

Appendix J

References and Sources for the Screening and Testing Chapter

Table of Contents

I. Recommended Mammalian <i>in vitro</i> and <i>in vivo</i> Assays	1
II. Thyroid Sections	14
III. Frog Metamorphosis Assay	18
IV. Fish Gonadal Recrudescence Assay	18
V. Uterotrophic Assay (intraperitoneal)	19
VI. 14-Day Intact Adult Male Assay	19
VII. Alternative Mammalian Reproduction Test	19
VIII. Avian Reproduction (EPA OPPTS 850.2300;OECD 206)	19
XI. Nest Attentiveness/Incubation Behavior Test References To Be Used For Protocol Development And Standardization	21
X. Visual Cliff Test References To Be Used For Protocol Development And Standardization	21
XI. Cold Stress References To Be Used For Protocol Development And Standardization	22
XII. Fish Life Cycle Test	22
XIII. Methods to Select the Target Doses for T2T	23
XIV. Methods to Select the Target Doses for T2T	23
XV. "Low Dose Consideration for T2T"	23
XVI. Documents Distributed to Screening and Testing Work Group Members	24

I. Recommended Mammalian *in vitro* and *in vivo* Assays

Aakvaag A., Utaaker E., Thorsen T., Lea O.A. and Lahooti H. (1990). Growth control of human mammary cancer cells (MCF-7 cells) in culture: effect of estradiol and growth factors in serum-containing medium. *Cancer Research* 50:7806-10.

Aitken S.C., Lippman M.E., Kasid A. and Schoenberg D.R. (1985). Relationship between the expression of estrogen-regulated genes and estrogen-stimulated proliferation of MCF-7 mammary tumor cells. *Cancer Research* 45:2608-15.

- Allegretto, E., and Heyman, R. 1996. Intracellular Receptor Characterization And Ligand Screening By Transactivation And Hormone-Binding Assays. *Methods in Molecular Genetics* 8, 405-420.
- Allen, E., and Doisy E. (1924). The induction of a sexually mature condition in immature females by injection of the ovarian follicular hormone. *American Journal of Physiology* 69, 577.
- Anderson J., Clark J.H. and Peck E.J. Jr (1972). Oestrogen and nuclear binding sites. Determination of specific sites by (3 H)oestradiol exchange. *Biochem J* 126:561-7.
- Anderson S., Pearce, S., Fail, P, McTaggart, B., Tyl, R., and Gray, L. E. (1995). Validation of the alternative reproductive test protocol (ART) to assess toxicity of methoxychlor in rats. *The Toxicologist* 15, 164.
- Anderson, S., Pearce. S., Fail, P., McTaggart, B, Tyl, R and Gray, L. (1995). Testicular and adrenal response in adult Long-Evans Hooded rats after antiandrogenic vinclozolin exposure. *Journal Andrology* 16, 43.
- Arai, Y., Mori, T., Suzuki, Y. and Bern. (1983). Long-term effects of perinatal exposure to sex steroids and diethylstilbestrol on the reproductive system of male mammals. *International Review of Cytology*, vol 84, 235-268.
- Armstrong, D.T., Dorrington, J.H., Robinson, J. (1976). Effects of indomethacin and aminoglutethimide phosphate *in vivo* on luteinizing-hormone-induced alterations of cyclic adenosine monophosphate, prostaglandin F, and steroid levels in preovulatory rat ovaries. *Canadian Journal Biochemistry* 54, 796-802.
- Arnold, S. F., Klotz, D. M., Collins, B. M., Vonier, P. M., Guillette, L. J., and Mclachlan, J. A. (1996). Synergistic activation of estrogen receptor with combinations of environmental chemicals. *Science* 272: 1489-1492.
- Arnold, S. F., Robinson, M. K., Notides, A. C., Guillette, L. J., and Mclachlan, J. A. (1996). A yeast estrogen screen for examining the relative exposure of cells to natural and xenoestrogens. *Environ Health Perspect* 104: 544-548.
- Astwood, W. (1939). As assay method for progesterone based upon the decidual reaction in the rat. *Journal of Endocrinology* 1, 49.
- Badia E. Duchesne MJ. Fournier-Bidoz S. Simar-Blanchet AE. Terouanne B. Nicolas JC. Pons M., 1994. Hydroxytamoxifen induces a rapid and irreversible inactivation of an estrogenic response in an MCF-7-derived cell line. *Cancer Research*. 54(22):5860-6.
- Balaguer P., Joyeux A., Denison M.S., Vincent R., Gillesby B.E. and Zacharewski T. (1996). Assessing the estrogenic and dioxin-like activities of chemicals and complex mixtures using *in vitro* recombinant receptor-reporter gene assays. *Canadian Journal of Physiology and Pharmacology* 74:216-222.
- Berman, E., and Laskey, J (1993). Altered steroidogenesis in whole-ovary and adrenal culture in cycling rats. *Reproductive Toxicology* 7, 349-358.

