1-x-yGexCy Layers Obtained by Pulsed Laser Induced Epitaxy", E. Finkman, J. Boulmer, P. Boucard, C. Guedj, D. Bouchier, K. Nugent and S. Prawer, Appl. Surf. Sci., 3496 (1996).

"The Effect of Ion-Beam Induced Strain on the Nucleation Density of Diamond", P. S. Weiser, S. Prawer, K. W. Nugent, A. A. Bettiol, L. I. Kostidis, S. P. Dooley and D. N. Jamieson, Ion Beam Modification Of Materials, Elsevier (1996) p752

"Systematic Variation of the Raman Spectrum of DLC Films as a Function of sp2:sp3 Composition" S. Prawer, K. W. Nugent, Y. Lifshitz, G. D. Lempert, E. Grossman, J. Kulik, I. Avigal and R. Kalish, Diamont Relat. Mater., 5 (1996), p433.

"Homo-epitaxial Diamond Film Growth on Ion Implanted Diamond Substrates"P. S. Weiser, S. Prawer, K. W. Nugent, A. A. Bettiol, L. I. Kostidis and D. N. Jamieson, Diamond Relat. Mater. 5 (1996) p272.

"Diamond Film Quality: The Effects of the Gas Phase Species Concentrations on the Raman Spectrum" S. J. Harris, A. M. Weiner, S. Prawer and K. W. Nugent,J. Appl. Phys. 80 (1996) p2187.

"Radiation Damage Induced by MeV alpha-particles in Polycrystalline Diamond Films" P. Gonon, S. Prawer, K. W. Nugent and D. N. Jamieson, J. Appl. Phys., 80 (1996) p5006.

"The Rubredoxin from Clostridium Pasteurianum - Mutation of the Conserved Glycine Residues 10 and 43 to Alanine and Valine" Z. Ayhan, Z. G. Xiao, M. J. Lavery, A. M. Hamer, K. W. Nugent

S. D. B. Scrofani, M. Guss and A. G. Wedd, Inorg. Chem., 35 (1996) p5902.

"An X-ray Crystallographic Study of the Ruthenium Blue Complexes, [Ru2Cl3(tacn)2](PF6)2.4H2O, [Ru2Br3(tacn)2](PF6)2.2H2O and [Ru2I3(tacn)2](PF6)2 : Steric Interactions and the Ru-Ru 'Bond Length'" W. A. Clucas, R. S. Armstrong, I. E. Buys, T. W. Hambly and K. W. Nugent, Inorg. Chem., 35 (1996) p6789.

"Analyzing the Growth and Form of Mollusc Shell Layers, In situ, by Cathodoluminescence Microscopy and Raman Spectroscopy" G. P. Hawkes, R. W. Day, M. W. Wallace, K. W. Nugent, A. A. Bettiol, D. N. Jamieson and M. C. Williams, J. Shellfish Res., 15 (1996) p659.

"Raman Laser Microprobe Spectroscopy and the Analysis of Materials from Oil Paintings" L. Mathieson and K. W. Nugent, AICCM Bull., 21 (1996)

"Radiation hardness of polycrystalline diamond" P. Gonon, S. Prawer, D. N. Jamieson and K. W. Nugent, Diamond Relat. Mater., 6 (1997) p314.

"Chromium Luminescence as a Probe of Site Effects in the Alum Lattice" R. S. Armstrong, A. J. Berry, B. D. Cole and K. W. Nugent, J. Chem. Soc., Dalton Trans. 1997 p363.

"The Characterisation of High-grade Synthetic Quartz, Corundum and Spinel Using Ionoluminescence (IL)"A. A. Bettiol, K. W. Nugent and D. N. Jamieson, Nucl. Instrum. Methods. B 131 (1997) p1.

"Effects of Damage on Diffusion of Implanted Helium in Diamond Measured by Nuclear Elastic Scattering" J. O. Orwa, D. N. Jamieson, K. W. Nugent, S. Prawer and R. Kalish, Nucl. Instrm. Methods B 124 (1997) p515.

"Formation of Buried p-type Conducting Layers in Diamond" R. Walker, S. Prawer, D. N. Jamieson, K. W. Nugent and R. Kalish, Appl. Phys. Lett., 71 (1997) p1492.

"Mechanical Properties and Raman Spectra of Tetrahedral Amorphous Carbon Films With High sp3 Fraction Deposited Using a Filtered Cathodic Arc" Shi Xu, D. Flynn, B. K. Tay, S. Prawer, K. W. Nugent, S. R. P. Silva. Y. Lifschitz and W. I. Milne, Philos. Mag. B 76 (1997) p351.

"Confocal Raman Strain Mapping of Isolated Single CVD Diamond Crystals." K. W. Nugent and S. Prawer, Diamond Relat. Mater, 7 (1998) p215.

"The Raman Spectrum of Amorphous Diamond" S. Prawer, K. W. Nugent and D. N. Jamieson, Diamond Relat. Mater., 7 (1998) p106.

"Structural Diversity in Thallium Chemistry, III. The First Structurally Characterized Examples of the Pentabromothallate(III) Anion in the 1,1,4,4-tetramethylpiperazinium and N,N`-diethyltriethylenediammonium Salts Contrasted with the Mixed Anions in the 1,1,3,3-tetramethylimidazoidinium Salt."A. Linden, K. W. Nugent, A. Petridis and B. D. James, Inorg. Chim. Acta, 285(1) (1999) p122.

"Steric Effects on Excited State Geometry. The Resonance Raman Spectra of [Ru2X3(tacn)2}2+ (X=Cl, Br or I) and [Ru2X3(Me3tacn)2}2+ (X=Cl or Br)", W. A. Clucas, R. S. Armstrong and K. W. Nugent, J. Raman Spect., 29(10-11) (1998) p881.

"Micro-Raman Scattering Properties of Highly Oriented AlN Films" M. S. Liu, K. W. Nugent, S. Prawer, L. A. Bursill, J. L. Peng, Y. Z. Tong, and P. Jewsbury, Int. J. Modern Phys. B, 12 (1998) p1963.

"Dependence on Al Concentration of the Optical Phonons of AlxGa1-xN Films" Liu, M. S., Tong, Y. Z., Bursill, L. A., Prawer, S., Nugent, K. W. and Zhang, G. Y., Solid State Comm., 108 (1998) p765.

"The Nature of Damage in Ion-Implanted and Annealed Diamond" R. Kalish, A. Reznik, K. Nugent and S. Prawer, Nucl. Instr. Methods B, 148 (1999) p626.

"Ëffective Activation of Dopants Using MeV Ion Implantation" S. Prawer, D. N. Jamieson, K. W. Nugent, R. Walker, C. Uzan-Saguy and R. Kalish, Diamond Films and Technology, 8 (1998) p195

"Thermal Stability and Relaxation in Diamond-Like Carbon. A Raman Study of Films with Different sp3 Fractions (ta-C to a-C)" R. Kalish, Y. Lifshitz, K. Nugent and S. Prawer, Appl. Phys. Lett., 74 (1999) p2936.

"Temperature Dependence of Raman Scattering in Single Crystal GaN Films" M. S. Liu, L. A. Bursill, S. Prawer, K. W. Nugent, Y. Z. Tong and Zhang, G. Y. Appl. Phys. Lett., 74 (1999) p3125.

"Diamond-Like Carbon Nanocrystals Formed By Implanting Fused Quartz and Sapphire (□-Al2O3) with Carbon Ions" J. O. Orwa, J. C. McCallum, S. Prawer, K. W. Nugent and D. N. Jamieson, Diamond Relat. Mater., 8 (1999) p1642.

"Clustering in Carbon Implanted, Laser Annealed Fused Quartz" R. Walker, S. Prawer, D. N. Jamieson and K. W. Nugent, Diamond Relat. Mater., 8 (1999) p2159.

"The Raman spectrum of nanocrystalline diamond" S. Prawer, K. W. Nugent, D. N. Jamieson, J. O. Orwa, L. A. Bursill and J. L. Peng Chem Phys Lett. 332 (2000) p 93.

"Raman investigation of damage caused by deep ion implantation in diamond." J. O. Orwa, K. W. Nugent, D. N. Jamieson and S. Prawer Phys Rev B. 62 (2000) p. 5461.

"Direct quantitative detection of the sp(3) bonding in diamond-like carbon films using ultraviolet and visible Raman spectroscopy." K. W. R. Gilkes, S. Prawer, K. W. Nugent, J. Robertson, H. S. Sands, Y. Lifshitz and X.Shi, J Appl Phys. 87(2000) p. 7283.

"Diamond nanocrystals formed by direct implantation of fused silica with carbon" J. O. Orwa, S. Prawer,a) D. N. Jamieson, J. L. Peng, J. C. McCallum, K. W. Nugent, Y. J. Li, L. A. Bursill and S. P. Withrow, J Appl Phys. 90 (2001) p. 3007.

"Ecotoxicities of polyquaterniums and their associated polyelectrolyte-surfactant aggregates (PSA) to Gambusia holbroki" J. L.Cumming, D. W. Hawker, H Chapman and K. W. Nugent, J. Env. Sci. Health, 43 (2008) p 113

CURRICULUM VITAE

Edward J. Perkins, Ph.D.

