Final Results of an International Validation Study of an *In Vitro* ER TA Test Method in BG-1 Cells

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The LUMI-CELL® ER (BG1Luc4E2) stably transfected estrogen receptor (ER) transcriptional activation (TA) assay uses the human ovarian cancer cell line, BG-1, that expresses both human hER-alpha and hER-beta to screen for substances that may induce or inhibit estrogenic activity *in vitro*. NICEATM, in collaboration with ECVAM and JaCVAM, coordinated an international validation study to evaluate the accuracy and reliability of the test method. Three laboratories (one each in the U.S., Europe and Japan) tested ICCVAM recommended reference substances with well-characterized *in vitro* ER TA data. Subsets of this list were used to evaluate test method accuracy and reliability. Phases 1 and 2 were used to demonstrate proficiency, establish historical databases in each laboratory, evaluate intra- and interlaboratory reproducibility, and identify protocol refinements prior to initiating Phases 3 and 4, where the remaining reference substances were tested. Overall accuracy for identifying *in vitro* ER agonists was 86% (36/42), with false positive and false negative rates of 20% (2/10) and 13% (4/32), respectively. For *in vitro* ER antagonists, overall accuracy was 89% (16/18), with false positive and false negative rates of 7% (1/15) and 33% (1/3), respectively. These results will be used to provide the basis for draft ICCVAM recommendations on the usefulness and limitations of the BG1Luc4E2 test method for review by an expert peer panel in March 2011, as well as to develop performance standards for the expedited validation of functionally and mechanistically similar test methods. Results from this study will also be used to support the development of an OECD performance based test guideline for ER TA test methods. Supported by NIEHS Contract N01-ES-35504.

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Poster Session: Alternatives to Mammalian Models for Testing