- Bjerke, D. and Peterson, R. (1994). Reproductive toxicity of 2,3,7,8 tetrachlorodibenzo-p-dioxin in male rats: Different effects of in utero versus lactational exposure. *Toxicology and applied Pharmacology* 127, 241-249.
- Briand P, Lykkesfeldt AE, 1986. Long-term cultivation of a human breast cancer cell line, MCF7, in chemically defined medium. Effect of estradiol. *Anticancer Res* 6:85-90.
- Brooks S.C., Locke E.R. and Soule H.D. (1973). Estrogen receptor in a human cell line (MCF-7) from breast carcinoma. *Journal of Biological Chemistry* 248:6251-3.
- Brotans JA, Olea-Serrano MF, Villalobos M, Pedraza, V, Olea N., 1995 Xenoestrogens released from lacquer coating in food cans. *Environ Health Perspect* 103:608-613.
- Butler W, Kirkland WL, Gargala T, Goran N, Kelsey WH, Berlinski P, 1983. Steroid stimulation of plasminogen activator production in a human breast cancer cell line (MCF-7). *Cancer Res* 43:1637-1641.
- Butler W.B. (1984). Preparing nuclei from cells in monolayer cultures suitable for counting and for following synchronized cells through the cell cycle. *Analytical Biochemistry* 141:70-3.
- Cavaillès V., Garcia M., Rochefort H. (1989). Regulation of Cathepsin-D and pS2 Gene Expression by Growth Factors in MCF7 Human Breast Cancer Cells. *Mol Endocrinology* 3:552-558.
- Chapin, R., Harris, M., Shelby, M., Smialowicz, R., Moser, V., Padilla, S., MacPhail, R., and Berone, S. The effects of perinatal/juvenile pesticide exposure on adult CNS, Immune and reproductive function in rats. *The Toxicologist* 30, 52.
- Clark M., Cramer R.D., Jones D.M., Patterson D.E., Simeroth P.E. (1990). Comparative Molecular Field Analysis (CoMFA). 2. Toward its use with 3D-Structural Databases. *Tetrahedron Comp Meth* 3:47-59.
- Conner, J., Cook, J., Craven. C., Van Pelt, C., and Obourn J. (1996). An *in vivo* battery for identifying endocrine modulators that are estrogenic or dopamine regulators. *Fundamental and Applied Toxicology* 33, in print.
- Connor K., Howell J., Chen I., Berhane K., Sciarretta C., Safe S. and Zacharewski T. (1996). Failure of chloro-S-triazine-derived compounds to induce estrogen receptor-mediated responses *in vivo* and *in vitro*. *Fund Appl Toxicol* 30:93-101.
- Cramer R.D.I., Patterson D.E., Bunce J.D. (1988). Comparative molecular field analysis (CoMFA). 1. Effect of shape on binding of steroids to carrier Proteins. *J Am Chem Soc* 110:5959-5967.
- Cummings, A. (1990). Toxicological mechanisms of implantation failure. *Fundamental and Applied Toxicology* 15, 571-579.
- Cummings, A., and Gray, L. (1989). Antifertility effect of methoxychlor in female rats: Dose- and time-dependent blockade of pregnancy. *Toxicology and Applied Pharmacology* 97, 454-462.

- Davis M.D., Butler W.B. and Brooks S.C. (1995). Induction of tissue plasminogen activator mRNA and activity by structurally altered estrogens. *J Steroid Biochem Mol Biol* 52:421-430.
- Dell'Aquila M.L., Pigott D.A., Bonaquist D.L. and Gaffney E.V. (1984). A factor from plasma-derived human serum that inhibits the growth of the mammary cell line MCF-7: characterization and purification. *Journal of the National Cancer Institute* 72:291-8.
- Desbrow, C., Waldock, M., Sheahan, D., Blackburn, M., Routledge, E., Sumpter, J., and Brighty G., The identification of compounds causing endocrine disruption in fish in UK rivers. 17th Annual Society of Environmental Toxicology and Chemistry Abstract 190.
- Devleeschouwer N., Legros N., Olea-Serrano N., Paridaens R. and Leclercq G. (1987). Estrogen conjugates and serum factors mediating the estrogenic trophic effect on MCF-7 cell growth. *Cancer Research* 47:5883-7.
- Dodds, E., Lawson, W., and Noble, R. (1938). Biological effects of the synthetic oestrogenic substance 4:4'-dihydroxy-1:B-diethylstilbene. *Lancet* 139, 627.
- Edgren, R. (1994). Issues in animal pharmacology. In: *Pharmacology of the contraceptive steroids*. Ed J. Goldzieher, Raven Press, Ltd., New York.
- Eisman J.A., Martin T.J., MacIntyre I., Frampton R.J., Moseley J.M. and Whitehead R. (1980). 1,25-Dihydroxyvitamin D3 receptor in a cultured human breast cancer cell line (MCF 7 cells). *Biochemical & Biophysical Research Communications* 93:9-15.
- Fail, P, Pearce, Anderson, S., Tyl, R., and Gray, L. (1995). Endocrine and reproductive toxicity of vinclozolin in male Long-Evans hooded rats. *The Toxicologist* 15, 293.
- Gagne D., Balaguer P., Demirpence E., Chabret C., Trousse F., Nicolas J.C. and Pons M. (1994). Stable luciferase transfected cells for studying steroid receptor biological activity. *Journal of Bioluminescence & Chemiluminescence* 9:201-9.
- Gaido, K.W., Leonard, L.S., Lovell, S., Gould, J.C., Babai, D., Portier, C.J., McDonnell, D.P. (1996). Evaluation of chemicals with endocrine modulating activity in a yeast-based steroid hormone receptor gene transcription assay. *Toxicol. Appl. Pharmacol.* (submitted).
- Gaido, K.W., Leonard, L.S., Lovell, S., Gould, J.C., Babai, D., Portier, C.J., McDonnell, D.P. (1996). Evaluation of chemicals with endocrine modulating activity in a yeast-based steroid hormone receptor gene transcription assay. *Toxicol. Appl. Pharmacol.* (submitted).
- Gellert, R. J., Heinrichs, W. L. and Swerdloff, R. 1974. Effects of neonatally-administered DDT homologs on reproductive function in male and female rats. *Neuroendocrinology* 16: 84-94.

- Gellert, R.J. 1978 a. Kepone, Mirex, Dieldrin and Aldrin: Estrogenic activity and the induction of persistent vaginal estrus and anovulation in rats following neonatal treatment. Environmental Research 16: 131-138.
- Gellert, R.J. 1978 b. Uterotrophic activity of polychlorinated biphenyls and induction of precocious reproductive aging in neonatally treated female rats. Environ. Res. 16: 123-130.
- Gellert, R.J. and Wilson, C. 1979. Reproductive function in rats exposed prenatally to pesticides and polychlorinated biphenyls (PCB). Environmental Research 18: 437-443.
- Gray, L.E., Jr. 1982. Neonatal chlordecone exposure alters behavioral sex differentiation in female hamsters. Neurotoxicology 3(2): 67-80.
- Gellert, R.J. and Wilson, C. 1979. Reproductive function in rats exposed prenatally to pesticides and polychlorinated biphenyls (PCB). Environmental Research 18: 437-443.
- Gillesby, B., and Zacharewski, T. (1996). Endocrine disrupters: Mechanism of action of promiscuous receptors and strategies for identification and assessment. 17th Annual Society of Environmental Toxicology and Chemistry Abstract 006.
- Glasser, S., Northcutt, R., Chytil, F. and Strott, C. (1972). The influence of an antisteroidogenic drug (aminoglutethimide phosphate) on pregnancy maintenance. Endocrinology 90, 1363-1370.
- Goldman, A.S., Eavey, R.D., Baker, M.K. 1976. Production of male pseudohermaphroditism in rats by two new inhibitors of steroid 17 α -hydroxylase and C17-20 lyase. J. Endocrinology 71, 289-297.
- Gonzalez M. D., Lopez, F., and Aguilar, E. (1984). Involvement of prolactin in the onset of puberty in female rats. Journal of Endocrinology 101; 63-68.
- Goodman and Gillman's, The Pharmacological basis of therapeutics. (1990). Eighth Edition, MacMillian.
- Gorski, R.A., Gordon, J.H. Shryne, J.E., and Southam, A.M. 1978. Evidence for a morphological sex difference within the medial preoptic area of the rat brain. Brain Research 148: 333-346.
- Gray, L. E., Ostby, J. s., and Kelce, W. R. (1994). Developmental effects of an environmental antiandrogen: The fungicide vinclozolin alters sex differentiation of the male rats. Toxicology and Applied Pharmacology 129, 46-52.
- Gray, L.E. Jr., J. Ostby, R. Sigmon, R. Linder (1991). A Fungicide (Fenarimol) That Inhibits Fungal Sterol Synthesis Also Reduces Mating Behavior and Fertility in Male Rats. Biol of Reproduction Supplement.
- Gray, L.E. Jr., Ostby, J., Ferrell, J., Rehnberg, G., Linder, R., Cooper, R., Goldman, J. Slott, V., and Laskey, J. 1989. A dose-response analysis of methoxychlor-induced alterations of

