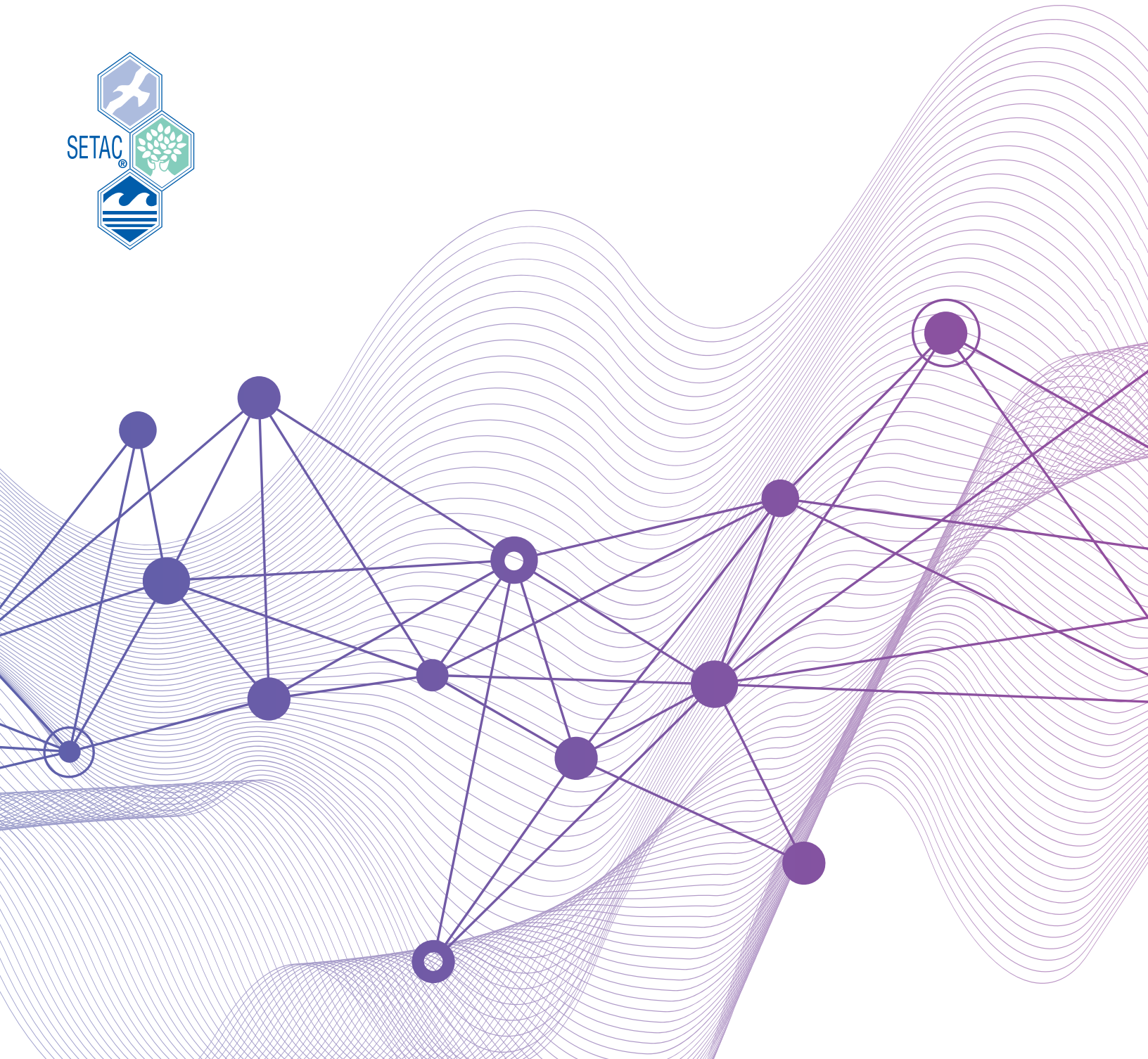
ABSTRACT BOOK

Advanced Approaches for Species Surrogacy in Chemical Risk Assessment

1–2 November 2026 • Montreal, Quebec

Toward a Weight of Evidence Approach for Cross Species Extrapolation



Abstract Book

Advanced Approaches for Species Surrogacy in Chemical Risk Assessment
SETAC Topical Symposium

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This book comprises the abstracts from the Society of Environmental Toxicology and Chemistry (SETAC) Topical Symposium on Advanced Approaches for Species Surrogacy in Chemical Risk Assessment, conducted from 1–2 November 2026 in Montreal, Quebec.

The abstracts are reproduced as accepted by SETAC staff and the program committee. They appear in order of abstract number per session. The presenting author of each abstract is highlighted in bold.