CONTACT INFORMATION

Environmental Laboratory
U.S. Army Engineer Research and Development Center (ERDC)
US Army Corps Engineers (USACE)
3909 Halls Ferry Rd.
Vicksburg, MS
T: (601) 415-0657
E-mail: edward.j.perkins@usace.army.mil

EDUCATION

Ph.D.: Washington State University, USA, 1987.
Genetics and Cell Biology

B.S.: University of Illinois, Champaign-Urbana, IL, Oct 1983.
Major in Genetics. Minor in Art

EMPLOYMENT HISTORY

Title	Affiliation	Dates
US Army Senior Research Scientist, Environmental Networks and Genetic Toxicology, ST-00 (SES equivalent)	Environmental Laboratory, US Army Engineer Research and Development Center, 3909 Halls Ferry Rd, Vicksburg, MS 39180	Sept 2009 - present
US Army Deputy Chief Scientist	Deputy Assistant Secretary Army Research & Technology, ASA ALT, Army	Nov 2019- Nov 2020
Team Leader, Environmental Genomics and Genetics Team, Research Biologist DB05, 401	Environmental Laboratory, US Army Engineer Research and Development Center, 3909 Halls Ferry Rd, Vicksburg, MS 39180	Aug. 2004 – Sept 2009
Research Biologist, DB04, 401	Environmental Laboratory, US Army Engineer Research and Development Center, 3909 Halls Ferry Rd, Vicksburg, MS 39180	Aug. 2000 – Aug. 2004
Research Geneticist	AScI Corporation (on-site contractor-ERDC EL), 3402 Wisconsin Ave., Vicksburg MS 39180	Oct. 1995 – Aug. 2000
Post-doctoral Research Fellow, GS-11	USDA-ARS, Land Management and Water Conservation Research Unit, 215 Johnson Hall, Washington State University, Pullman, WA 99164	Nov. 1993 – Sept. 1995

Title	Affiliation	Dates
Independent Research Consultant	Self-employed	Nov. 1991 –Nov. 1993
Post-Doctoral Research Fellow	Department of Biochemistry, University of Washington Seattle WA 98195	Oct. 1988 – June 1992
Post-Doctoral Research Fellow	Program in Genetics and Cell Biology, Washington State University, Pullman WA 99164.	Oct. 1987 – Sept 1988

PROFESSIONAL SOCIETIES

- Society of Environmental Toxicology and Chemistry
- Society of Toxicology
- International Association for Great Lakes Research
- American Association for Advancement of Science
- International Society for Computational Biology
- MidSouth Computational Biology and Bioinformatics Society
- DoD TriServices Toxicology Consortium
- Society for Advancement of Adverse Outcome Pathways

HONORS AND AWARDS	DATE
US Army ERDC Program Development Achievement Award for Asian Carp DNA Research Team	2013
US EPA, STAA, Level II, for contributions to a journal article related to *Description of a Conceptual Framework for Use of Mechanistic Toxicology Data for Ecological Risk Assessment.*	2011
US Army ERDC Research and Development Center Achievement Award for Remote Monitoring of Invasive Carp	2011
US EPA, STAA, Level III for contribution to journal article related to *Applying Mechanistic Toxicology to Ecological Risk Assessment of Endocrine-Active Chemicals.*	2010
US Army ERDC Commander's Award for Civilian Service,	2008
US Army ERDC Researcher of the Year	2006
US Army Corps Engineers Researcher of the Year	2006
US Army Corps Engineers Researcher of the Year	2006
US Army ERDC Research and Development Achievement Award	2003

RESEARCH INTERESTS

My interests center around understanding biological complexity and understanding chemical hazards in the environment. I also have a significant interests on combining

computational modeling, omic technologies, and alternative models for toxicity testing to enable more rapid and realistic risk and hazard assessment.
My research has examined the hazardous effects of chemicals to a wide range of species including rat, bobwhite quail, Japanese quail, earthworms, fish (fathead minnow and Zebrafish), invertebrates (daphnia) and coral. This has led to the development and application of new tools and alternative testing strategies for chemical hazard assessment in addition to understanding complexity and function in biological systems. Most recently I have focused on developing approaches for using alternative animal models for both ecological and human health assessment, the application of Adverse Outcome Pathways for risk assessment, and the development of next generation risk assessment approaches that incorporate omics technologies, High throughput assays, and other novel technologies. In collaboration with the USEPA, the Organization for Economic Cooperation and Economic Development (OECD), The European Union Joint Research Center, I am also involved in international efforts in development of Adverse Outcome Pathways for hazard characterization and risk assessment. As the Army ST for Environmental Networks and Genetic toxicology, I am the Army's lead Research Scientist for toxicology. For example, I am currently leading a large project focused on developing computational models that are parameterized using in vitro assays to predict the ecological and human health impacts of PFASs.

PROFESSIONAL APPOINTMENTS/COMMITTEES/WORKSHOPS

1. ***Invited Expert Panelist***: EPA Scientific Advisory Committee on Chemicals panel meeting Peer Review of the Draft Risk Evaluation for 1-Bromopropane, Sept 10-12, 2019, Arlington VA
2. ***Invited Expert Panelist***: FIFRA Scientific Advisory Panel Meeting on Continuing Development of Alternative High-Throughput Screens to Determine Endocrine Disruption, Focusing on Androgen Receptor, Steroidogenesis, and Thyroid Pathways, Nov 28-29, 2017 One Potomac Yard, Arlington, Virginia
3. ***Invited Expert Panelist***: FIFRA Scientific Advisory Panel Meeting on the EPA Integrated Bioactivity and Exposure Ranking: A Computational Approach for Prioritization and Screening of Chemicals in the Endocrine Disruptor Screening Program, Dec. 2-4, 2014, Arlington, Virginia
4. ***Co-Organizer International Symposium:*** Materials Research Society Symposium F: Reverse Engineering of Bio-Inspired Nanomaterials, Materials Research Society meeting, Boston, MA November 30-December 5, 2014
5. ***Co-organizer International workshop:*** Advancing AOPs for Integrated Toxicology and Regulatory Applications. Somma Lombardo, Italy. March 2-7, 2014.
6. ***Member Intergovernmental working group:*** Working group on Exposure Science for the 21ST Century, the Toxics and Risk Subcommittee on Environment, Natural Resources, and Sustainability, under the National Science and Technology Council.

7. ***Expert Participant***: Seventh meeting of the OECD Advisory group on Molecular Screening and Toxicogenomics, June 11-12, 2014 Paris, France
8. ***Invited Expert Panelist***: FIFRA Scientific Advisory Panel Meeting on the EPA Weight-of-Evidence: Evaluating Results of EDSP Tier 1 Screening, July 30, 2013 - August 2, 2013, Arlington, Virginia
9. ***Invited Expert Participant:*** EPA Office of Pesticide Programs' Stakeholder workshop: Where Vision Meets Action: Practical Application of 21st Century Methods, July 9, 2013, Arlington, VA.
10. ***Invited Expert Panelist***: FIFRA Scientific Advisory Panel Meeting on the EPA Proposed Endocrine Disruptor Screening Program (EDSP) Tier 2 Ecotoxicity Tests, June 25-28, 2013, Arlington, Virginia
11. ***Invited Expert Panelist*****:** FIFRA Scientific Advisory Panel Meeting on the Scientific Issues Associated with Prioritizing the Universe of Endocrine Disruptor Screening Program (EDSP) Chemicals Using Computational Toxicology Tools, June 25-28, 2013, Arlington, Virginia
12. ***International Collaboration***: International consortium for Adverse Outcome Pathways for Endocrine Disruption in Daphnia magna, a conceptual approach for mechanistically-based Risk assessment (EDRISK**)** May, 2013 to present [**international**]
13. ***Expert Participant***: Sixth meeting of the OECD Advisory group on Molecular Screening and Toxicogenomics, May 14-15, 2013. [**international**]
14. ***Co-organizer:*** MidSouth Computational Biology and Bioinformatics Society, Tenth Annual Conference, University of Missouri, Columbia Mo, April 5-6, 2013
15. ***President:*** MidSouth Computational Biology and Bioinformatics Society, March 2012 – April 2013
16. ***Expert Participant*****:** Fifth meeting of the OECD Advisory group on Molecular Screening and Toxicogenomics, 7-8 June, 2012. [**international**]
17. ***Co-organizer:*** *Society of Toxicology Contemporary Concepts in Toxicology Workshop*: Building for Better Decisions: Multi-Scale Integration of Human Health and Environmental Data—May 8–11, 2012
    US EPA, Research Triangle Park, North Carolina
18. ***Board of Directors:*** MidSouth Computational Biology and Bioinformatics Society, March 2011 – present.
19. ***Invited Expert Participant:*** International Workshop on Integrative Approaches to Molecular Network Inference, 19-21, January, 2011, Birmingham, UK [**international**].
20. ***Expert Participant***. OECD Workshop on Using Mechanistic Information in Forming Chemical Categories to Fill Data Gaps for Regulatory Purposes. 8-10 December, 2010, US EPA Potomac Yard, Arlington, VA, USA [**international**].
21. ***Expert Participant***: OECD/IPCS Advisory Group on Molecular Screening and Toxicogenomics. 6-7 December, 2010, US EPA Potomac Yards, Arlington, VA, USA [**international**].
22. ***Expert Participant***: Fifth meeting of the OECD Advisory group on Molecular Screening and Toxicogenomics. 26-27 October, 2009, OECD Headquarters, Paris, France [**international**].

23. ***Co-organizer SETAC Pellston Workshop***: A Vision and Strategy for Predictive Ecotoxicology in the 21st Century: Defining Adverse Outcome Pathways Associated with Ecological Risk. April 19-23, 2009, Forest Grove, OR, USA [**international**].