- reproductive development and function in the rat. Fundamental and Applied Toxicology (12) 92-108.
- Gray, L.E. Jr., Ostby, J., Ferrell, J., Rehnberg, G., Linder, R., Cooper, R., Goldman, J. Slott, V., and Laskey, J. 1989. A dose- response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fundamental and Applied Toxicology (12) 92-108.
- Gray, L.E. Jr., Ostby, J., Ferrell, J., Rehnberg, G., Linder, R., Cooper, R., Goldman, J. Slott, V., and Laskey, J. 1989. A dose- response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fundamental and Applied Toxicology (12) 92-108.
- Gray, L.E. Jr., Ostby, J., Ferrell, J., Rehnberg, G., Linder, R., Cooper, R., Goldman, J. Slott, V., and Laskey, J. 1989. A dose- response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fundamental and Applied Toxicology (12) 92-108.
- Gray, L.E. Jr., Ostby, J., Ferrell, J., Rehnberg, G., Linder, R., Cooper, R., Goldman, J. Slott, V., and Laskey, J. 1989. A dose- response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fundamental and Applied Toxicology (12) 92-108.
- Gray, L.E., Jr., Ostby, J., Ferrell, J., and Goldman, J., 1998. Methoxychlor- Induced Alterations of Estrogen-Dependent Running Wheel Activity, The Reproductive Tract and Pituitary Function in the Female Rat. Toxicology and Applied Pharmacology 96:525-540.
- Gray, L.E., Kelce, W.R., Monosson, E., Ostby, J.S., and Birnbaum, L.S. (1995). Exposure to TCDD during development permanently alters reproductive function in male LE rats and Hamsters: Reduced ejaculated and epididymal sperm numbers and sex accessory gland weights in offspring with normal androgenic status. Toxicol and Appl Pharmacol 131 (1), 108-118.
- Gray, L.E., Kelce, W.R., Monosson, E., Ostby, J.S., and Birnbaum, L.S. (1995). Exposure to TCDD during development permanently alters reproductive function in male LE rats and Hamsters: Reduced ejaculated and epididymal sperm numbers and sex accessory gland weights in offspring with normal androgenic status. Toxicol and Appl Pharmacol 131 (1), 108-118.
- Gray, L.E., Klinefelter, G., Kelce, W., Laskey, J., Ostby, J., Marshall, R., and Ewing, L. (1995). An *in vivo* and *in vitro* comparison of the effects of ethane dimethanesulfonate (EDS) on Leydig cell function in hamsters and rats. Tox. Appl. Pharmacol. 130:248-256.
- Gray, L.E., Monosson, E., and Kelce, W. (1996). Emerging issues: the effects of endocrine disrupters on reproductive development. In: Interconnections between human ;and

- ecosystem health. Eds. R. Di Giulio and E. Monosson. Chapman and Hall, London, Chapter 4.
- Gray, L.E., Ostby, J., Wolf, C., Miller, D., Kelce, W., Gordon, C., and Birnbaum, L. (1995 b). Functional developmental toxicity of low doses of 2,3,7,8 tetrachlorodibenzo-p-dioxin and a dioxin-like PCB (169) in Long Evans rats and Syrian hamsters: Reproductive, behavioral and thermoregulatory alterations. *Organohalogen Compounds* 25, 33-38.
- Gray, L.E., Jr. 1982. Neonatal chlordecone exposure alters behavioral sex differentiation in female hamsters. *Neurotoxicology* 3(2): 67-80.
- Gupta, C. The role of epidermal growth factor receptor (EGFR) in male reproductive tract differentiation. *Endocrinology* 137, 905-910.
- Gupta, C., Siegel, S., and Ellis., E. (1991). The role of EGF in testosterone-induced reproductive tract differentiation. *Developmental Biology* 146, 106-116.
- Hannon, W., Hill, F., Bernert J. et al., (1987). Premature thelarche in Puerto Rico: a search for environmental estrogenic contamination. *Arch. Environ. Contam. Toxicol.* 16, 255-262.
- Hardy, M.P., Kelce, W.R., Klinefelter, G.R., and Ewing, L.L. (1990). Differentiation of Leydig cell precursors *in vitro*: a role for androgen. *Endocrinology*. 127:488-490.
- Harris, M., Chapin, R., Haskins, J., Allen, J., Collins, B., Davis, B., Lockhart, A., and Mauney, M. The effects of perinatal/juvenile pesticide exposure on adult reproductive performance. *The Toxicologist* 30, 144.
- Harris, M., Chapin, R., Haskins, J., Allen, J., Collins, B., Davis, B., Lockhart, A., and Mauney, M. The effects of perinatal/juvenile pesticide exposure on adult reproductive performance. *The Toxicologist* 30, 144.
- Hausler, A., Schenkel, L., Krahenbuhl, C., Monnet, G., Bhatnagar, A. (1989). *Journal Steroid Biochemistry* 33, 125-131.
- Heinrichs, W.L., Gellert, R.J., Bakke, J.L., and Lawrence, N.L. 1971. DDT administered to neonatal rats induces persistent estrus syndrome. *Science* 173: 642-643.
- Hershberger, L., Shipley, E. Meyer, R. (1953). Myotrophic activity of 19-nortestosterone and other steroids determined by modified levator ani muscle method. *Proc Soc Exp Biol Med* 83, 175.
- Heywood, R., and Wadsworth, P. (1980). The experimental toxicology of estrogens. *Pharmacol. Ther.* 8, 125-142.
- Higashi, Y., Yoshida, K., and Oshima, H. (1990). In vitro inhibition by ketaconazole of human testicular steroid oxidoreductases. *Journal of Steroid Biochemistry* 36, 667-671.
- Hirsch, K., Weaver, D, Black, L, Falcone, J and MacLusky, N. (1987). Inhibition of central nervous system aromatase activity: A mechanism for fenarimol-induced infertility in the male rat. *Toxicology and Applied Pharmacology* 91, 235-245.

