Utilizing high-throughput bioassays associated with US EPA ToxCast Program to assess biological activity of environmental contaminants: A case study of chemical mixtures

B. Blackwell[1], A. Schroeder[2], M. Lee[3], K. Jensen[3], K. Houck[4], R. Judson[4], G. Ankley[3], D. Villeneuve[3]

[1]ORISE Research Participation Program, U.S. EPA, Duluth, MN; [2]University of Minnesota – Water Resources Center, St. Paul, MN; [3]U.S. EPA Mid-Continent Ecology Division, Duluth, MN; [4]U.S. EPA National Center for Computational Toxicology, Research Triangle Park, NC;

Effects-based monitoring and surveillance is increasingly being utilized in conjunction with chemical monitoring to determine potential biological activity associated with environmental contaminants. Supervised approaches targeting specific chemical activity or molecular pathways (e.g., estrogenic activity) have commonly been used; however, recent developments in the arena of in vitro high-throughput (HTP) assays allow screening of environmental samples for a wider array of biological targets in a rapid, cost effective manner. Ongoing work from our lab has focused on utilizing HTP assays to screen surface water samples for biological activity to help support linkage of measured environmental contaminants to potential adverse outcomes. As organisms are rarely exposed to single contaminants in the environment, it is important to understand how chemical mixtures potentially affect biological activity and lead to adverse outcomes in ecological receptors. Little is known as to how environmentally-relevant chemical mixtures behave in HTP assays, so a series of mixtures was specifically developed to assess in vitro response. The Attagene subset of assays from the US EPA ToxCast Program was selected to screen individual chemicals and mixtures of these chemicals for biological activity. The Attagene assays screen for chemical interactions with over 90 different transcription factors and 48 nuclear receptors. A total of 28 individual chemicals and 11 mixtures were screened for biological activity. Test chemicals and artificial mixtures were selected to consider one of the following situations: to address chemical specificity and activity alone versus in a mixture; to address response additivity in a mixture of chemicals sharing a common molecular target; or to mimic chemical composition previously observed in wastewater impacted surface waters. Response profiles of individual chemicals were compared against those of mixtures to assess system performance. Gene targets unique to specific chemicals remained detectable in the presence of a mixture. Individual mixtures of estrogen receptor agonists, antagonists, and combination of agonists/antagonists demonstrated apparent response additivity. The results demonstrate the utility of HTP assays in screening environmental contaminants for potential biological activity. *The contents of this abstract neither constitute, nor necessarily reflect, official US EPA policy.*