

NTP, NICEATM, and ICCVAM

Test Method evaluation for:

In Vitro Endocrine Disruptor Screening Assays

http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm

LUMI-CELL[®] ER Assay

ICCVAM completed a protocol standardization for the LUMI-CELL[®] ER assay.

- Standardized procedures for agonists and antagonists.
- Standardized procedures for cell viability.
- Developed two GLP-compliant protocols.
- Demonstrated the adequacy of the standardized protocols.

ICCVAM is currently conducting an international validation study of the LUMI-CELL[®] ER assay in association with:

- ◆ European Centre for the Validation of Alternative Methods (ECVAM).
- ◆ Japanese Center for the Validation of Alternative Methods (JaCVAM).
- Test the 78 ICCVAM recommended substances for the validation of *in vitro* ER TA test methods in three laboratories, one in Europe, Japan, and the U.S.
- Use the results to develop a high quality *in vitro* ER TA database that can might be used to further reduce the expected requirements for animal use in the screening of potential endocrine disruptors.

** For complete text see back and the above web site.

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Xenobiotic Detection Systems, Inc. LUMI-CELL[®] ER Assay

The LUMI-CELL[®] ER assay measures whether and to what extent a substance induces or inhibits TA activity via ER mediated pathways in recombinant BG-1Luc4E2 cells. The BG-1Luc4E2 cell line was derived from BG-1 immortalized adenocarcinoma cells that endogenously express ER and that have been stably transfected with the plasmid pGudLuc7.ERE. This plasmid contains four copies of a synthetic oligonucleotide containing the estrogen response element upstream of the mouse mammary tumor viral promoter and the firefly luciferase gene. BG-1Luc4E2 cells express luciferase activity in response to estrogen and estrogen-like substances.

ICCVAM has recently completed a protocol standardization study for the LUMI-CELL[®] ER assay which:

- standardized procedures for using the assay to identify ER agonists and antagonists
- standardized procedures for a quantitative assessment of cell viability for use with the agonist and antagonist assays
- developed two GLP-compliant protocols: one for the agonist assay, and one for the antagonist assay
- established a historical database for reference standards and controls used in the agonist and antagonist assay protocols
- demonstrated the adequacy of the standardized protocols for detecting ER agonists or antagonists using eight substances covering a range of ER agonist and antagonist activities, respectively.

ICCVAM is currently conducting an international validation study of the LUMI-CELL[®] ER assay using the standardized protocols in conjunction with the European Centre for the Validation of Alternative Methods (ECVAM) and the Japanese Center for the Validation of Alternative Methods (JaCVAM). The specific objectives of this validation study are:

- further standardize and optimize the LUMI-CELL[®] ER assay using the agonist and antagonist protocols to test the 78 ICCVAM recommended substances for the validation of *in vitro* ER TA test methods in three laboratories, one in Europe, Japan, and the U.S, to maximize test method reliability (intralaboratory repeatability, intra- and inter-laboratory reproducibility).
- use the results from the testing of the 78 ICCVAM recommended substances to develop a high quality *in vitro* ER TA database that can be used to characterize the extent to which other individual *in vitro* endocrine disruptor test methods (or test method batteries) might be used to further reduce the expected requirements for animal use in the screening of potential endocrine disruptors.

Draft Evaluation: Nomination of the LUMI-CELL[®] ER High-Throughput System for Screening Estrogen-Like Chemicals for Validation Studies (August 2004) [PDF]



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