- Horwitz K.B., Costlow M.E. and McGuire W.L. (1975). MCF-7; a human breast cancer cell line with estrogen, androgen, progesterone, and glucocorticoid receptors. *Steroids* 26:785-95.
- Hostetter, M. and Piacsek, B. (1977). The effect of prolactin deficiency during sexual maturation in the male rat. *Biology of Reproduction* 17, 574-577.
- Huhtaniemi, I., Amsterdam, A., and Naor, Z. (1986). Effect of postnatal treatment with a gonadotropin-releasing hormone antagonist on sexual maturation of male rats. *Biology of Reproduction* 35, 501-507.
- Iguchi, T. (1992). Cellular effects of early exposure to sex hormones and antihormones. *International review of Cytology* vol 139, 1-55.
- Ince B.A., Montano M.M. and Katzenellenbogen B.S. (1994). Activation of transcriptionally inactive human estrogen receptors by cyclic adenosine 3',5'-monophosphate and ligands including antiestrogens. *Mol Endocrinol* 8:1397-1406.
- Jain P.T. and Pento J.T. (1991). Growth medium for the evaluation of antiestrogenic compounds in MCF-7 cell culture. *Methods & Findings in Experimental & Clinical Pharmacology* 13:595-8.
- Jain P.T., Pento J.T. and Graves D.C. (1992). Cell-growth quantitation methods for the evaluation of antiestrogens in human breast cancer cells in culture. *Journal of Pharmacological & Toxicological Methods* 27:203-7.
- Jobling S, Reynolds T, White R, Parker MG, Sumpter J, 1995. A variety of environmentally persistent chemicals, including some phthalate plasticizers, are weakly estrogenic. *Environ Health Perspect* 103:582-587.
- Johnson, D., Kogo, H., Sen, M., and Dey, S. (1988). Multiple estrogenic action of o,p' DDT: Initiation and maintenance of pregnancy in the rat.
- Katzenellenbogen B.S., Kendra K.L., Norman M.J. and Berthois Y. (1987). Proliferation, hormonal responsiveness, and estrogen receptor content of MCF-7 human breast cancer cells grown in the short-term and long-term absence of estrogens. *Cancer Research* 47:4355-60.
- Katzenellenbogen B.S., Montano M.M., Le Goff P., Schodin D.J., Kraus W.L., Bhardwaj B. and Fujimoto N. (1995). Antiestrogens: Mechanisms and actions in target cells. *J Steroid Biochem Mol Biol* 53:387-393.
- Kelce WR, CR Stone, SC Laws, LE Gray, Jr. and EM Wilson. Persistent DDT Metabolite p,p'-DDE is a Potent Androgen Receptor Antagonist. *Nature* 375: 581-585, 1995.
- Kelce WR, Monosson E, Gamcsik MP, Laws SC and Gray LE, Jr. Environmental Hormone Disruptors: Evidence that Vinclozolin Developmental Toxicity is Mediated by Antiandrogenic Metabolites. *Toxicology and Applied Pharmacology* 126: 276-285, 1994.

- Kelce, W.R., Monosson, E., Gamcsik, M.P., Laws, S.C., and Gray, L.E. Jr. (1994). Environmental hormone disruptors: Evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites. *Toxicol Appl Pharmacol* 126, 275-285.
- Kelce, W.R., Stone, C., Laws, S., Gray, L.E., Kemppainen, J., and Wilson, E. (1995). Persistent DDT metabolite p,p' DDE is a potent androgen receptor antagonist. *Nature* 375 (15), 581-585.
- Kelce, W.R., Stone, C., Laws, S., Gray, L.E., Kemppainen, J., and Wilson, E. (1995). Persistent DDT metabolite p,p' DDE is a potent androgen receptor antagonist. *Nature* 375 (15), 581-585.
- Kitawaki J., Kim T., Kanno H., Noguchi T., Yamamoto T. and Okada H. (1993). Growth suppression of MCF-7 human breast cancer cells by aromatase inhibitors: a new system for aromatase inhibitor screening. *Journal of Steroid Biochemistry & Molecular Biology* 44:667-70.
- Klinefelter, G., Laskey, J., Ferrell, J., Roberts, N., Suarez, J. (1994). Chloroethylmethanesulfonate-induced effects on the epididymis seem unrelated to altered Leydig cell function. *Biol. Reprod.* 51:82-91.
- Klinefelter, G.R. and Ewing, L.L. (1988). Optimizing testosterone production by purified adult rat Leydig cells *in vitro*. *in vitro Cell. Dev. Biol.* 24:545-549.
- Klinefelter, G.R. and Ewing, L.L. (1989). Maintenance of testosterone production by purified adult rat Leydig cells for 3 days *in vitro*. *In Vitro Cell. Dev. Biol.* 25:283-288.
- Klinefelter, G.R., Hall, P.F. and Ewing, L.L. (1987). Effect of luteinizing hormone deprivation *in situ* on steroidogenesis of rat Leydig cells purified by a multistep procedure. *Biol. Reprod.* 36:769-783.
- Klinefelter, G.R., Kelce, W.R. (in press). A Comparison of Leydig Cell Responsiveness to Hormonal and Nonhormonal Factors *in vivo and in vitro*. In: *The Leydig Cell*, (Russel L. and Hardy M., eds.), Cache River Press.
- Klinefelter, G.R., Kelce, W.R., Hardy, M.P. (1993). The isolation and culture of Leydig cells from adult rats. In: *Methods in Toxicology*, Volume 3, Part A, (Heindel J. and Chapin R., eds.), Academic Press, pp 166-181.
- Klinefelter, G.R., Laskey, J.W., and Roberts, N.R. (1991). *in vivo/in vitro* effects of ethane dimethanesulphonate on Leydig Cells of adult rats. *Tox. Appl. Pharm.* 107:460-471.
- Klotz D.M., Castles C.G., Fuqua S.A., Spriggs L.L. and Hill S.M. (1995). Differential expression of wild-type and variant ER mRNAs by stocks of MCF-7 breast cancer cells may account for differences in estrogen responsiveness. *Biochemical & Biophysical Research Communications* 210:609-15.

