Evaluation report on the BG1Luc estrogen receptor (ER) transactivation (TA) test method (BG1Luc ER TA)

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Summary

The BG1Luc estrogen receptor (ER) transactivation (TA) test method (BG1Luc ER TA) was the subject of an international tripartisan interlaboratory validation study which evaluated its usefulness as a means to screen substances for *in vitro* ER agonist or antagonist activity. The BG1Luc ER TA test method differs from other ER binding assays in that it is capable of detecting transcriptional activation of DNA resulting from ligand binding as well as distinguishes between ER agonist and antagonist activities. The scientific validity and regulatory application of the BG1Luc ER TA test method was assessed with 78 reference chemicals selected by ICCVAM (the Interagency Coordinating Committee on the Validation of Alternative Methods). The ICCVAM validation report found the BG1Luc ER TA test method to be highly accurate, highly reliable, and equivalent to the Stably Transfected Transactivation *In Vitro* Assays (STTA) to Detect Estrogen Receptor Agonists.

The validation data did, however, exhibit certain inter-laboratory discrepancies, which indicate the need for quality control methods, such as individual laboratories retesting as necessary to clarify their proficiency with the method. Also, although a total of 78 reference chemicals were specified, comparative studies did not necessarily include data for all reference chemicals from all laboratories. Some of the reference chemicals failed to exhibit a clear reaction during testing and were excluded from consideration in the validation report. The reasons for these discrepancies need further study.

An advantage of the BG1Luc ER TA test method is its ability to observe native human ER response *in vitro* by making use of an ER-responsive reporter gene (luc) in the human ovarian adenocarcinoma cell line BG-1.

The presence in these cells of both ERα and ERβ, however, results in some ambiguity as to precisely what extent each isoform is responsible for test-induced TA response, which is a subject of some urgency for future research, as described in the ICCVAM validation report.