enable the prediction of exposure concentration needed to cause chemical concentrations at the tissue or assay levels and, as a result, levels below which no impact would be expected. Here, we present a framework where IVIVE can be applied in a screening-level context to develop threshold hazard levels in different fish species and how this may relate to human threshold levels. A chemical is first assessed by exposure of zebrafish embryos to five different concentrations of a chemical. Potential molecular initiating events, toxicity pathways, and adverse outcome pathways (AOPs) are identified based on effects observed at the morphological, behavioral, and transcriptional levels. Concentration-dependent changes in gene expression related to AOPs are then used to identify a transcriptional point of departure where a pathway is first significantly different from controls. A reverse toxicokinetic model for zebrafish adults is then used to calculate a transcriptional, pathway-based benchmark concentration below which no observed effect are expected in adult fish. We expect this framework to provide more accurate hazard-level screening, and enable the reduction and refinement of in vivo safety tests required for new chemical development, which will ultimately result in significant savings in money and time.

589 Incorporating Modeling and Visualization Tools to Assess Environmental Exposures and Fish Toxicokinetics following Deepwater Horizon Spill

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Widespread concern over aquatic exposures to polycyclic aromatic hydrocarbons (PAHs) has provided a broad yet disparate dataset assessing exposures to fish. Whereas early reports concluded PAH levels resident in the northern red snapper (*Lutjanus campechanus)* were below the level of concern, more recent studies have indicated that they are above USEPA-defined toxicity thresholds. Alternately, other studies have reported levels below thresholds but involve much longer exposures). Additional studies offer conflicting data on PAH partitioning into different matrices (e.g., water, sediment) that will also affect aquatic exposures Given that external exposures will dictate internal tissue concentrations, tools designed to model different exposure scenarios and resultant effects on chemical toxicokinetics will prove useful in environmental assessments. NOAA and USEPA sampling data were collated to capture environmental concentrations of a subset of PAHs (e.g., naphthalene, anthracene, , pyrene, and benzo[a]pyrene) in the air, vegetation, ocean, and sediment after the Deepwater Horizon spill. Concentration-data were collected pre-spill and at four times post-spill (i.e., early, mid, late, and 3+year post). At each of these time points, we run a physiologically-based toxicokinetic (PBTK) model on the red snapper to assess the impact of time- and matrix-dependent differences in exposure on the predicted internal fish tissue concentrations. . Finally, we compare the internal concentrations derived from the PBTK model to in vitro ToxCast concentrations on a subset of PAHs to determine whether modeled fish concentrations surpass ToxCast AC50 concentrations, used as a surrogate for an internal concentration that elicits bioactivity. This tool provides a visualization of geographically anchored PAH chemical concentrations plotted over time using GIS location and Google Map. To visualize the environmental concentrations and fish internal concentrations over time, we modified the PBTK exposures based on the revelant PAH concentration maps. The environmental media (vegetation, sediment, air, and ocean water) concentrations are displayed on a generic landscape model, and PAH distribution and concentrations in the different organ tissues of the red snapper are displayed on a model fish. This study demonstrates the utility of a visualization approach that communicates the effect that changes in exposure may have on aquatic toxicokinetics.

Ecotoxicity Technical Advisory Panel: Honoring 20 Years of Scientific Contributions to Metals Risk Assessment

590 Ecotoxicity Technical Advisory Panel - Purpose and Development

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This presentation will describe the creation of the metals' industry Ecotoxicity Technical Advisory Panel (ETAP), beginning with the state of metals risk assessment in the mid-1990s and the rationale and motivation for the creation of the panel. The development of the terms of reference for ETAP, and lessons that were learned with regard to ensuring that the deliberations and products of the panel had maximum credibility and impact will be shared. The evolution of ETAP provides a useful roadmap for the development of other scientific advisory panels. Examples will be provided of initiatives which contributed to meaningful, science based solutions to environmental problems and to advancing the risk assessment of metals in the environment.

591 Scientific advances in aquatic metal ecotoxicology

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The risk assessment of metals requires ecologically relevant environmental quality standards and monitoring instruments based upon a fundamental understanding of the processes controlling metal bioavailability, accumulation and toxicity. This is challenging given that environments differ in their physical and chemical characteristics and many different organisms coexist and form complex networks. The research developed over the years by the Ecotoxicology Technical Advisory Panel has increased our understanding of the different processes manifested across levels of organization with direct applications for risk assessment. Metal exposure involves different steps of which the first are the partitioning and speciation of the metals in the environment. Metal uptake and accumulation by organisms occurs via different routes and may result in different internal metal loadings and toxicological outcomes. Differences in water characteristics such as pH, hardness and temperature have profound effects on metal bioavailability and toxicity. In part these effects can be explained by changes in the chemical speciation of the metals, but effects on the molecular physiology of the organisms are equally important. Metal toxicity develops when a certain internal threshold concentration is reached and one or more essential processes are disturbed or damaged. The differences in structural and functional organization among aquatic organisms results in large differences in metal sensitivity spanning orders of magnitude. The species sensitivity distribution approach describes this variation and allows to set overall toxicological thresholds. Understanding the processes underlying the observed variation in sensitivity allows normalization and read across among species and environments. In this way informed environmental quality standards for different metals have been developed and implemented for freshwater and marine systems. Although considerable progress has been made and the risk assessment of metals has largely improved and become more site specific, a number of challenges remain. In the real world metal exposure generally involves mixtures of metals and other stressors. Recent work has shown that these interactions can be complex and of an antagonistic or synergistic nature. At this stage we only have a marginal understanding of this complexity, but given the expertise and instruments developed fast progress is expected in this important domain in the near future.

592 Scientific advances in sediment metal ecotoxicology

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During the past several years a large body of research has been developed and conducted by the Ecotoxicology Technical Advisory Panel (ETAP) regarding the risk of metals in sediments, surface waters and soils. This research was in response to the European Union's Water Framework Directive and REACH. The primary goal of the research has been