

ICCVAM Revised Recommended Substances for the Validation of *In Vitro* Estrogen Receptor and Androgen Receptor Binding and Transcriptional Activation Test

Methods

DG Hattan¹, ML Wind², P Ceger³, FH Deal³, RR Tice⁴, WS Stokes⁴

¹U.S. FDA, College Park, MD, US; ²U.S. Consumer Product Safety Commission, Bethesda, MD, US; ³ILS, Inc., Contractor Supporting NICEATM, RTP, NC, US;

⁴National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), NIEHS/NIH/DHHS, RTP, NC, US

Abstract

NICEATM recently re-assessed the commercial availability and cost for the 78 reference substances previously recommended by ICCVAM for validation of *in vitro* estrogen receptor (ER) and androgen receptor (AR) binding and transcriptional activation (TA) test methods (ICCVAM 2003). This re-assessment indicated that three substances (anastrozole, CGS 18320B, fadrozole) are no longer commercially available, one substance now has restricted commercial availability (ICI 182,780), and six substances (actinomycin D, hydroxyflutamide, 4-hydroxytamoxifen, methyltrienolone, 12-*O*-tetradecanoylphorbol-13-acetate [TPA], zearalenone) may be considered too expensive for use in validation studies. Where feasible, ICCVAM updated the list of reference substances with suitable replacements (4-hydroxyandrostenedione, chrysin, dicofol, raloxifene HCl, 19-nortestosterone and resveratrol) that have similar ER and AR activity profiles. Because of their unique activity profiles and/or chemical/physical properties, suitable replacements for four of the expensive substances (actinomycin D, hydroxyflutamide, 4-hydroxytamoxifen, and TPA) could not be identified. The revised list of reference substances has been published (ICCVAM 2006) and is being used for validation of ER TA test methods by NICEATM, the European Centre for the Validation of Alternative Methods, and the Japanese Center for the Validation of Alternative Methods. Supported by NIEHS Contract N01-ES-35504.