NICEATM/ECVAM/JaCVAM Multi-phased International Validation Study of an *In Vitro* Estrogen Receptor Transcriptional Activation Assay to Detect Agonist and Antagonist Activity

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Abstract

An *In Vitro* estrogen receptor (ER) transcriptional activation (TA) assay (LUMI-CELL® ER, Xenobiotic Detection Systems, Inc.) for the detection of ER agonists and antagonists was nominated to ICCVAM and recommended for validation. NICEATM, ECVAM, and JaCVAM designed and initiated a multi-phased international validation study to evaluate the reproducibility and accuracy of the assay, using laboratories in Japan, the US, and Europe. A standardized test method protocol is being used to evaluate 78 reference substances recommended by ICCVAM for validation of *in vitro* ER test methods (ICCVAM 2006). The first phase will establish test acceptance standards for each laboratory. The second phase will test 12 coded substances, from a subset of 53 that ICCVAM considered as minimum for validation, in each laboratory. Reproducibility and accuracy will be assessed continuously. Excessive variation will be investigated and protocols modified accordingly. The third phase will evaluate the performance of the optimized test method protocol using the remaining 41 minimum substances. The remaining 25 ICCVAM recommended substances will be tested during the final phase in the lead laboratory. By identifying and resolving sources of variability early in the validation process, the outcome of this multi-phased approach is expected to be a reproducible protocol that is suitable for international regulatory use. Supported by NIEHS Contract N01-ES-35504.