Representative Peer-reviewed Papers on Assays to Detect EDCs with EA

C.Z. Yang and G.D. Bittner. 2002. Dietary Phytoestrogens: a confusing landscape. Lab Animal. 31: 43-47.

C.Z. Yang, W. Casey, M. Stoner, G.J .Kollessery, A.W. Wong and G.D. Bittner. 2014. A robotic MCF-7:WS8 cell proliferation assay to detect agonist and antagonist estrogenic activity. Toxological Sci. 137:335-349.

M.A.Stoner, C.Z.Yang, and G.D.Bittner. 2014. A Robotic BG1Luc Reporter Assay to Detect Estrogen Receptor Agonists. Toxicology in Vitro. 28: 916–925.

The latter two papers describe our robotic assays for EA that have very high concordance with ICCVAM/ECCVAM metaanalyses for test chemicals. Specifically, our robotic BG1Luc assay has high (100%) concordance for the presence or absence of detectable EA with ICCVAM meta-analyses for 27 test chemicals. When chemicals tested in common by both assays are compared, this robotic BG1Luc assay has 100% concordance with the ICCVAM manual BG1 assay for 27 test chemicals, 100% concordance with CERI for 20 test chemicals, and 100% concordance with a robotic MCF-7 assay for 27 test chemicals. In contrast, the yeast estrogen screening (YES) assay has only 47% (7/15) concordance with any of these other assays for 15 test chemicals. When sensitivities of these different assays are compared to detect the EA of the same test chemical as defined by its EC50, our robotic BG1Luc assay is more sensitive for 15/20 and one tie out of 21 chemicals reported by ICCVAM meta-analyses , i.e., is more sensitive ($p < 0.001$, Chi Squared test) for 15 chemicals whose EC50s can be directly compared. Compared to ICCVAM BG1 manual data for 22 chemicals, our robotic BG1Luc assay is more sensitive for 14/22 ($p < 0.0.001$). Compared to CERI manual assays, the robotic BG1 is more sensitive for 18/20 test chemicals ($p <0.0001$). Compared to the YES assay, the robotic BG1 assay is more sensitive ($p < 0.0001$) for 15/15 chemicals whose EC50s can be directly compared. In contrast, with respect to the robotic MCF-7 assay as reported for ICCVAM validation results, the BG1Luc is more sensitive for only 4/27 chemicals whose EC50 can be directly compared, i.e. the MCF-7 assay is more sensitive (and has as high a concordance) with a high significance ($p < 0.0001$) compared to our EC50 from our robotic BG1Luc, ICCVAM manual BG1Luc, CERI, and YES assays and ICCVAM EC50 meta-analyses.

Representative Peer-reviewed Papers on Release of EDCs having EA from Various Consumer Products.

C. Z. Yang, S. I. Yaniger, V. C. Jordan, D. Klein and G.D. Bittner. 2011. Most Plastic Products Release Estrogenic Chemicals: A Potential Health Problem That Can Be Solved. EHP. 119: 989-996.

S.L. Myers, C.Z.Yang, G.D. Bittner, K.L. Witt, R.R. Tice, D.D. Baird. 2014. Estrogenic and Anti-Estrogenic Activity of Off –The-Shelf Hair and Skin Products. Journal of Exposure Science and Environmental Epidemiology. May 2014. Epub ahead of print. doi: 10.1038/jes.2014.32.

G.D.Bittner, M. A. Stoner, C. Z. Yang. 2014. Estrogenic chemicals often leach from BPA-free plastic products that are replacements for BPA-containing polycarbonate products. Environmental Health 13:41-54.

G.D. Bittner, M.S. Denison, C. Z. Yang· 2014. Chemicals having estrogenic activity can be released from some BPA-free, hard and clear, thermoplastic resins. Environmental Health. 13:103-121.

These papers report that consumer products in two general categories-—plastics and personal care products (PCPs) – release chemicals thast have easily-detectable EA as measured by our two robotic assays for EA. The data for PCPs are described in the body of this proposal. The results of our two hazard studies of BPA-replacement resins (aka polycarbonate or PC resins) and PC-replacement products. Like PC resins, these PC-replacement resins are “hard, clear, and reusable”. S ome (4/14) of these unstressed and stressed BPA-free resins

leached chemicals having significant levels of EA, including one polystyrene, and three Tritan™ resins, the latter reportedly EA-free. Exposure to UV radiation in natural sunlight resulted in an increased release of EA from Tritan™ resins. Ten unstressed or stressed glycol-modified polyethylene terephthalate (PETG), cyclic olefin polymer (COP) or copolymer (COC) thermoplastic resins did not release chemicals with detectable EA under any test condition. Similarly, many unstressed and stressed, PC-replacement-products made from acrylic, polystyrene, polyethersulfone, and Tritan™ resins leached chemicals with EA, including products made for use by babies. Exposure to various forms of UV radiation often increased the leaching of chemicals with EA. In contrast, some BPA-free PC-replacement products made from glycol-modified polyethylene terephthalate or cyclic olefin polymer or co-polymer resins did not release chemicals with detectable EA under any conditions tested.

These two hazard assessment surveys showed that many BPA-free PC- replacement resins and products still leached chemicals having significant levels of EA, as did their BPA-containing PC counterparts they were meant to replace. That is, BPA-free did not mean EA-free. However, this study also showed that some PC-replacement resins and products did ***not l***each chemicals having significant levels of EA. That is, EA-free PC-replacement resins and products could be made in commercial quantities at prices that compete with PC-replacement products that were not BPA-free. Since plastic products often have advantages (price, weight, shatter-resistance, etc.) compared to other materials such as steel or glass, our data show that is not necessary to forgo those advantages of plastics in order to avoid release into foodstuffs or the environment of chemicals having EA that may have potential adverse effects on our health or the health of future generations.