International Standard Serial Number 1087-8939

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About the Abstract Book

The titles, authors and abstracts of the presentations given at the meeting are summarized in this book. Acknowledgments and disclosures are not included for space considerations, though we recommend that authors include them in the presentations themselves. Abstracts are not peer-reviewed and therefore should not be cited.

For further information, contact one of our offices:

SETAC Africa
SETAC Europe
Avenue des Arts, 53
B-1000 Brussels, Belgium
T +32 2 772 72 81
E setac@setac.org

SETAC Latin America
SETAC North America
712 H Street NE, Suite 1889,
Washington, DC, USA
T +1 202 677 3001
E setac@setac.org

SETAC Asia-Pacific
2/290 Boundary Street, Spring Hill,
Brisbane, QLD 4000 Australia
ABN: 37 689 850 262
E setac@setac.org

www.setac.org

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Session 1: Toxicokinetics Across Species

1 Exploring Inter-Species Differences in Biotransformation Rates using In Vitro, In Vivo and In Silico Data

***Jon Arnot**, ARC Arnot Research and Consulting Inc., Alessandro Sangion, ARC Arnot Research and Consulting Inc., Aaron Redman, ExxonMobil Biomedical Sciences, Michelle Embry, Health and Environmental Sciences Institute*

Reliable toxicokinetic (TK) data are essential for bioaccumulation, exposure and risk assessment, interspecies toxicity extrapolation, and the in vitro–in vivo extrapolation (IVIVE) of New Approach Method (NAM) bioactivity data. However, in vivo TK data across species are limited and costly to generate, creating substantial uncertainty in chemical evaluations and hindering efforts to reduce animal testing. For many organic chemicals, the biotransformation half-life (HLB) is a key determinant of the total elimination half-life (HLT), yet interspecies similarities and differences in HLB and estimation methods remain poorly understood. This research compiled, critically evaluated, and compared biotransformation data for fish, rodents, and humans generated using in vivo, in vitro, and in silico approaches. More than 22,500 in vitro rates from hepatocyte, liver microsomal, and liver S9 assays for humans, rats, mice, and fish were evaluated for data quality. Approximately 680 new rodent in vivo HLB values were estimated from critically evaluated HLT data and compared with existing human (~913 chemicals) and fish (~628 chemicals) HLB data and OECD-validated HLB-QSARs for humans (n=5) and fish (n=6). This work provides the foundation for an Integrated Approach to Testing and Assessment (IATA) that systematically addresses uncertainty in biotransformation estimates and interspecies extrapolation.

2 Biodegradable Polymer Systems as Cross-Species Proxies for Microplastic Exposure and Fate in Soil Ecosystems

***Arya Upadhyay**, University of Texas at Austin*

Understanding how microplastics interact with diverse soil organisms remains a major challenge in chemical risk assessment due to species-specific variability in exposure and response. This study proposes biodegradable polymer systems as standardized surrogates to model microplastic fate and bioavailability across species. Thin films composed of polylactic acid, polyglycolic acid, and polycaprolactone were deployed in controlled soil environments to quantify degradation behavior under varying microbial activity. Structural integrity, mass loss, and fragmentation were tracked over time to approximate the physical transformation pathways of microplastics. These metrics were integrated with a predictive framework to estimate exposure likelihood across representative soil organisms with differing ecological traits. Results indicate that degradation rates and fragmentation patterns are strongly mediated by microbial density and polymer composition, suggesting that material-specific behavior can serve as a proxy for microplastic persistence and transport. By linking polymer degradation dynamics to functional traits such as feeding strategy and habitat depth, this approach provides a scalable method for extrapolating exposure across species without requiring organism-specific testing. This framework supports the development of surrogate-based models for chemical risk assessment, enabling more efficient evaluation of microplastic impacts in complex soil ecosystems while reducing reliance on species-by-species toxicity studies.

3 A Read-Across Approach Using Fish and Mammalian Toxicokinetic and Toxicity Data to Evaluate Reproductive Toxicity Risk in Fish for a Pharmaceutical

***Michael Lee**, Eli Lilly and Company, Alison Perkins, Eli Lilly and Company*

Teratogenicity is a known class effect of Bruton's tyrosine kinase (BTK) inhibitors, and BTK orthologs are present in fish and some invertebrates. During the environmental risk assessment (ERA) of pirtobrutinib, a BTK inhibitor for relapsed/refractory mantle cell lymphoma, the EMA requested additional information on potential reproductive effects in fish. Standard ERA indicated negligible risk (predicted environmental concentration [PEC] 0.0094 μg/L; risk quotient 0.0002; no effects in an OECD 210 fish early-life-stage