- Kohno, H., Gandidi, O., Curtis, S. W., and Korach, K. S. (1994). Anti-estrogen activity in the yeast transcription system: Estrogen receptor mediated agonist response. *Steroids* 1994: 572-578.
- Korach K.S. (1979). Estrogen action in the mouse uterus: characterization of the cytosol and nuclear receptor systems. *Endocrinology* 104:1324-32. Several Reviews By Katenellenbogen
- Korenbrot, C.C., Huhtaniemi, I., Weiner, R. (1977). Prepubertal separation as an external sign of pubertal development in the male rat. *Biology of Reproduction* 17, 298-303.
- Krall, A., and K.R. Yamamoto (1996). An FK506-sensitive transporter selectively decreases intracellular levels and potency of steroid hormones. *Journal of Biological Chemistry* 271, 17152-17156.
- Krishnan A.V., Stathis P., Permuth S.F., Tokes L. and Feldman D. (1993). Bisphenol-A: an estrogenic substance is released from polycarbonate flasks during autoclaving [see comments]. *Endocrinology* 132:2279-86.
- Krishnan AV, Starhis P, Permuth SF, Tokes L, Feldman D., 1993. Bisphenol-A. an estrogenic substance is released from polycarbonate flasks during autoclaving. *Endocrinology* 132:2279-2286.
- Kurebayashi J., Horiuchi R., Nakamura T., Iino Y., Ishida T., Takigawa H. and Izuo M. (1987). [Effects of estrogen and endocrine therapeutic agents on the estrogen receptor, progesterone receptor and DNA synthesis in MCF-7 human breast cancer cells using the whole cell uptake method]. [Japanese]. *Nippon Naibunpi Gakkai Zasshi - Folia Endocrinologica Japonica* 63:1351-63.
- Larsson, K (1979). Features of the neuroendocrine regulation of masculine sexual behavior. In: *Endocrine Control of Sexual Behavior*. Eds C. Beyer, Raven Press, New York, p 77-163.
- Laskey, J. and Berman, E. (1993). Steroidogenic assessment using ovary culture in cycling rats: Effects of bis (2-diethylhexyl) phthalate on ovarian steroid production. *Reproductive Toxicology* 7, 25-33.
- Laskey, J., Berman, E., and Ferrell J. (1995). The use of cultured ovarian fragments to assess toxicant alterations in steroidogenesis in Sprague-Dawley rat. *Reproductive Toxicology* 9, 131-141.
- Laskey, J.W. and Phelps, P.V. (1991). Effect of cadmium and other metal cations on *in vitro* Leydig cell testosterone production. *Toxicol. Appl. Pharmacol.* 108:296-306.
- Laskey, J.W., Klinefelter, G.R., Kelce, W.R., and Ewing, L.L. (1994). Effects of ethane dimethanesulfonate on adult and immature rabbit Leydig cells: comparison with EDS-treated rat Leydig cells. *Biol. Reprod.* 50:1151-1160.

- Lasky, J.W. et al. 1994. Effects of ethane dimethanesulfonate (EDS) on adult and immature rabbit Leydig cells: comparison with EDS-treated rat Leydig cells. *Biol. Reprod.* 50: 1151-1160.
- Laursen I, Briand P, Lykkesfeldt AE., 1990. Serum albumin as a modulator on growth of the human breast cancer cell line, MCF-7. *Anticancer Res* 10:343-351.
- Laws, S., Carey, S., Huey, O., and Gray, L. E. (1995). 4-tert-octylphenol: in vitro and *in vivo* assessments of potential estrogenicity in rats. *The Toxicologist* 30, 132.
- Laws, S., Carey, S., Huey, O., and Gray, L. E. (1995). 4-tert-octylphenol: in vitro and *in vivo* assessments of potential estrogenicity in rats. *The Toxicologist* 30, 132.
- Leung, P. and Armstrong, D. (1979). Estrogen treatment of immature rats inhibits ovarian androgen production in vitro. *Journal Endocrinology* 104, 1411-1417.
- Lippman M., Bolan G. and Huff K. (1976). The effects of estrogens and antiestrogens on hormone-responsive human breast cancer in long-term tissue culture. *Cancer Research* 36:4595-601.
- Luke M. and Coffey, D. (1994). The male sex accessory tissues. Chapter 23. In: *The physiology of reproduction*, second edition. Ed Knobil, E. and J. Neill, Raven Press, New York.
- Lykkesfeldt AE, Briand P., 1986 Indirect mechanism of oestradiol stimulation of cell proliferation of human breast cancer cell lines. *Br J Cancer* 53:29-35.
- MacIndoe J.H. and Woods G.R. (1981). Steroid-metabolizing enzymes in human breast cancer cells. II. 5 alpha-Reductase, 3 alpha-hydroxysteroid oxidoreductase, and 17 beta-hydroxysteroid oxidoreductase. *Endocrinology* 108:1407-13.
- MacIndoe J.H., Hinkhouse M. and Woods G. (1990). Dehydroepiandrosterone and estrone 17-ketosteroid reductases in MCF-7 human breast cancer cells. *Breast Cancer Research & Treatment* 16:261-72.
- Masamura S., Santner S.J., Heitjan D.F. and Santen R.J. (1995). Estrogen deprivation causes estradiol hypersensitivity in human breast cancer cells. *Journal of Clinical Endocrinology & Metabolism* 80:2918-25.
- Mayr U., Butsch A. and Schneider S. (1992). Validation of two *in vitro* test systems for estrogenic activities with zearalenone, phytoestrogens and cereal extracts. *Toxicology* 74:135-49.
- McDonnell, D. P., Pike, J. W., Drutz, D. J., Butt, T. R., and O'Malley, B. W. (1989). Reconstitution of the vitamin D-responsive osteocalcin transcription unit in *Saccharomyces cerevisiae*. *Mol Cell Biol* 9: 3517-3523.
- Medlock, K., Branham, W., and Sheehan D. (1995). The effects of phytoestrogens on neonatal rat growth and development. *Proceedings of the Society for Experimental Biology and Medicine* 208, 307-313.

