International Validation of two Human Recombinant Estrogen Receptor (ERα) Binding Assays.

Vickie Wilson[1], Susan Laws[1], Alexius Freyberger[2], Yumi Akahori[3], Masahiro Takeyoshi[3], Miriam Jacobs[4], Daniel Dietrich[5],Karen Hamernik[6], Mary Manibusan[6].

US EP, [1]Office of Research & Development, [6]Office of Science Coordination & Policy, A. [2]Bayer HealthCare, Germany. [3]Chemicals Evaluation and Research Institute, Japan. [4]Centre for Radiation, Chemical and Environmental Hazards Centre, Public Health England, UK. [5]U. Konstanz, Germany.

An international validation study has been successfully completed for 2 competitive binding assays using human recombinant ERα. Assays evaluated included the Freyberger-Wilson (FW) assay using a full length human ER, and the Chemical Evaluation and Research Institute (CERI) assay using a ligand-binding domain of the human ER. Twenty three compounds were tested in 6 laboratories for the FW assay and 5 for the CERI assay, which included three controls (used with every run), 9 uncoded, and 14 coded chemicals across 3 subtasks. The overall goal of this validation study was to demonstrate the ability of each of the two assays to reliably classify the test chemicals as binders or non-binders. Laboratories had little trouble with the ER binders that produced a full binding curve when using either the CERI or FW assays. As is typical with all ER competitive binding assays, the weak binders proved to be more challenging. However, overall results from both the FW and CERI assays were consistent and in agreement with expected classifications regardless of the form of the hrER (i.e., full length ER versus an ER ligand binding domain) or the subtle differences in the protocols for conducting each assay. The reproducibility and accuracy for classification of chemicals as potential ER binders and non-binders using the FW and CERI hrER binding assays were comparable to that of the U.S.EPA's existing ER binding test guideline OPPTS 890.1250, while providing an improved, higher throughput method that does not require animal tissue as the source of receptor. An OECD test guideline is currently being drafted. *This abstract does not reflect US EPA policy.*