[FELS] study up to ≥9950 µg/L). To address the reproductive concern directly, we applied a read-across from the extensive mammalian toxicity dataset to fish, anchored on internal exposure. A fish toxicokinetic study (adult fathead minnow, 160 and 2500 µg/L) measured plasma and whole-body concentrations; measured plasma was 16- to 100-fold below Fish Plasma Model predictions and whole-body concentrations indicated bioconcentration factors were ≤1 L/kg. Mammalian internal exposures at reproductive effect levels (rat embryo-fetal development NOEL and LOEL; repeat-dose studies with no reproductive or endocrine organ effects) and human therapeutic plasma were compared against fish plasma at the PEC. Internal exposures producing effects in mammals exceeded fish internal exposure at the PEC by ~4.7×105, and FELS embryos were directly exposed to ~1×109 times the PEC without toxicity or teratogenicity across organogenesis. Because FELS evaluates only waterborne and chorionic exposure, maternal transfer was also considered; producing in ovo concentrations equivalent to the mammalian effect level would require water concentrations exceeding the limit of solubility. Read-across integrating fish and mammalian toxicokinetic and toxicity data alleviated the regulatory concern for reproductive toxicity in fish, illustrating how mechanistic target conservation plus internal-dose comparison can extrapolate mammalian hazard information across a large taxonomic gap.

Session 2: Toxicodynamics and Pathway Conservation

4 Which Fish? Comparative Receptor Pharmacology and Toxicokinetics for Selecting and Interpreting a Fish Full-Life Cycle Study with an Estrogen Receptor Degrader

***Michael Lee**, Eli Lilly and Company, Alison Perkins, Eli Lilly and Company*

Imlunestrant is a potent, selective estrogen receptor alpha (ERα) degrader approved for breast cancer. To evaluate environmental risk, EMA effectively requires a fish full-life cycle study (FFLC). Draft and validated FFLC guidelines vary in recommended fish species but don't consider underlying biology. Since physiological roles of ER and pharmacological specificity vary between fish species, we asked which species is most sensitive to imlunestrant. In vitro reporter-gene assays characterized potency at three ER subtypes (ESR1, ESR2a, ESR2b) across three fish species in agonist and antagonist mode. No subtype showed agonism; ESR2b was ~7-fold more potent than other subtypes and most potent to fathead minnow. In vivo adult reproductive assays confirmed fathead minnow was more sensitive (≥10-fold). The FFLC was conducted with fathead minnow alongside a complementary toxicokinetics study. Apical effects (primarily increased weight in males) occurred mainly at the highest doses. Diagnostic endpoints revealed vitellogenin induction and Leydig cell hyperplasia in males, while females showed a non-significant decrease in vitellogenin – responses that appear estrogenic, but are mechanistically antagonistic. In males ER antagonism disinhibits hypothalamic-pituitary-gonadal feedback, driving an aromatized testicular estradiol surge; while ovarian estradiol is reduced in females. Receptor pharmacology supports male vitellogenin induction as antagonism-driven, not agonistic. Sex-divergent toxicokinetics explain the predominant male response. The comparative pharmacology demonstrates a mechanism-based species surrogate selection within a taxon, the complement to extrapolating hazard across taxa.

5 Transcriptomic Assay Assesses Hazard of 6PPD-Quinone to Fish Species-At-Risk

***Ryan Chui**, McGill University, Janet Cermak, Florence Pagé-Larivière, Allison Dunn, Rebecca Dalton Environment and Climate Change Canada, Kristin K. Mueller, Ministère de l'Environnement, de la Lutte contre les changements climatiques, de la Faune et des Parcs, Aylish Marshall, Emily Boulanger, Hugo Marchand, Jessica Head, McGill University*

Transcriptomic novel approach methodologies can support the assessment of emerging contaminants by quickly producing hazard data. Hazard data for 6PPD-Quinone, a degradation product of a key constituent of tires and contaminant of emerging concern. Here, we combine early-life stage fish assays and transcriptomic benchmarking to rapidly test the toxicity of 6PPD-Quinone in fish species of interest. Our study included model species, as well as species at risk that are native to Canada. Eleutheroembryos (<24 hours post-hatch) for each species were exposed for 24-hours across 12 concentrations of 6PPD-Quinone. We designed the dose-