- Mellanen P., Petanen T., Lehtimaki J., Makela S., Bylund G., Holmbom B., Mannila E., Oikari A. and Santti R. (1996). Wood-derived estrogens: Studies *in vitro* with breast cancer cell lines and *in vivo* in trout. *Toxicol Appl Pharmacol* 136:381-388.
- Metzger, D., White, J. H., and Chambon, P. (1988). The human oestrogen receptor functions in yeast. *Nature* 334: 31-36.
- Meyer T., Koop R., von Angerer E., Schonenberger H. and Holler E. (1994). A rapid luciferase transfection assay for transcription activation effects and stability control of estrogens in cell cultures. *Journal of Cancer Research & Clinical Oncology* 120:359-64.
- Milen, C., Hasmall, R., Russell, A., Watson, S., Vaughan, Z., and Middleton, M. (1987). Reduced estradiol production by a substituted triazole results in delayed ovulation in rats. *Toxicology and Applied Pharmacology* 90, 427-435.
- Miyazaki, K., Dambrosia, J., and Kebabian, J. (1985). Dopaminergic modulation of DES-induced proliferation of the anterior pituitary of the Fisher 344 rat. *Neuroendocrinology* 41, 405-408.
- Moore M., Mustain M., Daniel K., Chen I., Safe S. and Zacharewski T. (1996). Antiestrogenic activity of hydroxylated polychlorinated biphenyl congeners identified in human serum. *Toxicology and Applied Pharmacology* In Press:.
- Morali, G., and Beyer, C. (1979). Neuroendocrine control of mammalian estrous behavior. In: *Endocrine Control of Sexual Behavior*. Eds C. Beyer, Raven Press, New York, p 33-75.
- Murray, M. and Reidy, G. 1990. Selectivity in the inhibition of mammalian cytochromes P-450 by chemical agents. *Pharmacol. Rev.* 42:85-101.
- Murray, M., and Reidy, G. (1990). Selectivity in the inhibition of mammalian cytochromes P-450 by chemical agents. *Pharmacological Reviews* 42, 85-101.
- Nawata H., Chong M.T., Bronzert D. and Lippman M.E. (1981). Estradiol-independent growth of a subline of MCF-7 human breast cancer cells in culture. *Journal of Biological Chemistry* 256:6895-902.
- Nelson, K., Takahashi, T., Bossert, N., Walmer, D., and McLachlan, J. (1991). Epidermal growth factor replaces estrogen in the stimulation of female genital-tract growth and differentiation.
- Nelson, K., Takahashi, T., Bossert, N., Walmer, D., and McLachlan, J. (1991). Epidermal growth factor replaces estrogen in the stimulation of female genital-tract growth and differentiation.
- Nimrod, A.C. and W.H. Benson. (1998). Xenobiotic-induced alterations in estrogen receptor function and characterization. *Toxicology and Applied Pharmacology* 147:381-390.
- Nunez A., Berry M., Imler J., Chambon P. (1989). The 5' flanking region of the pS2 Gene contains a complex enhancer region responsive to oestrogens, epidermal growth factor, a

- tumor promoter (TPA), the *c-Ha-ras* oncoprotein and the *c-jun* protein. *EMBO J* 8:823-829.
- Osborne CK, Boldt DH, Estrada P., 1984. Human breast cancer cell cycle synchronization by estrogens and antiestrogens in culture. *Cancer Research*. 44(4):1433-9.
- Parker, A. (1966). *Marshall's Physiology of Reproduction*. Edited by A. Parkes, Volume III, Longmans Green and Co. Ltd., London.
- Pepper, G., Brenner, S., and Gabilove, J. (1990). Ketoconazole use in the treatment of ovarian hyperandrogenism. *Fertility and Sterility* 54, 438-444.
- Perez, P., Pulgar, R., Olea-Serrano, F., Villalobos, M., Rivas, A., Metzler, M., Pedraza, V. and Olea, N., 1998. The estrogenicity of bisphenol-A related diphenyl alkanes with various substituents at the central carbon and the hydroxy groups. In press, *EHP*, March issue.
- Piasek, M. and Laskey, J. (1994). Acute cadmium exposure and ovarian steroidogenesis in cycling and pregnant rats. *Reproductive Toxicology* 8, 495-507.
- Pilat M.J., Hafner M.S., Kral L.G., Brooks S.C. (1993). Differential induction of pS2 and cathepsin D mRNAs by structurally altered estrogens. *Biochemistry* 32:7009-7015.
- Pons M., Gagne D., Nicolas J.C. and Mehtali M. (1990). A new cellular model of response to estrogens: a bioluminescent test to characterize (anti) estrogen molecules. *Biotechniques* 9:450-9.
- Purvis, I. J., Chotai, D., Dykes, C. W., Lubahn, D. B., French, F. S., Wilson, E. M., and Hobden, A. N. (1991). An androgen-inducible expression system for *Saccharomyces cerevisiae*. *Gene* 106: 35-42.
- Ramely, J. and Phares, C. (1983). Delay of puberty onset in males due to suppression of growth hormone. *Neuroendocrinology* 36, 321-329.
- Ramirez, V., and Sawyer, C. (1964). Advancement of puberty in the female rat by estrogen. *Endocrinology* 76, 1158-1168.
- Reel, J., Lamb, J., and Neal, B. (1996). Survey and assessment of mammalian estrogen biological assays for hazard characterization. *Fundamental and Applied Toxicology* 33, (in press).
- Reel, J., Lawton, A., Wolkowski-Tyl, R., Davis, G., and Lamb, J. (1985). Evaluation of a new reproductive toxicology protocol using diethylstilbestrol (DES) as a positive control compound. *Journal of the American College of Toxicology* 4, 147.
- Robaire, B., Ewing, L.L., Irby, D.C. and Desjardins, C. (1979). Interactions of testosterone and estradiol-17 β on the reproductive tract of the male rat. *Biology of Reproduction* 21, 455-463.
- Ruh M.F., Zacharewski T., Connor K., Howell J., Chen I. and Safe S. (1995). Naringenin: A weakly estrogenic bioflavonoid that exhibits antiestrogenic activity. *Biochem Pharmacol* 50:1485-1493.
- Salamon, V. (1938). The effect of testosterone propionate on the genital tract of the immature female rat. *Endocrinology* 23, 779-783.