Service in Academia: EDUCATION, OUTREACH, AND TEACHING ACTIVITIES

1. University of Liverpool, Liverpool UK. Dates served: 2014-16. Rank/position: Honorary Chair in Integrative Biology, Department of Functional and Comparative Genomics in the Institute of Integrative Biology.
2. Keck Graduate Institute, Claremont CA. Dates served: 2008-12. Rank/position: Adjunct faculty/Mentor. Service: Served on PhD thesis committee. Supervised and mentored research of Christopher Warner, DoD Science, Math, and Research for Transformation graduate student.
3. University of Southern Mississippi, Dept of Computer Science and Dept of Biology, Dates served: 2008-Current. Rank/position: Adjunct faculty. Supervised research and served on Ph.D. thesis committees of A. Ruwat and Y. Lee,
4. Jackson State University, Dept of Chemistry, Dates served: 2008-2011. Rank/position: Adjunct Professor. Service: Supervising research and Ph.D. thesis committee, Jason Ford-Green.
5. University of Mississippi, Dept of Computer and Information Sciences, Dates served: 2006-2007. Rank/position: Adjunct Professor. Service: Served on Ph.D. committee. Yuanyuan Ding.
6. University of Louisiana at Lafayette, Dates served: 2006-2007. Rank/position: NA. Service: Supervised and mentored Ph.D. thesis research, Curt Elderkin, 2001.
7. Alcorn State University, Department of Biology. Dates served: 1999-2002. Rank/position: Adjunct Professor. Service: Supervised research and served on M.S. committees (Valencia Knight, M.S. 2000; Regina O'Leary, M.S. 2002)
8. University of Idaho, Department of Biological Sciences. Dates served: 1998-2000. Rank/position: Adjunct Professor. Service: Supervised research and served on M.S. committee of Karl Diedrich (M.S. 2000).

GRANT REVIEWER

- US Army ERDC basic research grants (2009 - present)
- US Army Independent Laboratory Research Grants
- US Environmental Protection Agency
- US Army Research Office academic grants
- US Army Research Laboratory Collaborative Technologies Alliance grants
- Natural Sciences and Engineering Research Council of Canada (NSERC)
- Alternatives Research & Development Foundation
- UK Natural Environment Research Council (NERC)
- The Netherlands Organization for Scientific Research (NWO)

AD HOC REVIEWER

Ecotoxicology and Environmental Safety
PLOS ONE
Environmental Science and Technology
Environmental Toxicology and Chemistry
Ecotoxicology and Environmental Safety
Environmental and Molecular Mutagenesis
Environmental Research
BMC Bioinformatics
Toxicology
Toxicological Letters
Chemosphere
Environmental Health Perspectives
Defence Technology
HELIYON

PEER-REVIEWED JOURNAL ARTICLES: (146)

1. Mylroie JE, Wilbanks MS, Kimble AN, To KT, Cox CS, McLeod SJ, Gust KA, Moore DW, **Perkins EJ**, Garcia-Reyero N. Perfluorooctanesulfonic acid induced toxicity on zebrafish embryos in the presence or absence of the chorion. Environ Toxicol Chem. 2020 Oct 12. doi: 10.1002/etc.4899. Online ahead of print.PMID: 33044770
2. Rycroft TE, Foran CM, Thrash A, Cegan JC, Zollinger R, Linkov I, **Perkins EJ**, Garcia-Reyero N. AOPERA: A proposed methodology and inventory of effective tools to link chemicals to adverse outcome pathways. ALTEX. 2020;37(1):64-74. doi: 10.14573/altex.1906201. Epub 2019 Aug 26.
3. Bannon DI , Bao W , Turner SD , McCain WC , Dennis W , Wolfinger R , **Perkins E** , Abounader R. Gene expression in mouse muscle over time after nickel pellet implantation. Metallomics. 2020 Apr 1;12(4):528-538. doi: 10.1039/c9mt00289h. Epub 2020 Feb 17.PMID: 32065191
4. Burgoon LD, Angrish M, Garcia-Reyero N, Pollesch N, Zupanic A, **Perkins E.** Predicting the Probability that a Chemical Causes Steatosis Using Adverse Outcome Pathway Bayesian Networks (AOPBNs). Risk Anal. 2020 Mar;40(3):512-523. doi: 10.1111/risa.13423. Epub 2019 Nov 13.PMID: 31721239
5. Jeong J, Garcia-Reyero N, Burgoon L, **Perkins E**, Park T, Kim C, Roh JY, Choi J. Development of Adverse Outcome Pathway for PPARγ Antagonism Leading to Pulmonary Fibrosis and Chemical Selection for Its Validation: ToxCast Database and a Deep Learning Artificial Neural Network Model-Based Approach. Chem Res Toxicol. 2019 Jun 17;32(6):1212-1222. doi: 10.1021/acs.chemrestox.9b00040. Epub 2019 Jun 7.
6. Rowland MA, Mayo ML, Perkins EJ, Garcia-Reyero N. Stochastically modeling multiscale stationary biological processes. PLoS One. 2019 Dec 26;14(12):e0226687. doi: 10.1371/journal.pone.0226687. eCollection 2019.PMID: 31877201
7. Perkins EJ, Ashauer R, Burgoon L, Conolly R, Landesmann B, Mackay C, Murphy CA, Pollesch N, Wheeler JR, Zupanic A, Scholz S. Building and Applying Quantitative Adverse Outcome Pathway Models for Chemical Hazard and Risk Assessment. Environ Toxicol Chem. 2019 Sep;38(9):1850-1865. doi: 10.1002/etc.4505. Epub 2019 Aug 8.PMID: 31127958
8. Thrash A, Arick M 2nd, Barbato RA, Jones RM, Douglas TA, Esdale J, **Perkins EJ**, Garcia-Reyero N. Keanu: a novel visualization tool to explore biodiversity in metagenomes. BMC Bioinformatics. 2019 Mar 14;20(Suppl 2):103. doi: 10.1186/s12859-019-2629-4.PMID: 30871459
9. Patel R, Riveros G,Thompson D, Perkins EJ, Hoover JJ, Peters J, Tordesillas A. 2019. A Transdisciplinary Approach for Analyzing Stress Flow Patterns in Biostructures *Math. Comput. Appl. 24*(2),47; https://doi.org/10.3390/mca24020047
10. Linkov I, Trump BD, Anklam E, Berube D, Boisseasu P, Cummings C, Ferson S, Florin MV, Goldstein B, Hristozov D, Jensen KA, Katalagarianakis G, Kuzma J, Lambert JH, Malloy T, Malsch I, Marcomini A, Merad M, Palma-Oliveira J, Perkins EJ, Renn O, Seager T, Stone V, Vallero D, Vermeire T. Comparative, Collaborative,

and Integrative Risk Governance for Emerging Technologies. Environ Syst Decis (2018) 38: 170. https://doi.org/10.1007/s10669-018-9686-5

11. Trump BD, Foran C, Rycroft T, Wood MD, Bandolin N, Cains M, Cary T, Crocker F, Friedenberg NA, Gurian P, Hamilton K, Hoover JJ, Meyer C, Pokrzywinski K, Ritterson R, Schulte P, Warner C, Perkins EJ, Linkov I. Development of community of practice to support quantitative risk assessment for synthetic biology products: contaminant bioremediation and invasive carp control as cases. Environ Syst Decis (2018) 38: 517. https://doi.org/10.1007/s10669-018-9710-9
12. Trump BD, Cegan J, Wells E, Poinsatte-Jones K, Rycroft T, Warner C, Martin D, Perkins E, Wood MD, Linkov I. Co-evolution of physical and social sciences in synthetic biology. Critical Reviews in Biotechnology, Published online: 06 Feb 2019. https://doi.org/10.1080/07388551.2019.1566203
13. Foran CM, Rycroft T, Keisler J, **Perkins EJ**, Linkov I, Garcia-Reyero N. A modular approach for assembly of quantitative adverse outcome pathways. ALTEX. 2019 Jan 20. doi: 10.14573/altex.1810181. [Epub ahead of print]
14. Gust KA, Chaitankar V, Ghosh P, Wilbanks MS, Chen X, Barker ND, Pham D, Scanlan LD, Rawat A, Talent LG, Quinn MJ Jr, Vulpe CD, Elasri MO, Johnson MS, **Perkins EJ**, McFarland CA. Multiple environmental stressors induce complex transcriptomic responses indicative of phenotypic outcomes in Western fence lizard. BMC Genomics. 2018 Dec 5;19(1):877. doi: 10.1186/s12864-018-5270-0.
15. **Perkins EJ**, Gayen K, Shoemaker JE, Antczak P, Burgoon L, Falciani F, Gutsell S, Hodges G, Kienzler A, Knapen D, McBride M, Willett C, Doyle FJ, Garcia-Reyero N. Chemical hazard prediction and hypothesis testing using quantitative adverse outcome pathways. ALTEX. 2019;36(1):91-102. doi: 10.14573/altex.1808241. Epub 2018 Oct 16.
16. **R. R. Patel**, D. Valles, G. A. Riveros, D. S. Thompson, E. J. Perkins, J. J. Hoover, J. F. Peters "*Stress flow analysis of biostructures using finite element method and flow network approach*", Finite Elements in Analysis and Design ,152 (2018) 46-54.
17. Schroeder AL, Ankley GT, Habib T, Garcia-Reyero N, Escalon BL, Jensen KM, Kahl MD, Durhan EJ, Makynen EA, Cavallin JE, Martinovic-Weigelt D, **Perkins EJ**, Villeneuve DL Rapid effects of the aromatase inhibitor fadrozole on steroid production and gene expression in the ovary of female fathead minnows (Pimephales promelas). Gen Comp Endocrinol. 2017 Oct 1;252:79-87. doi: 10.1016/j.ygcen.2017.07.022. Epub 2017 Jul 21.
18. Lee JH, Warner CM, Jin HE, Barnes E, Poda AR, **Perkins EJ**, Lee SW. 2017. Production of tunable nanomaterials using hierarchically assembled bacteriophages. Nat Protoc. 2017 Sep;12(9):1999-2013. doi: 10.1038/nprot.2017.085. Epub 2017 Aug 31.
19. **Perkins EJ**, Habib T, Escalon BL, Cavallin JE, Thomas L, Weberg M, Hughes MN, Jensen KM, Kahl MD, Villeneuve DL, Ankley GT, Garcia-Reyero N. 2017. Prioritization of Contaminants of Emerging Concern in Wastewater Treatment Plant Discharges Using Chemical:Gene Interactions in Caged Fish. Environ Sci Technol. Aug 1;51(15):8701-8712. doi: 10.1021/acs.est.7b01567. Epub 2017 Jul 17.

