

# Comparison of the Manual and Quantitative High Throughput Versions of the BG1Luc Estrogen Receptor Transactivation Test Method

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## Abstract

NICEATM conducted an international validation study of the BG1Luc estrogen receptor (ER) transactivation (TA) test method. The test method evaluation report was reviewed and the method accepted by U.S. regulatory agencies and the Organisation for Economic Co-operation and Development. In 2011, NICEATM nominated the BG1Luc ER TA to Tox21 to be evaluated for adaptation into a quantitative high throughput screening (qHTS) assay. The Tox21 collaboration, an effort by the National Toxicology Program, NIH Chemical Genomics Center, Environmental Protection Agency, and Food and Drug Administration, was formed to advance toxicity testing by shifting from traditional *in vivo* tests to *in vitro* methods. A major goal of Tox21 is to prioritize chemicals for in-depth toxicity testing. One method for prioritization is the use of qHTS assays using cell- and biochemical-based assays to construct concentration–response curves for thousands of chemicals. The Tox21 consortium adapted the BG1Luc ER TA manual method to a qHTS format, making it the first assay validated for regulatory use to be adapted to Tox21. Data from qHTS assays have been generated for approximately 10,000 chemicals in both the agonist and antagonist versions of the qHTS assay. Seventy-six chemicals had been tested in both the manual and qHTS methods. Data from both methods were used to evaluate the degree to which classifications of test chemicals in the BG1 manual and qHTS methods matched reference classifications (accuracy) and the degree to which chemical classifications were identical between the two methods (concordance). Except for a few discrepancies attributable to different test concentrations used in the two methods, the BG1Luc ER TA manual and qHTS methods produced almost identical results in terms of accuracy, with a high degree of concordance.