range to capture mortality and concentrations at which no transcriptomic response was expected. Mortality was noted and surviving eleutheroembryos were pooled (n = 3 per concentration) prior to RNA extraction and sequencing. Sequenced RNA fragments were aligned to a curated fish protein database using Seq2Fun to obtain count tables. Dose-responsive genes were then modelled to obtain a benchmark dose for each of them. Benchmark doses were used to derive the concentration at which significant molecular changes occur, hereafter known as the transcriptomic point-of-departure (tPOD). The first peak of the distribution of logged-transformed benchmark doses was used as the tPOD. Acute 24-hour LC50s were obtained for two species, rainbow trout (Oncorhynchus mykiss; 5.6 µg/L, all concentrations hereafter in nominal) and chinook salmon (Oncorhynchus tshawytscha; 9048 µg/L). tPODs were obtained for four species, rainbow trout (0.00528 µg/L), chinook salmon (34.9 µg/L), zebrafish (Danio rerio; 0.607 µg/L) and copper redhorse (Moxostoma hubbsi; 0.135 µg/L). No tPODs were obtained for Atlantic salmon (Salmo salar), and river redhorse (Moxostoma carinatum). Notably, the tPODs of rainbow trout, zebrafish and copper redhorse are below the concentrations detected in some environments, raising concerns as more tire-wear particles are washed into their habitat. Our study demonstrates that transcriptomic approaches can be combined with early-life stage fish assays to quickly generate hazard data for a variety of fish species, including species-at-risk. With further validation, these data, such as the tPOD for copper redhorse, could become part of the weight-of-evidence for rapid prioritization, and even maybe for the risk assessment, of these emerging contaminants.

6 Semantic Similarity Analysis of Developmental Zebrafish Transcriptomes to Support Pathway-Based Species Surrogacy

Lindsey St. Mary*, Exponent Inc., Ryan McClure, Pacific Northwest National Laboratory (PNNL), Lisa Truong, Oregon State University (OSU), Steven J. Carrell, Oregon State University (OSU), Katrina M. Waters, Pacific Northwest National Laboratory (PNNL), Robyn L. Tanguay, Oregon State University (OSU)*

Species surrogacy in chemical risk assessment requires confidence that toxicodynamic pathways observed in model organisms are relevant across taxa. We used phenotypically anchored transcriptomics in developing zebrafish to evaluate 45 structurally diverse agrichemicals from U.S. EPA ToxCast libraries. Embryos were exposed from 6 to 120 hours post fertilization, morphological outcomes were scored at 120 hours, and RNA sequencing was conducted at 48 hours, linking early transcriptional perturbations to later adverse developmental outcomes through a phenotypic anchoring approach based on concentrations causing effects in 60-80% of animals at 120 hours. Agrichemicals produced highly chemical-specific transcriptional profiles, yet these responses converged on shared biological processes including neurodevelopment, cytoskeletal organization, and GTPase-mediated signaling. Semantic similarity analysis reduced 726 enriched gene ontology terms into 45 biologically interpretable parent categories and revealed 409 pathway associations not represented in existing data found in the Comparative Toxicogenomics Database (CTD). The strong convergence of diverse chemicals on conserved developmental pathways suggests that phenotypically anchored zebrafish transcriptomics can capture biologically relevant toxicodynamic responses that may be applicable across species. Collectively, these findings support the use of developmental zebrafish as a species surrogate for identifying conserved mechanisms of toxicity, demonstrating how phenotypically anchored transcriptomics can strengthen pathway-based cross-species extrapolation and inform next-generation chemical risk assessment.

7 Developing a Soil Nematode System as a Predictive Surrogate Platform for Mammalian Gut Barrier Vulnerability to Metabolic Toxicity

Ki-Hyung Kim, Pusan National University, Juil Kim, Pusan National University, ***Yuseok Moon****, Pusan National University*

Modern chemical safety assessment requires a paradigm shift from traditional in vivo rodent testing toward predictive, cost-effective New Approach Methodologies. The complex intestinal interface, which coordinates nutrient processing, barrier maintenance, and cellular energy homeostasis, is a major target for environmental and metabolic toxicants. However, high-throughput screening of gut-metabolic disruption remains highly challenging due to the lack of physiological, non-mammalian surrogate systems with conserved chemical-

sensing pathways. To address this methodological gap, we evaluated the soil nematode Caenorhabditis elegans as an alternative, non-vertebrate surrogate platform for assessing chemical-induced gut-barrier and metabolic distress. We focused on characterizing how a highly conserved xenobiotic receptor—the ancestral counterpart to mammalian environmental sensors—coordinates intestinal resilience under physiological stress. Utilizing wild-type and xenobiotic receptor-deficient nematode strains, we monitored changes in epithelial permeability, microbial colonization, and mitochondrial superoxide generation under modulated metabolic demands. Our assays demonstrated that functional activation of the conserved xenobiotic receptor is essential to protect the gut against cellular damage. In receptor-deficient models, metabolic stress triggered acute epithelial breakdown, resulting in marked structural leaking, high susceptibility to opportunistic bacterial colonization, and severe mitochondrial redox failure. Conversely, intact xenobiotic receptor signaling successfully preserved barrier homeostasis and mitochondrial efficiency. These results demonstrate that the nematode xenobiotic receptor operates as a critical biological sensor integrating metabolic stress with barrier protection. By demonstrating the functional conservation of this toxicological pathway, this work validates the soil nematode as a reliable, animal-free species surrogate for predicting mammalian gut barrier vulnerability. Integrating this in vertebrate platform into early-stage chemical risk assessment provides a scalable, high-throughput approach for screening environmental compounds that disrupt mammalian immunometabolic and barrier integrity.