- Salamon, V. (1938). The effect of testosterone propionate on the genital tract of the immature female rat. *Endocrinology* 23, 779-783.
- Schardein, J.L. (1993). Hormones and hormonal antagonists. In *Chemically induced birth defects*. pp. 271-339. Marcel Dekker, New York.
- Schena, M., and Yamamoto, K. R. (1988). Mammalian glucocorticoid receptor derivatives enhance transcription in yeast. *Science* 241: 965-967.
- Schurmeyer, T., and Nieschlag, E. (1984). Effect of ketoconazole and other imidazole fungicides on testosterone biosynthesis. *Acta Endocrinologica* 105, 275-280.
- Shaban M. and Terranova, P. (1986). 2-Bromo-1-ergocryptine mesylate (CB-154) inhibits prolactin and luteinizing hormone secretion in the prepubertal female rat. *Biology of Reproduction* 34, 788-795.
- Shafie S. and Brooks S.C. (1979). Characteristics of the dextran-coated charcoal assay for estradiol receptor in breast cancer preparations. *Journal of Laboratory & Clinical Medicine* 94:784-98.
- Sheehan, D. (1995). The case for expanded phytoestrogen research. *Proceedings of the Society for Experimental Biology and Medicine* 208, 3-5.
- Sonnenschein C, Szelei J, Nye TL, Soto AM., 1994. Control of cell proliferation of human breast MCF7 cells; serum and estrogen resistant variants. *Oncology Research* 6:373-381
- Sonnenschein C., Szelei J., Nye T.L. and Soto A.M. (1994). Control of cell proliferation of human breast MCF7 cells; serum and estrogen resistant variants. *Oncology Research* 6:373-81.
- Sonnenschein, C., Papendorp, J.T. and Soto, A.M., 1985. Estrogenic effect of Tamoxifen and its derivatives on the proliferation of MCF7 human breast tumor cells. *Life Sciences* 37:387-394.
- Sonnenschein, C., Soto, A.M. and Michaelson, C.L., 1996. Human serum albumin shares the properties of estrocolonyone-I, the inhibitor of the proliferation of estrogen-target cells. *Journal of Steroid Biochemistry and Molecular Biology* 59:147-154.
- Soto A.M. and Sonnenschein C. (1984). Mechanism of estrogen action on cellular proliferation: evidence for indirect and negative control on cloned breast tumor cells. *Biochemical & Biophysical Research Communications* 122:1097-103.
- Soto A.M., Justicia H., Wray J.W. and Sonnenschein C. (1991). p-Nonyl-phenol: an estrogenic xenobiotic released from "modified" polystyrene. *Environmental Health Perspectives* 92:167-73.
- Soto A.M., Silvia R.M. and Sonnenschein C. (1992). A plasma-borne specific inhibitor of the proliferation of human estrogen-sensitive breast tumor cells (estrolycone-I). *Journal of Steroid Biochemistry & Molecular Biology* 43:703-12.

- Soto A.M., Sonnenschein C., Chung K.L., Fernandez M.F., Olea N. and Serrano F.O. (1995). The E-SCREEN assay as a tool to identify estrogens: an update on estrogenic environmental pollutants. *Environmental Health Perspectives* 103 Suppl 7:113-22.
- Soto, A.M. and Sonnenschein, C., 1984. Mechanism of estrogen action on cellular proliferation: Evidence for indirect and negative control on cloned breast tumor cells. *Biochem. Biophys. Res. Commun.* 122:1097-1103.
- Soto, A.M. and Sonnenschein, C., 1985. The role of estrogens on the proliferation of human breast tumor cells (MCF-7). *J. Steroid Biochem.* 37:87-94.
- Soto, A.M., Fernandez, M.F., Luizzi, M.F., Oles Karasko, A. S., and Sonnenschein, C., 1997. Developing a marker of exposure to xenoestrogen mixtures in human serum. *Environmental Health Perspectives* 105: 647-654.
- Soto, A.M., Lin, T-M., Justicia, H., Silvia, R.M. and Sonnenschein, C., 1992. An "in culture" bioassay to assess the estrogenicity of xenobiotics. In: *Chemically induced alterations in sexual development: The wildlife/human connection*, ed. T. Colborn and C. R. Clement. Princeton Scientific Publishing Co. Princeton, NJ., pp. 295-309.
- Soto, A.M., Wray, J., Justicia, H. and Sonnenschein, C., 1991. p-Nonyl phenol: an estrogenic xenobiotic released from modified polystyrene. *Environ. Health Perspect.*, 92:167-173.
- Soule H.D., Vazquez J., Long A., Albert S. and Brennan M. (1973). A human cell line from a pleural effusion derived from a breast carcinoma. *Journal of the National Cancer Institute* 51:1409-16.
- Spencer, J., Torrado, T., Sanchez, R., Vaughn E., and Imperato-McGinley, J. (1991). Effects of flutamide and finasteride on rat testicular descent. *Endocrinology* 129, 741-748.
- Steinberger, A. and Klinefelter G. (1993). Sensitivity of Sertoli and Leydig cells to xenobiotics in *in vitro* models. *Reprod. Toxicol.*, Volume 7, pp 23-37.
- Szelei, J., Jimenez, J., Soto, A.M., Luizzi, M.F. and Sonnenschein, C., 1997. Androgen-induced inhibition of proliferation in human breast cancer MCF7 Cells Transfected with Androgen Receptor. *Endocrinology* 138:1406-1412.
- Takenawa T., Ueda H., Millan J.C. and Brandes D. (1980). Retinoic acid-binding protein in a human cell (MCF-7) from breast carcinoma. *Laboratory Investigation* 42:490-4.
- Taton M., et al. 1988. Interaction of Triazole fungicides and plant growth regulators with microsomal cytochrome P-450-dependent obtusifoliol 14a-Methyl Demethylase. *Pestic Biochem. Physiol.* 90:1363-1370.
- Taton, M., Ullmann, P., Benveniste, P., and Rahier, A. (1988). *Pesticide Biochemistry and Physiology* 30, 178-189.
- Tayeb, E., Salih, Y., Pillay, A. (1985). Effects of aminoglutethimide on ovarian histology in the rat. *Acta anat.* 122, 212-215.