20. Brockmeier EK, Hodges G, Hutchinson TH, Butler E, Hecker M, Tollefsen KE, Garcia-Reyero N, Kille P, Becker D, Chipman K, Colbourne J, Collette TW, Cossins A, Cronin M, Graystock P, Gutsell S, Knapen D, Katsiadaki I, Lange A, Marshall S, Owen SF, **Perkins EJ**, Plaistow S, Schroeder A, Taylor D, Viant M, Ankley G, Falciani F. 2017. The Role of Omics in the Application of Adverse Outcome Pathways for Chemical Risk Assessment. Toxicol Sci. 2017 Aug 1;158(2):252-262. doi: 10.1093/toxsci/kfx097.
21. LaLone CA, Ankley GT, Belanger SE, Embry MR, Hodges G, Knapen D, Munn S, **Perkins EJ**, Rudd MA, Villeneuve DL, Whelan M, Willett C, Zhang X, Hecker M. 2017. Advancing the adverse outcome pathway framework-An international horizon scanning approach. Environ Toxicol Chem. Jun;36(6):1411-1421. doi: 10.1002/etc.3805.
22. Conolly RB, Ankley GT, Cheng W, Mayo ML, Miller DH, **Perkins EJ**, Villeneuve DL, Watanabe KH. 2017. Quantitative Adverse Outcome Pathways and Their Application to Predictive Toxicology. Environ Sci Technol. 51(8):4661-4672. doi: 10.1021/acs.est.6b06230. Epub 2017 Apr 7. PMID:28355063
23. Rowland MA, **Perkins EJ**, Mayo ML. 2017. Physiological fidelity or model parsimony? The relative performance of reverse-toxicokinetic modeling approaches. BMC Syst Biol. Mar 11;11(1):35. doi: 10.1186/s12918-017-0407-3. PMID: 28284215
24. Schroeder AL, Martinović-Weigelt D, Ankley GT, Lee KE, Garcia-Reyero N, **Perkins EJ**, Schoenfuss HL, Villeneuve DL. 2017. Prior knowledge-based approach for associating contaminants with biological effects: A case study in the St. Croix River basin, MN, WI, USA. Environ Pollut. Feb;221:427-436. doi: 10.1016/j.envpol.2016.12.005. PMID: 27939634
25. Wittwehr C, Aladjov H, Ankley G, Byrne HJ, de Knecht J, Heinzle E, Klambauer G, Landesmann B, Luijten M, MacKay C, Maxwell G, Meek ME, Paini A, **Perkins E**, Sobanski T, Villeneuve D, Waters KM, Whelan M. 2017. How Adverse Outcome Pathways Can Aid the Development and Use of Computational Prediction Models for Regulatory Toxicology. Toxicol Sci.155(2):326-336. doi: 10.1093/toxsci/kfw207. Review. PMID:27994170
26. Barbato RA, Garcia-Reyero N, Foley K, Jones R, Courville Z, Douglas T, **Perkins E**, Reynolds CM. 2016. Removal of Exogenous Materials from the Outer Portion of Frozen Cores to Investigate the Ancient Biological Communities Harbored Inside. J Vis Exp. (113). doi: 10.3791/54091. PMID:27403572
27. Klimenko K, Kuz'min V, Ognichenko L, Gorb L, Shukla M, Vinas N, **Perkins E**, Polishchuk P, Artemenko A, Leszczynski J. 2016. Novel enhanced applications of QSPR models: Temperature dependence of aqueous solubility. J Comput Chem. Aug 15;37(22):2045-51. doi: 10.1002/jcc.24424.PMID:27338156
28. Villeneuve DL, Jensen KM, Cavallin JE, Durhan EJ, Garcia-Reyero N, Kahl MD, Leino RL, Makynen EA, Wehmas LC, **Perkins EJ**, Ankley GT. 2016. Effects of the antimicrobial contaminant triclocarban, and co-exposure with the androgen 17β-trenbolone, on reproductive function and ovarian transcriptome of the fathead minnow (Pimephales promelas). Environ Toxicol Chem. Jun 17. doi: 10.1002/etc.3531.

29. Johnston TK, **Perkins E**, Ferguson DC, Cropek DM. 2016. Tissue explant coculture model of the hypothalamic-pituitary-gonadal-liver axis of the fathead minnow (Pimephales promelas) as a predictive tool for endocrine disruption. Environ Toxicol Chem. 2016 Oct;35(10):2530-2541. doi: 10.1002/etc.3415. PMID: 26931821

30. Gust KA, Kennedy AJ, Melby NL, Wilbanks MS, Laird J, Meeks B, Muller EB, Nisbet RM, **Perkins EJ**. 2016. Daphnia magna's sense of competition: intra-specific interactions (ISI) alter life history strategies and increase metals toxicity. Ecotoxicology. Aug;25(6):1126-35.

31. Cote I, Andersen ME, Ankley GT, Barone S, Birnbaum LS, Boekelheide K, Bois FY, Burgoon LD, Chiu WA, Crawford-Brown D, Crofton KM, DeVito M, Devlin RB, Edwards SW, Guyton KZ, Hattis D, Judson RS, Knight D, Krewski D, Lambert J, Maull EA, Mendrick D, Paoli GM, Patel CJ, **Perkins EJ**, Poje G, Portier CJ, Rusyn I, Schulte PA, Simeonov A, Smith MT, Thayer KA, Thomas RS, Thomas R, Tice RR, Vandenberg JJ, Villeneuve DL, Wesselkamper S, Whelan M, Whittaker C, White R, Xia M, Yauk C, Zeise L, Zhao J, DeWoskin RS. 2016. The Next Generation of Risk Assessment Multiyear Study- Highlights of Findings, Applications to Risk Assessment and Future Directions. Environ Health Perspect. Apr 19. DOI:10.1289/EHP233. Review.

32. Gong P, Nan X, Barker ND, Boyd RE, Chen Y, Wilkins DE, Johnson DR, Suedel BC, **Perkins EJ**. 2016. Predicting chemical bioavailability using microarray gene expression data and regression modeling: A tale of three explosive compounds. BMC Genomics. Mar 8;17:205.

33. Wang RL, Biales AD, Garcia-Reyero N, **Perkins EJ**, Villeneuve DL, Ankley GT, Bencic DC. 2016. Fish connectivity mapping: linking chemical stressors by their mechanisms of action-driven transcriptomic profiles. BMC Genomics. Jan 28;17:84. doi: 10.1186/s12864-016-2406-y.

34. Watanabe KH, Mayo M, Jensen KM, Villeneuve DL, Ankley GT, **Perkins EJ**. 2016. Predicting Fecundity of Fathead Minnows (Pimephales promelas) Exposed to Endocrine-Disrupting Chemicals Using a MATLAB®-Based Model of Oocyte Growth Dynamics. PLoS One. Jan 12;11(1):e0146594. doi: 10.1371/journal.pone.0146594. eCollection 2016.

35. Collier ZA, Gust KA, Gonzalez-Morales B, Gong P, Wilbanks MS, Linkov I, **Perkins EJ**. 2016. A weight of evidence assessment approach for adverse outcome pathways. Regul Toxicol Pharmacol. 2016 Mar;75:46-57. doi: 10.1016/j.yrtph.2015.12.014.

36. Abdelzaher AF, Al-Musawi AF, Ghosh P, Mayo ML, **Perkins EJ**. 2015. Transcriptional Network growing Models using Motif-based Preferential Attachment. Frontiers in Bioengineering and Biotechnology. Oct 12;3:157. doi: 10.3389/fbioe.2015.00157. eCollection 2015

37. Gong P, Hong H, **Perkins EJ**. 2015. Ionotropic GABA receptor antagonism-induced adverse outcome pathways for potential neurotoxicity biomarkers. Biomark Med.;9(11):1225-39. doi: 10.2217/bmm.15.58. Epub 2015 Oct 28. Review.

38. **Perkins E**, Antczak P, Burgoon L, Falciani F, Garcia-Reyero N, Gutsell S, Hodges G, Kienzler A, Knapen D, McBride M, Willett. 2015. Adverse Outcome Pathways for Regulatory Applications: Examination of Four Case Studies With Different Degrees of Completeness and Scientific Confidence. Toxicological Sciences. in press. doi:10.1093/toxsci/kfv181

39. Gust KA, Nanduri B, Rawat A, Wilbanks MS, Ang CY, Johnson DR, Pendarvis K, Chen X, Quinn MJ Jr, Johnson MS, Burgess SC, **Perkins EJ**. 2015. Systems toxicology identifies mechanistic impacts of 2-amino-4,6-dinitrotoluene (2A-DNT) exposure in Northern Bobwhite. BMC Genomics. Aug 7;16:587. doi: 10.1186/s12864-015-1798-4.