8 Challenges in Species Surrogacy – A 6PPD-Quinone Case Study

***Markus Hecker**, Junyi Lin, Catherine Roberts, Alper James Alcaraz, Markus Brinkmann*

Species surrogacy underpins ecological risk assessment by extrapolating hazards across species based on the assumption of conservation of biological processes and associated vulnerabilities. Mechanism-based new approach methods (NAMs) aim to reduce some of the uncertainties associated with traditional species extrapolation approaches that can rely on order-of-magnitude safety factors. Using N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine-quinone (6PPD-quinone), a recently identified contaminant of emerging concern, as a case study, we illustrate both the limitations of traditional species surrogacy and the opportunities NAMs may provide to address them. 6PPD-quinone is one of the most toxic chemicals known to fish, an observation that would have been overlooked by traditional, surrogacy-dependent standard fish toxicity tests. This study employed quantitative whole-body transcriptomics approach to characterize molecular responses to 6PPD-quinone across early life stages of four fish species with contrasting sensitivity. Transcriptomic dose-response modeling was used to derive transcriptomic points of departure (tPOD) for each species, yielding molecular effect thresholds. Sensitive species (lake trout and rainbow trout) had significantly lower tPODs insensitive species (brown trout and largemouth bass), consistent with previously reported apical toxicity thresholds. Sensitive species had the greatest number of significantly enriched pathways, primarily related to immune and inflammatory response and cell death processes, whereas insensitive species only displayed changes in energy metabolism. This work highlights the potential of quantitative transcriptomics in fish embryo models for identifying susceptible species while being protective and predictive of acute and sub-chronic toxicity.

Session 3: Ecological and Organismal Traits

9 Implications of Population Vital rates for the Use of Surrogate Species in Ecological Risk Assessment

***John D. Stark**, Washington State University, WA, John E. Banks, California State University, Monterey Bay, CA*

The USEPA often develops ecological risk assessments for pesticides using toxicity data developed for surrogate species. Surrogate species are a small number of species that are supposed to be representative of other species in their response to toxic insult. Examples include cladocerans in the family Daphniidae that are used to represent all aquatic invertebrates, rainbow trout or fathead minnow data that represent all fish and amphibian species, and Bobwhite quail or Mallard ducks that are used to represent all birds and reptiles. Additionally, the honeybee is used to represent all insects. All too often, these surrogate species are used because they are easy to rear in the laboratory rather than being particularly representative of other species. Although vast differences in toxicokinetics and toxicodynamics have been identified even among closely

related species, we argue that another critical factor that should be considered in risk assessments are differences among population vital rates such as time to first reproduction, number of broods, number of offspring produced per female, generation times, death rates, longevity, and population growth rates. Differences in vital rates can make one species much more resilient to stress than other species, which in turn can influence the assessment of chemical risk. In this study, we will present population models of fish and cladoceran species that show how important differences in vital rates are in terms of ecological risk assessment, and how they should be incorporated in the development of ecological risk assessment.

10 Developing a Framework For Identifying Sentinel Taxa for the Non-Target Arthropod Risk Assessment Using Field Effect Studies – A Case Study with Carabidae

***Charlotte Elston**, Syngenta, Saskia Aldershof, Bioresearch & Evaluation, Ed Pilling, Corteva Agriscience, Frank Bakker, Bakker Onderzoeks Beheer*

Non-target arthropod (NTA) field studies represent the highest tier of study available in the tiered regulatory process. Field studies have the highest degree of realism, but also a high degree of variability and unlike higher tier bee studies, NTA field studies are conducted with naturally occurring populations of multiple species. This results in large, complex datasets involving hundreds of different taxa with differing compositions,abundances and phenologies, as a result these studies can be difficult to interpret and ascertain what is a potential effect of a plant protection product (PPP) on populations and communities versus natural background and seasonal variability. We have compiled an NTA field effect database and its analysis represent a powerful resource for the development of the future risk assessment scheme for NTAs. In the first instance, it allows to derive recommendations for future field trial design and for its data analysis and interpretation. Further, the identification of sentinel taxa is not only relevant for the evaluation of field effect studies but also for the development of ecological models. Considering the spatial and temporal scale of NTA field studies and the number of taxa that are observed, ecological models are expected to gain in importance in the future NTA higher tier risk assessment in Europe. As it will not be feasible to develop models for all taxa potentially present in an area, a framework to understand the key representative taxa is therefore essential for model development. In addition, the database is valuable for analysing the spatial and temporal variability of taxa or ecological traits, thus making it a valuable resource for establishment of Normal Operating Ranges or/and Specific Protection Goals. We present a case study using Carabidae ground beetles, highlighting both the challenges of identifying sentinel taxa but also possible solutions including pooling of species based on analysis of traits and chemical sensitivity.

