

ICCVAM Performance Standards for the BG1Luc ER TA Test Method

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Performance standards can be used to evaluate the accuracy and reliability of proposed test methods that are functionally and mechanistically similar to an accepted test method. ICCVAM recently recommended performance standards for the BG1Luc estrogen receptor (ER) transactivation (TA) test method. The performance standards were based on results from an international interlaboratory validation study and include essential test method components, reference substances, and standards for accuracy and reliability. Essential components include a cell line that endogenously expresses human ERs and is stably transfected with a reporter gene, use of a solvent miscible with cell culture media, a defined concentration limit for agonist (1 mM) or antagonist (10 µM) testing, evaluation of cytotoxicity, a reference estrogen, anti-estrogen, and positive and solvent controls. The reference substances should cover the range of ER responses, both positive and negative. ICCVAM selected 34 agonist and 10 antagonist reference substances. The evaluation of these reference substances yielded the following results for agonists: accuracy of 100% (34/34), sensitivity of 100% (27/27), specificity of 100% (7/7), false positive rate of 0% (0/7), and false negative rate of 0% (0/27). For antagonists, results were: accuracy of 100% (10/10), sensitivity of 100% (3/3), specificity of 100% (7/7), a false positive rate of 0% (0/7), and false negative rate of 0% (0/3). Evaluation of reference substances by a newly proposed method should yield similar results. Although it is not realistic to expect test methods to perform identically, the basis for any discordant results should be discussed along with the impact on the proposed use. These ICCVAM performance standards are expected to facilitate the efficient evaluation of new test methods proposed for evaluation of ER agonist and/or antagonist activity.