40. Vidal-Dorsch DE, Bay SM, Moore S, Layton B, Mehinto AC, Vulpe CD, Brown-Augustine M, Loguinov A, Poynton H, Garcia-Reyero N, **Perkins EJ**, Escalon L, Denslow ND, Cristina CR, Doan T, Shukradas S, Bruno J, Brown L, Van Agglen G, Jackman P, Bauer M. 2015. Ecotoxicogenomics: Microarray interlaboratory comparability. Chemosphere. Sep 9;144:193-200. doi: 10.1016/j.chemosphere.2015.08.019

41. McConnell ER, Bell SM, Cote I, Wang RL, **Perkins EJ**, Garcia-Reyero N, Gong P, Burgoon LD. 2014 Systematic Omics Analysis Review (SOAR) tool to support risk assessment. PLoS One. Dec 22;9(12):e110379.

42. Deng Y, Ai J, Guan X, Wang Z, Yan B, Zhang D, Liu C, Wilbanks MS, Escalon BL, Meyers SA, Yang MQ, **Perkins EJ**. 2014. MicroRNA and messenger RNA profiling reveals new biomarkers and mechanisms for RDX induced neurotoxicity. BMC Genomics.;15 Suppl 11:S1. doi: 10.1186/1471-2164-15-S11-S1.

43. Wang RL, Bencic DC, Garcia-Reyero N, **Perkins EJ**, Villeneuve DL, Ankley GT, Biales AD. 2014. Natural Variation in Fish Transcriptomes: Comparative Analysis of the Fathead Minnow (Pimephales promelas) and Zebrafish (Danio rerio).PLoS One. 2014 Dec 10;9(12):e114178. doi: 10.1371/journal.pone.0114178. eCollection 2014.

44. Ananthasubramaniam B, McCauley E, Gust KA, Kennedy AJ, Muller EB, **Perkins EJ**, Nisbet RM. 2015. Relating suborganismal processes to ecotoxicological and population level endpoints using a bioenergetic model. Ecological Applications. 25:1691–1710. http://dx.doi.org/10.1890/14-0498.1

45. Mayo M, Abdelzaher A, **Perkins EJ**, Ghosh P. 2014. Top-level dynamics and the regulated gene response of feed-forward loop transcriptional motifs. Phys Rev E Stat Nonlin Soft Matter Phys. Sep;90(3-1):032706. Epub 2014 Sep 10.

46. Wilbanks MS, Gust KA, Atwa S, Sunesara I, Johnson D, Ang CY, Meyer SA, **Perkins EJ**. 2014. Validation of a Genomics-Based Hypothetical Adverse Outcome Pathway: 2,4-Dinitrotoluene Perturbs PPAR Signaling Thus Impairing

Energy Metabolism and Exercise Endurance. Toxicol Sci. 2014 Jun 3. pii: kfu104. [Epub ahead of print]

47. Gust KA, Najar FZ, Habib T, Lotufo GR, Piggot AM, Fouke BW, Laird JG, Wilbanks MS, Rawat A, Indest KJ, Roe BA, **Perkins EJ**. 2014. Coral-zooxanthellae meta-transcriptomics reveals integrated response to pollutant stress. BMC Genomics. 2014 Jul 12;15(1):591.

48. Warner CM, Barker N, Lee SW, **Perkins EJ**. 2014 Bacteriophage production for large-scale applications. Bioprocess Biosyst Eng. Apr 13. [Epub ahead of print]

49. Garcia-Reyero N, Tingaud-Sequeira A, Cao M, Zhu Z, **Perkins EJ**, Hu W. 2014. Endocrinology: Advances through omics and related technologies.. Gen Comp Endocrinol. Apr 12. pii: S0016-6480(14)00116-6. doi: 10.1016/j.ygcen.2014.03.042. [Epub ahead of print]

50. Allison PG, Deang JF, Diaz AJ, Poda AR, Hoover JJ, Horstemeyer MF, **Perkins EJ.** 2013. Characterization of paddlefish (*Polyodon spathula*) rostrum stellate bones. Bioinspired, Biomimetic and Nanobiomaterials. 3:63-68. Available online: 31 October 2013. DOI: 10.1680/bbn.13.00024

51. Stanley JK, **Perkins EJ**, Habib T, Sims JG, Chappell P, Escalon BL, Wilbanks M, Garcia-Reyero N. 2013. The Good, the Bad, and the Toxic: Approaching Hormesis in Daphnia magna Exposed to an Energetic Compound. Environ Sci Technol. 2013 Aug 20;47(16):9424-33. doi: 10.1021/es401115q.

52. Garcia-Reyero N, Ekman DR, Habib T, Villeneuve DL, Collette TW, Bencic DC, Ankley GT, **Perkins EJ**. 2014. Integrated approach to explore the mechanisms of aromatase inhibition and recovery in fathead minnows (Pimephales promelas). Gen Comp Endocrinol. Apr 1. pii: S0016-6480(14)00096-3. doi: 10.1016/j.ygcen.2014.03.022. [Epub ahead of print]

53. Garcia-Reyero N, Kennedy AJ, Escalon BL, Habib T, Laird JG, Rawat A, Wiseman S, Hecker M, Denslow N, Steevens JA, **Perkins EJ**. 2014. Differential effects and potential adverse outcomes of ionic silver and silver nanoparticles in vivo and in vitro. Environ Sci Technol. Apr 15;48(8):4546-55. doi: 10.1021/es4042258. Epub 2014 Mar 31.

54. Wei X, Ai J, Deng Y, Guan X, Johnson DR, Ang CY, Zhang C, **Perkins EJ**. 2014. Identification of biomarkers that distinguish chemical contaminants based on gene expression profiles. BMC Genomics. Mar 31;15(1):248. doi: 10.1186/1471-2164-15-248.

55. Berninger JP, Martinović-Weigelt D, Garcia-Reyero N, Escalon L, **Perkins EJ**, Ankley GT, Villeneuve DL. 2014. Using transcriptomic tools to evaluate biological effects across effluent gradients at a diverse set of study sites in Minnesota, USA. Environ Sci Technol. Feb 18;48(4):2404-12. doi: 10.1021/es4040254. Epub 2014 Jan 27.

56. Garcia-Reyero N, Escalon BL, Prats E, Stanley JK, Thienpont B, Melby NL, Barón E, Eljarrat E, Barceló D, Mestres J, Babin PJ, **Perkins EJ**, Raldúa D. 2014. Effects of BDE-209 contaminated sediments on zebrafish development and potential

implications to human health. Environ Int. Feb;63:216-23. doi: 10.1016/j.envint.2013.11.012. Epub 2013 Dec 6.

57. Yang Y, Maxwell A, Zhang X, Wang N, **Perkins EJ**, Zhang C, Gong P. 2013. Differential reconstructed gene interaction networks for deriving toxicity threshold in chemical risk assessment. BMC Bioinformatics.;14 Suppl 14:S3. doi: 10.1186/1471-2105-14-S14-S3. Epub 2013 Oct 9.

58. **Perkins EJ**, Ankley GT, Crofton KM, Garcia-Reyero N, Lalone CA, Johnson MS, Tietge JE, Villeneuve DL 2013. Current Perspectives on the Use of Alternative Species in Human Health and Ecological Hazard Assessments. Environ Health Perspect. 121(9):1002-10.

59. Jaligama S, Kale VM, Wilbanks MS, Perkins EJ, Meyer SA. 2013. Delayed myelosuppression with acute exposure to hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) and environmental degradation product hexahydro-1-nitroso-3,5-dinitro-1,3,5-triazine (MNX) in rats. Toxicol Appl Pharmacol. Feb 1;266(3):443-51. doi: 10.1016/j.taap.2012.11.022.

60. Quinn MJ, Hanna TL, Shiflett AA, McFarland CA, Cook ME, Johnson MS, Gust KA, Perkins EJ. 2013. Interspecific effects of 4A-DNT (4-amino-2,6-dinitrotoluene) and RDX (1,3,5-trinitro-1,3,5-triazine) in Japanese quail, Northern bobwhite, and Zebra finch. Ecotoxicology. 2013 Mar;22(2):231-9. doi: 10.1007/s10646-012-1019-8.

61. McFarland CA, Talent LG, Quinn MJ Jr, Bazar MA, Wilbanks MS, Nisanian M, Gogal RM Jr, Johnson MS, Perkins EJ, Gust KA. 2012. Multiple environmental stressors elicit complex interactive effects in the western fence lizard (Sceloporus occidentalis). Ecotoxicology, 21(8):2372-90. doi: 10.1007/s10646-012-0993-1.

62. Schuster BE, Roszell LE, Murr LE, Ramirez DA, Demaree JD, Klotz BR, Rosencrance AB, Dennis WE, Bao W, Perkins EJ, Dillman JF, Bannon DI. 2012. In vivo corrosion, tumor outcome, and microarray gene expression for two types of muscle-implanted tungsten alloys. Toxicol Appl Pharmacol. Nov 15;265(1):128-38. doi: 10.1016/j.taap.2012.08.025.

63. Adedeji OB, Durhan EJ, Garcia-Reyero N, Kahl MD, Jensen KM, Lalone CA, Makynen EA, Perkins EJ, Thomas L, Villeneuve DL, Ankley GT. 2012. Short-Term Study Investigating the Estrogenic Potency of Diethylstilbesterol in the Fathead Minnow (Pimephales promelas). Environ Sci Technol. Jul 17;46(14):7826-35. Epub 2012 Jun 29.

64. Wu X, Li P, Wang N, Gong P, Perkins EJ, Deng Y, Zhang C. 2011. State Space Model with hidden variables for reconstruction of gene regulatory networks. BMC Syst Biol. Dec 23;5 Suppl 3:S3. Epub 2011 Dec 23.

65. Warner CM, Gust KA, Stanley JK, Habib T, Wilbanks MS, Garcia-Reyero N, Perkins EJ. 2012. A Systems Toxicology Approach to Elucidate the Mechanisms Involved in RDX Species-Specific Sensitivity. Environ Sci Technol. Jul 17;46(14):7790-8. Epub 2012 Jun 27.