11 Trait-Based Clustering of North American Lepidoptera to Support Ecological Risk Assessment

*Paul Glaum, Waterborne Environmental, Maura Roberts, Waterborne Environmental, Eric Peterson, Syngenta, **Maxime Vaugeois**, Syngenta*

Ecological risk assessment (ERA) often requires extrapolation from limited species-specific ecotoxicological data, particularly for listed or data-poor taxa. This challenge is particularly relevant for Lepidoptera, a diverse group of ecologically important pollinators and herbivores that may be exposed to plant protection products across different life stages, habitats, and host-plant associations, and that represents 42% %) of all threatened and endangered terrestrial arthropod species in the United States. In this work, we developed a trait-based analysis to organize North American Lepidoptera species into ecologically relevant groups that can support ERA. We compiled trait data from LepTraits database and supplemented these records with a cropland association metric derived from Global Biodiversity Information Facility occurrence records and land cover data. After filtering for data completeness, ecological relevance, and reduced collinearity, six traits were retained for 376 species: flight period start, flight period end, host-plant family number, cropland association, upper wingspan, and voltinism. We applied k-prototype clustering to accommodate mixed quantitative and ordinal data and used Factor Analysis of Mixed Data to visualize and corroborate cluster structure. Three clusters were identified, with flight phenology, diet breadth, and voltinism contributing most strongly to group separation. The clusters distinguished species with more constrained flight periods and lower cropland association from

multivoltine species with extended phenology and greater association with agricultural landscapes, as well as a smaller group of larger-bodied, broad-diet species. Cluster membership and proximity to cluster centroids provide a reproducible way to identify ecologically representative species or trait profiles for further evaluation. However, ecological similarity should not be interpreted as toxicological equivalence without additional sensitivity, toxicokinetic-toxicodynamic, and exposure-response information. This framework demonstrates how unsupervised learning and trait data can improve transparency in species organization and help structure ecological reasoning for data-poor or listed Lepidoptera in ecological risk assessment.

Session 4: Integration of Existing Data

12 Bio-QSARs: Enhancing Ecotoxicity Predictions for Untested Species

Jochen Zubrod, Zubrod Environmental Data Science, Nika Galic, Syngenta, ***Maxime Vaugeois****, Syngenta*

Estimating chemical-induced effects across diverse taxa without species-specific testing poses a significant challenge in the ecological risk assessment of agrochemicals, particularly for species listed under the Endangered Species Act (ESA). To address this, we introduced the Bio-QSAR concept for multispecies toxicity predictions. This approach aims to overcome limitations of traditional machine learning-based quantitative structure-activity relationship (QSAR) approaches by incorporating biological information, such as taxonomic distances and physiological features. While physiology is known to drive species sensitivity, understanding the relative contribution of specific underlying processes remains elusive. Our study aimed to utilize existing knowledge about organismal physiology and phylogeny to both understand and predict differences in species sensitivity. We trained machine learning models to predict chemical- and species-specific endpoints using chemical fingerprints/descriptors and physiological variables, including dynamic energy budget (DEB) properties, life history traits, and taxonomic/phylogenetic relationships. Initially, we used publicly available data from the EnviroTox database, with ToxPrints and DEB parameters as predictor variables for chemistry and physiology, respectively. We then broadened the models' applicability by increasing species diversity, incorporating life history traits and taxonomic/phylogenetic relationships, and supplementing the models with broadened ecotoxicology data from EnviroTox database. Bio-QSAR models demonstrate the capability for flexible cross-chemical and cross-species predictions beyond the levels present in the training data while meeting criteria for consideration in regulatory contexts. This advanced approach holds significant promise for applications in environmental risk assessment and chemical research and development, particularly in the context of ESA.

