14 September 2007

Dr. Jerry Smrchek
U.S. National Coordinator for the
OECD Test Guidelines Program
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Mail Code 7403M
Washington, DC 20460

Dear Dr. Smrchek:

On behalf of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), we are pleased to provide the enclosed OECD Standard Project Submission Form (SPSF) for a Stably Transfected Transcriptional Activation (TA) Assay for the Detection of Estrogen Receptor (ER) Agonists and Antagonists. The submission of this SPSF is in response to the 13 July 2007 notification from the OECD Secretariat requesting SPSFs for ongoing OECD Validation Management Group Non-Animal (VMG NA) projects that have gone through prevalidation so they can be added to the rolling work plan of the OECD Test Guidelines Program.

The SPSF is based on the LUMI-CELL® ER TA Assay developed by Xenobiotic Detection Systems, Inc., for the detection of estrogenic agonists and antagonists. The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) conducted a prevalidation study of the assay to develop standardized protocols for detecting ER agonists and antagonists that can be easily transferred to other laboratories and be used to obtain reproducible results. The study was completed in July 2006 and results indicated that intralaboratory reproducibility and the comparative performance of the standardized protocols were adequate for moving forward to a multi-laboratory validation study.

NICEATM, the European Centre for the Validation of Alternative Methods (ECVAM), and the Japanese Center for the Validation of Alternative Methods (JaCVAM) initiated the multi-laboratory validation study in March 2007. The study is scheduled for completion in April 2008 and a Background Review Document (BRD) summarizing the results of the study will be completed shortly thereafter. An independent, international expert peer review panel meeting will be convened in the

fall of 2008, with observers from ICCVAM, ECVAM, and JaCVAM. The panel will evaluate the extent to which the BRD supports draft recommendations for (1) test method usefulness and limitations, (2) standardized test method protocols, (3) performance standards, and (4) future studies. ICCVAM will consider the panel report, public comments, and recommendations from ICCVAM's advisory committee, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM), when finalizing the ICCVAM test method recommendations. These recommendations will be used to develop a generic Test Guideline for a Level 2 *in vitro* test method to detect substances with ER agonist and antagonist activity, as described in the OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals. The Test Guideline will be based on the validated test method protocol and will include performance standards for structurally, functionally, and mechanistically similar ER TA assays. A draft Test Guideline and supporting materials are scheduled for submission to the OECD Secretariat in early 2009.

We appreciate the opportunity for NICEATM and ICCVAM to submit the SPSF for this assay. Please feel free to contact me at any time if you have questions regarding any of the information provided in the attached documents.

Sincerely,

William S. Stokes, D.V.M, D.A.C.L.A.M.
Rear Admiral, U.S. Public Health Service
Director, NICEATM
Executive Director, ICCVAM

Add Wind as a signer