66. Mayo M, Abdelzaher AF, Perkins EJ, Ghosh P. 2012. Motif Participation by Genes in E. coli Transcriptional Networks. Front Physiol. 2012;3:357. doi: 10.3389/fphys.2012.00357. Epub 2012 Sep 24.

67. Kamapantula BK, Abdelzaher A, Ghosh P, Mayo M, Perkins E, Das SK. 2012. Performance of wireless sensor topologies inspired by E. coli genetic networks. Pervasive Computing and Communications Workshops (PERCOM Workshops), 2012 IEEE International Conference. Proceedings pp 302 – 307. DOI: 10.1109/PerComW.2012.6197500

68. Rawat A, Elasri MO, Gust KA, George G, Pham D, Scanlan LD, Vulpe C, Perkins EJ. 2012. CAPRG: sequence assembling pipeline for next generation sequencing of non-model organisms. PLoS One. 2012;7(2):e30370. Epub 2012 Feb 3.

69. Gong P, Guan X, Pirooznia M, Liang C, Perkins EJ. 2012. Gene expression analysis of CL-20-induced reversible neurotoxicity reveals GABA(A) receptors as potential targets in the earthworm Eisenia fetida. Environ Sci Technol. 2012 Jan 17;46(2):1223-32. Epub 2012 Jan 6.

70. Li Y, Gong P, Perkins EJ, Zhang C, Wang N. 2011. RefNetBuilder: a platform for construction of integrated reference gene regulatory networks from expressed sequence tags. BMC Bioinformatics. 2011 Oct 18;12 Suppl 10:S20.

71. Li H, Wang N, Gong P, Perkins EJ, Zhang C. 2011. Learning the structure of transition gene regulatory networks from time series gene expression data. BMC Genomics. 2011 Dec 23; 12 Suppl 5:S13. Epub 2011 Dec 23.

72. Villeneuve DL, Garcia-Reyero N, Martinović-Weigelt D, Li Z, Watanabe KH, Orlando EF, Lalone CA, Edwards SW, Burgoon LD, Denslow ND, Perkins EJ, Ankley GT. 2012. A graphical systems model and tissue-specific functional gene sets to aid transcriptomic analysis of chemical impacts on the female teleost reproductive axis. Mutat Res. 746:151–162.

73. Mayo ML, Perkins EJ, Ghosh P. 2011. First-passage time analysis of a one-dimensional diffusion-reaction model: application to protein transport along DNA. BMC Bioinformatics. 12 Suppl 10:S18.

74. Wren JD, Kupfer DM, Perkins EJ, Bridges S, Winters-Hilt S, Dozmorov MG, Braga-Neto U. 2011. Proceedings of the 2011 MidSouth Computational Biology and Bioinformatics Society (MCBIOS) conference. Introduction. BMC Bioinformatics. Oct 18;12 Suppl 10:S1.

75. Ghosh P, Mayo M, Chaitankar V, Habib T, Perkins E, Das SK. 2011. Principles of genomic robustness inspire fault-tolerant WSN topologies: A network science based case study. Pervasive Computing and Communications Workshops (PERCOM Workshops), 2011 IEEE International Conference Digital Object Identifier: 10.1109/PERCOMW.2011.5766861 Page160 – 165.

76. Ford-Green J, Isayev O, Gorb L, Perkins EJ, Leszczynski J. 2012. Evaluation of natural and nitramine binding energies to 3-D models of the S1S2 domains in the N-methyl-D: -aspartate receptor. J Mol Model. 18:1273-84

77. Gong P, Loh P-R, Barker N, Tucker G, Wang N, Zhang C, Escalon BL, Berger B, Perkins EJ. 2011. Building quantitative prediction models for tissue residue of two explosives compounds in earthworms from microarray gene expression data. Environ Sci Technol. 46:19-26.

78. Villeneuve DL, Garcia-Reyero N, Jensen KM, Cavallin JE, Makynen EA, Durhan EJ, Kahl MD, Thomas LM, Perkins EJ, Ankley GT. 2011. Ecotoxicogenomics to support ecological risk assessment: A case study with bisphenol A in fish. Environ Sci Technol. 46:51-59.

79. Garcia-Reyero N, Escalon BL, Loh P-R, Laird JD, Kennedy AJ, Berger B, Perkins EJ. 2011. Assessment of chemical mixtures and ground water effects on Daphnia magna transcriptomics. Environ Sci Technol. 46:42–50.

80. Gust KA, Brasfield, SM, Stanley JK, Wilbanks MS, Chappell P, Perkins EJ, Lotufo GR, Lance RF. 2011. Genomic investigation of year-long and multigenerational exposures of fathead minnow to the munitions compound RDX. Environ Toxicol Chem. 2011 Aug;30(8):1852-64. doi: 10.1002/etc.558. Epub 2011 Jun 14.

81. Garcia-Reyero N, Habib T, Pirooznia M, Gust KA, Gong P, Warner C, Wilbanks M, Perkins EJ. 2011. Conserved toxic responses across divergent phylogenetic lineages: a meta-analysis of the neurotoxic effects of RDX among multiple species using toxicogenomics. Ecotoxicology May;20(3):580-94. Epub 2011 Mar 29.

82. Chaitankar V, Zhang C, Ghosh P, Gong P, Perkins EJ, Deng Y. 2011. Predictive Minimum Description Length Principle Approach to Inferring Gene Regulatory Networks. Adv Exp Med Biol. 696:37-43.

83. Deng Y, Meyer SA**,** Guan X**,** Escalon BL, Ai J, Wilbanks MS, Welti R, Garcia-Reyero N, Perkins EJ. 2011. Analysis of common and specific mechanisms of liver function affected by nitrotoluene compounds. PLoS ONE. 6(2):e14662.

84. Gust KA, Wilbanks MS, Guan X, Pirooznia M, Habib T, Yoo L, Wintz H, Vulpe CD, Perkins EJ. 2011. Investigations of transcript expression in fathead minnow (Pimephales promelas) brain tissue reveal toxicological impacts of RDX exposure. Aquat Toxicol. 101(1):135-45. Epub 2010 Sep 29.

85. Garcia Reyero N, Perkins EJ. 2011. Systems biology: leading the revolution in ecotoxicology. Environ Toxicol Chem. 30(2):265-73.

86. Perkins EJ, Chipman K, Edwards SW, Habib T, Falciani F, Taylor R, Van Aggelen G, Vulpe C, Antczak P, Luginov A. 2011. Reverse Engineering Adverse Outcome Pathways. Environ Toxicol Chem. 30(1):22-38.

87. Skolness SY, Durhan EJ, Garcia-Reyero N, Jensen KM, Kahl MD, Makynen EA, Martinovic D, Perkins E, Villeneuve D, Ankley GT. 2011. Effects of a short-term exposure to the fungicide prochloraz on endocrine function and gene expression in female fathead minnows (Pimephales promelas).Aquatic Toxicology. 103, 170-178.

88. Chowbina S, Deng Y, Ai J, Wu X, Guan X, Wilbanks MS, Escalon BL, Meyer SA, Perkins EJ, Chen JY. 2010. A new approach to construct pathway connected networks and its application in dose responsive gene expression profiles of rat liver regulated by 2,4DNT. BMC Genomics. 2010 Dec 1;11 Suppl 3:S4.

89. Pirooznia M, Pozhitkov A, Perkins EJ, Deng Y, Brouwer M. 2010. Generation, analysis and functional annotation of expressed sequence tags from the sheepshead minnow (Cyprinodon variegatus). BMC Genomics. Nov 2; 11 Suppl 2:S4.
90. Deng Y, Johnson DR, Guan X, Ang CY, Ai J, Perkins EJ. 2010. In vitro gene regulatory networks predict in vivo function of liver. BMC Syst Biol. Nov 12; 4:153.
91. Gong P, Pirooznia M, Guan X, Perkins EJ. 2010. Design, Validation and Annotation of Transcriptome-Wide Oligonucleotide Probes for the Oligochaete Annelid Eisenia fetida. PLoS One. Dec 8;5(12):e14266
92. Gong P, Xie F, Zhang B, Perkins EJ. 2010. In silico identification of conserved microRNAs and their target transcripts from expressed sequence tags of three earthworm species. Comput Biol Chem. Dec; 34(5-6):313-9
93. Pirooznia M, Pozhitkov A, Perkins EJ, Deng Y, Brouwer M. 2010. Generation, analysis and functional annotation of expressed sequence tags from the sheepshead minnow (Cyprinodon variegatus). BMC Genomics. 11 Suppl 2:S4.
94. Li Y, Wang N, Perkins EJ, Zhang C, Gong P, 2010 Identification and Optimization of Classifier Genes from Multi-Class Earthworm Microarray Dataset. PLoS ONE Oct 28 5(10): e13715. *
95. Wren JD, Kupfer DM, Perkins EJ, Bridges S, Berleant D. 2010. Proceedings of the 2010 MidSouth Computational Biology and Bioinformatics Society (MCBIOS) Conference. BMC Bioinformatics, 2010. Oct 7;11 Suppl 6: p.1
96. Chaitankar V, Ghosh P, Perkins EJ, Gong P, Zhang C. 2010. Time lagged information theoretic approaches to the reverse engineering of gene regulatory networks. BMC Bioinformatics, 2010. Oct 7;11 Suppl 6: p. S19.
97. Rawat A, Gust KA, Elasri MO, Perkins EJ. 2010. Quail Genomics: a knowledgebase for Northern bobwhite. BMC Bioinformatics, Oct 7;11 Suppl 6: p. S13.
98. Shoemaker JE, Gayen K, Garcia-Reyero N, Perkins EJ, Villeneuve D L, Liu L, Doyle III FJ. 2010. Fathead minnow steroidogenesis: in silico analyses reveals tradeoffs between nominal target efficacy and robustness to cross-talk. BMC Systems Biology 4:89 (28 June 2010).
99. Chaitankar V, Ghosh P, Perkins EJ, Gong P, Deng Y, Zhang C. 2010. A novel gene regulatory inference algorithm using predictive minimum description length approach. BMC Systems Biology. May 28;4 Suppl 1:S7.
100. Rawat A, Gust KA, Deng Y, Garcia-Reyero N, Quinn Jr. M, Johnson M, Indest K, Elasri MO, Perkins EJ. 2010. From raw materials to validated system: The construction of a genomic library and microarray to interpret systemic perturbations in Northern bobwhite. Physiological Genomics. 42(2):219-35. Epub 2010 Apr 2.
101. Villeneuve DL, Garcia-Reyero N, Martinović D, Cavallin JE, Mueller ND, Wehmas LC, Kahl MD, Linnum AL, Perkins EJ, Ankley GT. 2010. Influence of ovarian stage on transcript profiles in fathead minnow (Pimephales promelas) ovary tissue. Aquat Toxicol. 98(4):354-66.