13 Predicting Chemical Potency and Species Sensitivity to AhR2 Activation Across Phylogenetically Diverse Fishes using In Silico Approaches

Justin Dubiel*, University of Lethbridge, Cameron Collins, Louisiana State University, Fernando Calahorro Nunez, University of Southampton, Nic Bury, University of Southampton, Jon Doering, Louisiana State University, Steve Wiseman, University of Lethbridge*

Species can vary dramatically in sensitivity to activation of the aryl hydrocarbon receptor (AhR) by structurally diverse chemical pollutants. As a result, predictive tools referred to as quantitative adverse outcome pathways (AOPs) have been developed to link in vitro AhR activation to early life-stage mortality to aid in risk assessment. However, the in vitro assay used to generate model predictions still requires considerable time and resources to perform limiting the ability to perform mass screening. This research aims to leverage published data for activation of the AhR of fishes to develop a fully computational predictive model that, in combination with existing in vitro to in vivo predictive frameworks, can accurately predict early life-stage mortality. As the existing predictive frameworks are based on half maximal effect concentrations (EC50s) for AhR activation, an in silico model to predict these EC50s was developed. There was a significant correlation between in silico predicted EC50s and experimental EC50s for activation of the AhR2 by more than 50 ligands representing 6 chemical classes in over 20 species of fish ($R2 = 0.78$). Computationally derived EC50s were used as an input for the qAOP enabling predictions of early life-stage mortality to be made using purely in silico data with an

average accuracy of 4.4-fold, demonstrating the utility of integrating in silico methods into the AOP framework. This model represents an important advancement in predictive toxicology, enabling high-throughput generation of species-specific toxicity data for any AhR agonist in any fish species without the use of animals or cell-based assays and serves as proof of concept for future research with additional receptors.

14 Bridging Data Gaps in Terrestrial Insect Ecotoxicity Across Species and Experimental Variables

***Tom Purucker**, U.S. Environmental Protection Agency, Cassandra Strauch, Oak Ridge Institute for Science and Education, Gage Sachs, General Dynamics Information Technology, Matthew Etterson, U.S. Environmental Protection Agency, Kristina Garber, U.S. Environmental Protection Agency, Margaret Murphy, U.S. Environmental Protection Agency*

Terrestrial insects provide critical ecosystem services, yet their vulnerability to pesticides remains poorly characterized across taxa, endpoints, and test designs. We compiled an integrated terrestrial insect ecotoxicity database by curating and merging >50 years of data from USEPA's ECOTOXicology (ECOTOX) Knowledgebase and the Office of Pesticide Programs' Pesticide Ecotoxicity Database, yielding 120,034 records spanning 2,082 species and 2,262 chemicals. Nearly half of the records report mortality, though alternative measurement endpoints (e.g., navigation, oviposition behavior, thermal tolerance) have increased in recent years. The Western honey bee (Apis mellifera) is the most frequently tested species (18% of records). Using this dataset, we evaluated how organism size (weight), life stage (adult, larval), chemical grade (technical grade active ingredient, formulated end-use product), and exposure type (contact, oral) influence LD50 values. Body size and chemical grade were influential predictors: larger organisms had higher LD50s and formulated products were more toxic than technical-grade active ingredients. Exposure type had a minor effect, and life stage showed no consistent influence. Despite the large dataset, species sensitivity distributions and 5th percentile hazard concentration/dose (HC05) estimates were feasible for only 47 pesticides due to limited species coverage per pesticide, constraining broader interpretation of trends due to uneven data coverage. We further assessed how well A. mellifera represents the sensitivity of non-Apis pollinators and other terrestrial invertebrates across pesticide classes. A. mellifera generally exhibited median sensitivity relative to other taxa, but its variability across chemicals highlights substantial mode of action and species-level variability that has been linked to metabolic detoxication capacity, life history traits, and phylogeny differences. Collectively, this work delivers an accessible, reusable resource to support meta-analyses and provides an empirical basis for using A. mellifera as a surrogate, thereby strengthening terrestrial insect risk assessment by incorporating non-Apis data, applying taxonomic extrapolation or cross-species models where data are sparse, and supplying an initial basis for systematic literature reviews to better characterize risks for data-poor and listed species.

15 Leveraging Existing Aquatic Toxicity Data and Integrating Multiple Lines of Evidence to Evaluate Species Surrogacy for Asian Species

***Adriana C Bejarano**, ExxonMobil Biomedical Sciences Inc., Biyao Han, ExxonMobil Biomedical Sciences Inc.*

Chemical evaluations frequently rely on a limited number of surrogate species to characterize hazard for a broader range of taxa. However, uncertainty remains regarding the representativeness of standard test organisms for regionally important species used across regulatory frameworks. China and other countries in the Asia-Pacific region have increasingly incorporated data from native aquatic species into chemical registration and environmental management programs, creating an opportunity to quantitatively evaluate their relative sensitivity within a global context. This case study compiles aquatic toxicity data for Asian freshwater and marine species from regulatory and public databases, and compares species responses with those of standard and non-standard aquatic organisms commonly used in North America, Europe, and other jurisdictions. For chemicals with sufficient taxonomic coverage, species sensitivity distributions (SSDs) are developed to evaluate the relative placement of Asian species across diverse chemical classes and modes of action. These analyses leverage existing ecotoxicity data to assess the extent to which commonly tested surrogate species are protective of regionally relevant aquatic taxa. To address data limitations, SSDs are supplemented with Interspecies Correlation Estimation (ICE) models, providing an additional predictive line of evidence for chemicals and taxa

