Estrogen Receptor Expert System – Overview and Examples

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The estrogen receptor expert system (ERES) is a rule-based system developed to prioritize chemicals based upon their potential for binding to the ER. The ERES was initially developed to predict ER affinity of chemicals from two specific EPA chemical inventories, antimicrobial pesticides and pesticide inert ingredients. These are industrial use chemicals that if active were likely to have low affinity for the ER. To build the ERES, selected chemicals from these inventories and chemicals with structural attributes known to be involved in interactions within the binding pocket of the ER were tested in two separate estrogenicity assays: (1) a trout-based estrogen receptor competitive binding assay and (2) an ER-mediated vitellogenin mRNA expression assay in metabolically competent trout liver slices. These assays were optimized to detect low affinity ER binders and to minimize false negatives. The data from these two assays were integrated to define chemical structural parameters important for activity and to develop effects-based chemical categories. By using an effects-based chemical category approach and strategically testing chemicals within chemical classes, inferences can be made about ER affinity of untested chemicals. The ERES is visualized as a logic-based decision tree, currently with seven major nodes, with multiple chemical categories within each node. The ERES has been incorporated as a component of the OECD QSAR toolbox and is publicly accessible at http://www.qsartoolbox.org/download. This presentation will provide a brief overview of how the system was developed and provide two examples of predicted ER affinity. *This abstract does not necessarily reflect U.S. EPA policy.*

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