102. Van Aggelen G, Ankley GT, Baldwin WS, Bearden DW, Benson WH, Chipman JK, Collette TW, Craft JA, Denslow ND, Embry MR, Falciani F, George SG, Helbing CC, Hoekstra PF, Iguchi T, Kagami Y, Katsiadaki I, Kille P, Liu L, Lord PG, McIntyre T, O'Neill A, Osachoff H, Perkins EJ, Santos EM, Skirrow RC, Snape JR, Tyler CR, Versteeg D, Viant MR, Volz DC, Williams TD, Yu L. 2010. Integrating omic technologies into aquatic ecological risk assessment and environmental monitoring: hurdles, achievements, and future outlook. Environ Health Perspect. 118:1-5.

103. Bannon DI, Johnson M, Williams L, Adams V, Perkins EJ, Gust K, Gong P. 2009. Comment on RDX and miRNA Expression in B6C3F1 Mice. Environmental Health Perspectives. 117: A97-98 *doi:10.1289/ehp.0800276*

104. Villeneuve DL, Garcia-Reyero N, Martinović D, Mueller ND, Cavallin JE, Durhan EJ, Makynen EA, Jensen KM, Kahl MD, Blake LS, Perkins EJ, Ankley GT. 2009. II: Effects of a dopamine receptor antagonist on fathead minnow dominance behavior and ovarian gene expression in the fathead minnow and zebrafish. Ecotoxicol Environ Saf. 73(4):478-85.

105. Gong P, Basu N, Scheuhammer AM, Perkins EJ. 2009. Neurochemical and electrophysiological diagnosis of reversible neurotoxicity in earthworms exposed to sublethal concentrations of CL-20. Environ Sci Pollut Res Int. 17(1):181-6.

106. Villeneuve DL, Garcia-Reyero N, Martinović D, Mueller ND, Cavallin JE, Durhan EJ, Makynen EA, Jensen KM, Kahl MD, Blake LS, Perkins EJ, Ankley GT. 2009 I. Effects of a dopamine receptor antagonist on fathead minnow, Pimephales promelas, reproduction. Ecotoxicol Environ Saf. Sep 25. [Epub ahead of print]

107. Gust K, Pirooznia M, Quinn Jr. MJ, Johnson MS, Escalon L, Indest K, Guan X, Deng Y, Gong P, Perkins EJ. 2009. Neurotoxicogenomic Investigations to Assess Mechanisms of Action of the Munitions Constituents RDX and 2,6-DNT in Northern Bobwhite (*Colinus virginianus*). Toxicological Sciences. 110:168-80

108. Garcia-Reyero N, Poynton HC, Kennedy AJ, Guan X, Escalon BL, Chang B, Varshavsky J, Loguinov AV, Vulpe CD, Perkins EJ. 2009. Biomarker discovery and transcriptomic Responses in *Daphnia magna* exposed to munitions constituents. Environ Science Technol. 43:4188–4193.

109. Garcia-Reyero N, Kroll KJ, Liu L, Orlando EF, Watanabe KH, Sepulveda M, Villeneuve DL, Perkins EJ, Ankley GT, Denslow ND. 2009. Gene expression responses in male fathead minnows exposed to binary mixtures of an estrogen and anti-estrogen. BMC Genomics. 10:308

110. Bannon DI, Dillman JF, Hable MA, Phillips CS, Perkins EJ. 2009. Global Gene Expression in Rat Brain and Liver after Oral Exposure to the Explosive Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX). *Chem. Res. Toxicol.*, 22(4):620-5

111. Ankley, Bencic D, Breen M, Collette T, Conolly R, Denslow N, Ekman D, Jensen K, Lazorchak J, Martinovic D, Miller D, Perkins E, Orlando E, Garcia-Reyero N, Villeneuve D, Wang R, Watanabe K. 2009. Endocrine-Disrupting Chemicals in Fish: Developing Exposure Indicators and Predictive Models of Effects based on Mechanism of Action. Aquat Toxicol. 2009 92(3):168-78

112. Quinn Jr MJ, Bazar MA, McFarland CA, Perkins EJ, Gust KA, Johnson MS. 2009. Sublethal Effects of Subacute Exposure to RDX (1,3,5-trinitro-1,3,5-triazine) in the Northern Bobwhite, *Colinus virginianus*. *Environ. Toxicol. Chem*. 10:2202-7.

113. Pirooznia M, Gong P, Yang JY, Yang MQ, Perkins EJ, Deng Y. 2008. ILOOP--a web application for two-channel microarray interwoven loop design. BMC Genomics. 9 Suppl 2:S11.

114. Pirooznia M, Perkins EJ, Deng Y. 2008. Batch Blast Extractor: an automated blastx parser application. BMC Genomics. 9 Suppl 2:S10.

115. Pirooznia M, Habib T, Perkins EJ, Deng Y. 2008. GOfetcher: A Database with Complex Searching Facility for Gene Ontology. Bioinformatics. 24(21):2561-3

116. Poynton HC, Loguinov AV, Varshavsky J, Chan S, Perkins EJ, Vulpe CD. 2008. Gene Expression Profiling in *Daphnia magna* Part 1: Concentration Dependent Profiles Provide Support for a No Observed Transcriptional Effect Level. Environ. Sci Technol. 42(16):6250-6.

117. Poynton HC, Zuzow R, Loguinov AV, Perkins EJ, Vulpe CD. 2008. Gene expression profiling in *Daphnia magna* Part II: Validation of a copper specific gene expression signature with effluent from two copper mines in California. Environ. Sci Technol. 15;42(16):6257-63.

118. Li B, Shang L, Marcus MS, Clare TM, Perkins E, Hamers RJ. 2008. Chemoselective Nanowire Fuses: Chemically Induced Cleavage and Electrical Detection of Carbon Nanofiber Bridges. *Small* 4(6):795-801.

119. Perkins E, Garcia-Reyero N, Villeneuve DL, Martinovic D, Brasfield SM, Blake LS, Brodin J, Denslow ND, Ankley GT. 2008. Perturbation of Gene expression and steroidogenesis with in vitro exposure of fathead minnow ovaries to ketoconazole. Mar. Environ. Res 66(1):113-5.

120. Gong P, Guan X, Inouye LS, Deng Y, Pirooznia M, Perkins EJ. 2008 Transcriptomic analysis of RDX and TNT interactive sublethal effects in the earthworm *Eisenia fetida BMC Genomics*, **9** (Suppl 1):S15 (20 March 2008).

121. Gong P, Escalon BL, Hayes CA, Perkins EJ. 2008. Uptake of hexanitrohexaazaisowurtzitane (CL-20) by the earthworm Eisenia fetida through dermal contact. Sci Total Environ. 2008 Feb 1;390(1):295-9. Epub 2007 Nov 8.

122. Gong P, Guan X, Inouye LS, Pirooznia M, Indest K, Athow R, Deng Y, Perkins EJ. 2007. Toxicogenomic Analysis Provides New Insights into Molecular Mechanisms of the Sublethal Toxicity of 2,4,6-Trinitrotoluene in *Eisenia fetida*. Environ Sci Technol. 41(23):8195-202.

123. Quinn MJ, Bazar M, McFarland C, Perkins E, Gust K, Gogal RM, Johnson RM. 2007.Effects of subchronic exposure to 2,6-dinitrotoluene (DNT) in the northern bobwhite (*Colinus virginianus*). Environ Toxicol Chem. 26:2202-2207

124. Li P, Zhang C, Perkins EJ, Gong P, Deng Y. 2007. Comparison of PBN and DBN Approaches for Inferring Gene Regulatory Networks. BMC Bioinformatics. Nov 1;8 Suppl 7:S13

125. Perkins EJ, Gust K, Steevens J. 2007. Toxicogenomic assessment of the population level impacts of contaminants. Integr Environ Assess Manag, 3:559-566

126. Pirooznia M, Gong P, Guan X, Athow R, Inouye L, Yang K, Perkins EJ, Deng Y. 2007. Analysis and Functional Annotation of Expressed Sequence Tags from the Earthworm Eisenia fetida. BMC Bioinformatics Nov 1;8 Suppl 7:S7

127. Marcus MS, Shang L, Li B, Streifer JA, Beck JD, Perkins E, Eriksson MA, Hamers RJ. 2007. Dielectrophoretic manipulation and real-time electrical detection of single nanowire bridges in aqueous saline solutions. Small. 3 (9):1610-1617

128. Johnson MS, Quinn MJ, Bazar MA, Gust KA, Escalon BL, Perkins EJ. 2007. Subacute toxicity of oral 2,6-dinitrotoluene and 1,3,5-trinitro-1,3,5-triazine (RDX) exposure to the northern bobwhite (*Colinus virginianus*). Environ Toxicol Chem. 26:1481-7.