with sparse empirical data. The integration of empirical toxicity data, SSDs and ICE predictions incorporates multiple lines of evidence to evaluate species surrogacy and extrapolate sensitivity to untested species. The analysis builds upon previous research demonstrating the utility of SSDs, cross-species comparisons, and predictive approaches for evaluating taxonomic sensitivity and improving chemical hazard assessments. Results are used to determine whether Asian species tend to be more sensitive, less sensitive or similarly sensitive than species routinely used in regulatory testing programs. By integrating multiple lines of evidence from empirical toxicity data, SSDs and ICE model predictions, the analysis evaluates the robustness of surrogate-species assumptions across taxa, chemical classes and geographic regions. The resulting framework strengthens species surrogacy assessments, improves cross-species extrapolation for data-limited taxa and provides insights to support chemical registration and hazard assessment in China and the broader Asia-Pacific region while maximizing the value of existing ecotoxicity data.

16 From Fish to Frogs: Leveraging Fish Toxicity Data to Predict Chronic Pesticide Effects on Aquatic Amphibian Life Stages

Elena Adams, Bayer AG Crop Science, Monheim am Rhein, Germany, Eric Bruns, Bayer AG Crop Science, Monheim am Rhein, Germany, Lennart Weltje, BASF SE, Agricultural Solutions - Ecotoxicology, Limburgerhof, Germany Georg-August University, Division of Plant Pathology and Crop Protection, Göttingen, Germany, ***Katherine K. Coady****, Bayer AG Crop Science, Chesterfield, United States of America, Julie C. Brodeur, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Centro de Investigaciones de Recursos Naturales (CIRN), Instituto Nacional de Tecnologia Agropecuaria, Hurlingham, Argentina, Dominic Englert, Bayer AG Crop Science, Monheim am Rhein, Germany*

Comparison of chronic aquatic toxicity between amphibians and fish has been historically limited due to a lack of amphibian data. However, with more amphibian metamorphosis assays being conducted for pesticide endocrine assessments, there is increasing data available. We investigated the relative chronic sensitivity of X. laevis from amphibian metamorphosis assays for 90 pesticides (33 herbicides, 31 insecticides, 26 fungicides) compared to various fish species in the fish early life stage test. Comparisons were made between taxa based on survival, body weight, and length endpoints. Statistical correlations between endpoints of the two test systems were assessed using Pearson's correlation coefficient. Additionally, responses between taxa were compared to their respective counterparts using paired t-tests. Using multiple linear regression, an interspecies extrapolation model was derived to predict a chronic surrogate endpoint for larval aquatic amphibian life stages. Results showed strong and statistically significant correlations between endpoints of the two test systems across all parameters ($rP \geq 0.78$) and pesticide classes ($rP \geq 0.67$). Paired t-tests identified the ELS as significantly more sensitive than the AMA for all investigated metrics ($p < 0.001$). The derived interspecies correlation model demonstrates reasonable prediction accuracy and moderate fit to the data; however, it may require further validation considering other pesticides and amphibian species.

17 Ecotoxicological Assessments of Over-The-Counter NSAIDs and Antipyretic Pharmaceuticals: Looking at Existing Data on Effects for Crustacean Models

Delezia Singh*, Stephan Pflugmacher*

Commonly used, over-the-counter nonsteroidal anti-inflammatory drugs (OTC NSAIDs) and antipyretic pharmaceuticals represent emerging contaminants with high global consumption. Concerns surround their harmful impacts on aquatic biota, especially because waterbodies represent the predominant receiving matrices for drug-imbued effluents and waste disposal. To support the growing evidence of testing for toxicity effects of OTC drugs on non-target organisms, ecotoxicological assessments have been conducted using biological models, like crustaceans. To shed light on the scope of toxicity data on common OTC drugs available for this group while identifying research limits that need future research attention, the aim was to examine existing literature that involved crustaceans and commonly used NSAID and antipyretic OTC medications represented by ibuprofen, diclofenac, acetylsalicylic acid and acetaminophen. A total of 814 records resulted, with 68 meeting relevance following their eligibility screening against a defined workflow criteria. Assimilated

information revealed that most studies focused on acute toxicity testing for the focus pharmaceuticals using largely microcrustaceans as test models, especially daphnids. Ibuprofen was the most investigated across all taxa (32.9%) and relatively less studies assessed mixtures, metabolites and sublethal effects. To supplement these information deficiencies, recommendations on research efforts are discussed in relation to efficient nontraditional methodologies within ethical frameworks to support risk management for NSAID and antipyretic pharmaceuticals.

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