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Application of an integrated strategy for monitoring of contaminants, including endocrine active chemicals, in Great Lakes Areas of Concern.

Chemical monitoring strategies are most effective for those chemicals whose hazards are well understood and for which sensitive and cost effective analytical methods are available. Unfortunately, such chemicals represent a minor fraction of those that may currently occur in the environment and impact biological systems. However, in cases such as endocrine disruption, where specific types of biological perturbation have been plausibly and/or empirically-linked to adverse outcomes (i.e., adverse outcome pathways have been characterized), effects-based monitoring approaches can serve as a powerful complement to analytical environmental chemistry for exposure monitoring and diagnostic risk assessments. This presentation describes an integrated research strategy that was employed in five different Great Lakes Areas of Concern (AOCs). The strategy used a combination of four day *in situ* exposures with fathead minnows (*Pimephales promelas*), in vitro bioassay-based screening of surface water samples, and analytical quantification of over 150 analytes in surface water and sediment samples to characterize contamination at selected sites within the five AOCs. Biological effects monitoring focused on endpoints associated with reproductive endocrine adverse outcome pathways as well as xenobiotic and steroid metabolism. In vitro screening with the MDA-kb2 cell bioassay detected weak androgenic activity at several sites within the lower Fox River and Green Bay AOC. Hepatic cytochrome p4501a1 mRNA induction was observed in fish exposed *in situ* at most sites examined within the St. Louis River, Detroit River, and Maumee River AOCs. In contrast, hepatic vitellogenin mRNA concentrations were rarely elevated in male fathead minnows exposed *in situ*. Ovarian expression of steriodogenesis-related genes was largely un-impacted by *in situ* exposure within the St. Louis River AOC, despite detection of a variety of known endocrine active chemicals and pharmaceuticals in surface waters collected during the period of exposure. On-going research includes the application of unsupervised analyses (e.g., transcriptomics) as well as construction of chemical-gene interaction networks as a means to aid selection of biological endpoints for future effects-based monitoring at these sites. *The contents of this abstract neither constitute nor reflect official US EPA policy.*

Keywords: Weight-of-evidence, effects-based monitoring, in vitro, fish

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