129. Gong P, Inouye L, Perkins E. 2007. Comparative neurotoxicity of two energetic compounds, CL-20 and RDX, in the earthworm Eisenia fetida. Environ Toxicol Chem. 2007 26:954-9.

130. Poynton HC, Varshavsky JR, Chang B, Cavigiolio G, Chan S, Holman PS, Loguinov AV, Bauer DJ, Colbourne JK, Komachi K, Theil EC, Perkins EJ, Hughes O, and Vulpe CD. 2007. Daphnia magna Ecotoxicogenomics Provides Mechanistic Insights into Metal Toxicity. Environ Science Technol. 41:1044-50.

131. Wintz H, Yoo LJ, Loguinov A, Wu YY, Steevens JA, Holland RD, Beger RD, Perkins EJ, Hughes O, Vulpe CD. 2006. Gene expression profiles in fathead minnow exposed to 2,4-DNT: correlation with toxicity in mammals. Toxicol Sci. 2006 94:71-82.

132. Perkins EJ, Bao W, Guan X, Ang CY, Wolfinger RD, Chu TM, Meyer SA, Inouye LS 2006. Comparison of transcriptional responses in liver tissue and primary hepatocyte cell cultures after exposure to hexahydro-1, 3, 5-trinitro-1, 3, 5-triazine. *BMC Bioinformatics*. 7 Suppl 4:S22.

133. Ankley GT, Daston GP, Degitz SJ, Denslow ND, Hoke RA, Kennedy SW, Miracle AL, Perkins EJ, Snape J, Tillitt DE, Tyler CR, Versteeg D. 2006. Toxicogenomics in regulatory ecotoxicology. *Environ Sci Technol*. 40(13):4055-65.

134. Elderkin, CL, Perkins EJ, Leberg PL, Klerks PL, and Lance R F (2004) Amplified fragment length polymorphism (AFLP) analysis of the genetic structure of the zebra mussel, *Dreissena polymorpha*, in the Mississippi River. Freshwater Biology 49: 1487-1494.

135. Perkins E, Furey J, Davis E. 2004. The Potential of Screening for Agents of Toxicity Using Gene Expression Fingerprinting in *Chironomus tentans*. *Aquatic Ecosys Health Man* 7:399-406.

136. Perkins E, Lotufo G. 2003. Playing in the mud- using gene expression to assess contaminant effects on sediment dwelling invertebrates. *Ecotoxicology* 12:453-456.

137. Perkins E, Streever WJ, Davis E, Fredrickson H.L. 2002. Development of amplified fragment length polymorphism markers for *Spartina alterniflora. Aquatic Botany* 1582:1–11

138. Perkins EJ. 2001. Enhanced detection of multiplex PCR products using SYBR Green I and an automated DNA sequencer. *BioTechniques* 31(2)278-280

139. Fredrickson H, Perkins E, Bridges T, Tonucci R, Fleming J, Nagel A, Diedrich K, Mendez-Tenorio A, Doktycz M, Beattie K. 2001. Towards environmental toxicogenomics: development of a flow-through, high-density DNA hybridization array and its application to ecotoxicity assessment. *Science Tot Environ*, 274:137-149

140. Ringelberg D, Talley JW, Perkins EJ, Tucker SG, Luthy R, Bouwer EJ, Fredrickson HL. 2001. Succession of Phenotypic, Genotypic and Metabolic Community Characteristics During the in vitro Bioslurry Treatment of PAH-Contaminated Sediments, *Appl Env Microbiol* 67:1542-50

141. Pennington JC, Brannon J, Gunnison D, Harrelson D, Zakikhani M, Miyares P, Jenkins T, Clarke J, Hayes C, Ringelberg D, Perkins E, Fredrickson H. 2001. Monitored natural attenuation of explosives. *Soil Sed Contam*, 10:45-75.

142. Perkins EJ, Gordon M, Cacares O, Lurquin P. 1990. Organization and sequence analysis of the 2,4-dichlorophenol hydroxylase and chlorocatechol oxidative operons of the plasmid pJP4. *J. Bacteriol* 172:2351-2359.

143. Perkins E, Bolton G, Gordon M, Lurquin P. 1988. Partial nucleotide sequence of the chlorocatechol degradative open tfdCDEF and similarities to promoters of the chlorinated aromatic degradative operons tfdA and clcABD. *Nucl. Acids Res*. 16:7200.

144. Perkins E, Lurquin P. 1988. Duplication of a 2,4-D monooxygenase gene on the plasmid pJP4. *J. Bacteriol*. 170:5669-5672.

145. Perkins E, Stiff C, Lurquin P. 1987. Use of *Alcaligenes eutrophus* as a source of genes for 2,4-D resistance in plants. *Weed Sci*. 35:12-18.

146. Rebeiz CA, Wu SM, Kuhadja M, Daniell H, Perkins EJ. 1983. Chlorophyll a biosynthetic routes and chlorophyll a chemical heterogeneity in plants. Mol Cell Biochem. 1983;57(2):97-125.

BOOK CHAPTERS:

1. Watanabe-Sailor K H, H Aladjov, S M Bell, L Burgoon, W-Y Cheng, R Conolly, S W Edwards, N Garcia-Reyero, ML Mayo, A Schroeder, C Wittwehr and EJ Perkins. 2019.Big Data Integration and Inference, in *Big Data in Predictive Toxicology. Royal soc. Chemistry. ISBN:* 978-1-78262-298-7
2. Perkins E, Garcia-Reyero N. 2013. Computational Translation of Non-Mammalian Species Data to mammalian species to meet REACH and Next generation risk assessment needs. In *Computational toxicology: Applications for risk assessment.* Springer
3. Garcia-Reyero N, Perkins E. 2010. The endocrine disruption forecast: are adverse effects predictable? Book Chapter in *Recent advances in fish reproduction biology*. 191-226 ISBN: 978-81-308-0397-5.
4. Chaitankar V, Zhang C, Ghosh P, Gong P, Perkins EJ, Deng Y. 2010. Predictive Minimum Description Length Principle Approach to Inferring Gene Regulatory Networks. In *Software Tools and Algorithms for Biological Systems*. Springer
5. Perkins E, Denslow D, Chipman K, Guiney PD, Oris J, Poynton H, Robidoux PY, Scroggins R, Van Der Kraak G. 2007. Application of Genomics to Assessment of the Ecological Risk of Complex Environmental Mixtures, in Toxicogenomics in Ecological Risk Assessment. Ankley GT, Miracle A, Perkins EJ, Daston GP. (Eds.) Taylor and Francis, SETAC Press.
6. Ankley GT, Miracle A, Perkins EJ, Daston GP (Eds.) 2007. Toxicogenomics in Ecological Risk Assessment. Taylor and Francis, SETAC Press.
7. Ringelberg D, Perkins E, Hansen L, Talley J, Fredrickson H. 1999. Relating biodegradation potentials to in-situ microbial community composition. In: B.C. Alleman and A. Leeson (eds.) *In Situ Bioremediation of Petroleum Hydrocarbons and Other Organic Compounds,* Battelle Press, Columbus, OH. 545-550.

Other publications

1. Wade R, Lotufo GR, Steevens JA, Houston JG, Fredrickson HL, Perkins EJ, Morrow AB, Weiss CA, Furey JS, Felt D, Duke M, Talley JW. 2002. Assessment of DDT Bioavailability in the Little Sunflower River Sediment and Agricultural Soil. ERDC TR -02-6, U.S. Army Engineer Research and Development Center, Vicksburg, MS.
2. Perkins E, Fredrickson H, Lotufo G. 2002. Development of a Rapid, inexpensive bioassay for screening contaminant bioavailability in sediment using mRNA profiling. EEDP Technical Notes collection (ERDC/TN EEDP-04-34, December 2002, U.S. Army Research and Development Center, Vicksburg, MS.
3. Streever W, Perkins E. 2000. Importing Plant Stock for Wetland Restoration and Creation: Maintaining Genetic Diversity and Integrity. ERDC TN-WRAP-00-03, U.S. Army Engineer Research and Development Center, Vicksburg, MS.

4. Pennington, JC, Brannon J, Gunnison D, Harrelson D., Jenkins T, Reynolds M, Zakikhani M, Clarke J, Coffin R, Fredrickson H, Hayes C, McGrath C, May J, Miyares P, Meyers T, Perkins E, Ringelberg D, Townsend D. 1999. Natural attenuation of explosives in soil and water systems at Department of Defense sites: Interim report. Technical report, U.S. Army Engineer Waterways Experiment Station, Vicksburg MS
5. Inouye L, McFarland V, Perkins E. 1999. Development of a Transgenic Model to Assess Bioavailable Genotoxicity in Sediments. Dredging Research Technical Note EEDP-01-43 Waterways Experiment Station, Vicksburg, MS.
6. Fredrickson, H., D. Gunnison, E. Perkins, and D. Ringelberg. 1999. Screening assays for assessing the bioreclamation of dredged materials. DOER Technical note collection (TN DOER-C4) U.S. Army Engineer Research and Development Center, Vicksburg, MS.
7. Pennington,J.C., D.Harrelson, M. Zakikhani, D.Gunnison, J.U.Clarke, C.McGrath, H.Fredrickson, J.M.May, E.Perkins, C.Hayes, and D. Ringelberg. 1998. Feasibility of using natural attenuation as a remedial alternative for explosives-contaminated groundwater at site L1, Joliet Army Ammunition Plant, Joliet Illinois. Prepared for U.S. Army Industrial Operations Command, Rock Island, IL, Technical report EL-98-8