Session: Applying Bioaccumulation Data to Better Inform Human and Ecological Risk Assessment of Chemicals (P)
Poster
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In vitro to in vivo extrapolation of hepatic metabolism in fish: update on development of OECD Test Guidelines and Guidance Document

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Chemical biotransformation represents the largest source of uncertainty in chemical bioaccumulation assessments, and model-based estimates of chemical bioconcentration in fish may be greatly improved by including biotransformation rates, as measured in vitro. In vitro substrate depletion assays, using rainbow trout hepatocytes or liver subcellular fractions (S9), have been successfully developed to provide estimates of fish biotransformation. A multi-laboratory ring trial, coordinated by the ILSI Health and Environmental Sciences Institute (HESI), was recently completed. This study involved six laboratories, each of which performed substrate depletion assays on six test chemicals in both systems (rainbow trout liver S9 fractions and rainbow trout cryopreserved hepatocytes) to determine in vitro intrinsic clearance ($CL_{\text{in vitro int}}$). Results successfully demonstrated assay reliability within and across laboratories and similar performance of substrate depletion assays using the two biological systems. For all test chemicals, hepatic clearance values determined by the two test systems were in good agreement (within 2-fold). Based on the successful results of this ring-trial, the two test guidelines ("*Determination of in vitro intrinsic clearance using cryopreserved rainbow trout hepatocytes*" and "*Determination of in vitro intrinsic clearance using rainbow trout liver S9 sub-cellular fractions*") have been drafted and are accompanied by by a Guidance Document. The launch of OECD WNT review of these draft documents is planned for 2017. The Guidance Document provides additional information on how to conduct the tests as well as how to apply the measured in vitro biotransformation rates to predict bioconcentration factors (BCFs). This includes guidance on the selection of the assay system (e.g., primary hepatocytes vs. liver S9 fractions), specific

considerations for testing chemicals, use of negative and positive controls, BCF extrapolation models, and application of the two test methods to other fields beyond BCF prediction. This poster will provide an overview of the Test Guidelines and Guidance Document, as well as an update on progress and timelines. chemicals, use of negative and positive controls, BCF extrapolation models, and application of the two test methods to other fields beyond BCF prediction. This poster will provide an overview of the Test Guidelines and Guidance Document, as well as an update on progress and timelines.