- Taylor C.M., Blanchard B. and Zava D.T. (1984). A simple method to determine whole cell uptake of radiolabelled oestrogen and progesterone and their subcellular localization in breast cancer cell lines in monolayer culture. *Journal of Steroid Biochemistry* 20:1083-8.
- Toppiari, et al., (1996). Male reproductive health and environmental xenoestrogens. *Environmental Health Perspectives* 104, 741-803.
- Tsai M.J. and O'Malley B.W. (1994). Molecular mechanisms of action of steroid/thyroid receptor superfamily members. [Review]. *Annual Review of Biochemistry* 63:451-86.
- van Ravenzwaay, B. Discussion of prenatal and reproduction toxicity of Reg. No. 83-258 (Vinclozolin). Data Submission to USEPA from BASF Corporation, MRID 425813-02, 1992.
- VanderKuur J.A., Hafner M.S., Christman J.K., Brooks S.C. (1993b). Effects of estradiol-17beta analogues on activation of estrogen response element regulated chloramphenicol acetyltransferase expression. *Biochemistry* 32:7016-7021.
- VanderKuur J.A., Wiese T., Brooks S.C. (1993a). Influence of estrogen structure on nuclear binding and progesterone receptor induction by the receptor complex. *Biochemistry* 32:7002-7008.
- Vickers P.J., Dickson R.B., Shoemaker R. and Cowan K.H. (1988). A multidrug-resistant MCF-7 human breast cancer cell line which exhibits cross-resistance to antiestrogens and hormone-independent tumor growth *in vivo*. *Molecular Endocrinology* 2:886-92.
- Villalobos M., Olea N., Brotons J.A., Olea-Serrano M.F., Ruiz de Almodovar J.M. and Pedraza V. (1995). The E-screen assay: a comparison of different MCF7 cell stocks. *Environ Health Perspect* 103:844-50.
- Vom Saal, F. (1995). Effects of exposure to estrogenic chemicals during fetal life on the reproductive system of male mice. *International School of Ethology* 11th
- Vom Saal, F., Montano, M. Wang, M. (1992). Sexual differentiation in mammals. In: *Advances in modern environmental toxicology vol XXI. Chemically-induced alterations in sexual and functional development: The wildlife/human connection*. Eds. T. Colborn and C. Clement. Princeton Scientific Publishing Co. Inc. p 203-230.
- Wakeling A.E. and Bowler J. (1988). Novel antioestrogens without partial agonist activity. *Journal of Steroid Biochemistry* 31:645-53.
- Wakeling A.E. and Bowler J. (1992). ICI 182,780, a new antioestrogen with clinical potential. [Review]. *Journal of Steroid Biochemistry & Molecular Biology* 43:173-7.
- Wakeling A.E., Newbould E. and Peters S.W. (1989). Effects of antioestrogens on the proliferation of MCF-7 human breast cancer cells. *Journal of Molecular Endocrinology* 2:225-34.

- Waller C.L., Juma B.W., Gray L.E. and Kelce W.R. (1996a). Three-dimensional quantitative structure-activity relationships for androgen receptor ligands. *Toxicology and Applied Pharmacology* 137:219-227.
- Waller C.L., Minor D.L. and McKinney J.D. (1995). Using three-dimensional quantitative structure-activity relationships to examine estrogen receptor binding affinities of polychlorinated hydroxybiphenyls. *Environ Health Perspect* 103:702-707.
- Waller C.L., Oprea T.I., Chae K., Park H., Korach K.S., Laws S.C., Wiese T.E., Kelce W.R. and Gray L.E. (1996b). Ligand-Based Identification of Environmental Estrogens. *Chemical Research in Toxicology* In Press:.
- Waller CL, Juma BW, Gray LE and Kelce WR. Three-Dimensional Quantitative Structure Activity Relationships for Androgen Receptor Ligands. *Toxicology and Applied Pharmacology* 137: 219-227, 1996.
- Welshons W.V. and Jordan V.C. (1987). Adaptation of estrogen-dependent MCF-7 cells to low estrogen (phenol red-free) culture. *European Journal of Cancer & Clinical Oncology* 23:1935-9.
- Welshons W.V., Grady L.H., Engler K.S. and Judy B.M. (1992). Control of proliferation of MCF-7 breast cancer cells in a commercial preparation of charcoal-stripped adult bovine serum. *Breast Cancer Research & Treatment* 23:97-104.
- Welshons W.V., Rottinghaus G.E., Nonneman D.J., Dolan-Timpe M. and Ross P.F. (1990). A sensitive bioassay for detection of dietary estrogens in animal feeds. *Journal of Veterinary Diagnostic Investigation* 2:268-73.
- White R, Jobling S, Hoare SA, Sumpter JP, Parker MG., 1994. Environmentally persistent alkylphenolic compounds. *Endocrinology* 135:175-182.
- Wiese T.E., Kral L.G., Dennis K.E., Butler W.B. and Brooks S.C. (1992). Optimization of estrogen growth response in MCF-7 cells. *in vitro Cellular & Developmental Biology* 28A:595-602.
- Wiese T.E., Polin L.A., Palomino E., Horwitz J.P., Brooks S.C. (1996). Induction of the Estrogen Specific Mitogenic Response in MCF-7 Cells by Selected Analogues of Estradiol-17 β : A 3D QSAR Study. *25th National Medicinal Chemistry Symposium, Ann Arbor, MI* Abstract 24.
- Wilson EM and French FS. Binding properties of androgen receptors. Evidence for identical receptors in rat testis, epididymis and prostate. *J Biol Chem* 25: 5620-5629, 1976.
- Wong C-I, WR Kelce, M Sar and EM Wilson. Androgen Receptor Antagonist versus Agonist Activities of the Fungicide Vinclozolin Relative to Hydroxyflutamide. *Journal of Biological Chemistry* 270: 19998-20003, 1995.
- Workshop: Environmental Endocrine Disrupting Chemicals: Erice, Sicily, Nov 5-10, 1995. Abstract.

- Yarbrough WG, Quarmby VE, Simental JA, Joseph DJ, Sar M, Lubahn DB, Olsen KL, French FS and Wilson EM. A single base mutation in the androgen receptor gene causes androgen insensitivity in the testicular feminized rat. *J Biol Chem* 265: 8893-8900, 1990.
- Young, W., and Fish, W. (1945). The ovarian hormones and spontaneous running activity in the female rat. *Endocrinology* 36, 181-189.
- Z.-X. Zhou, M. Sar, J.A. Simental, M.V. Lane, and E.M. Wilson. A ligand-dependent bipartite nuclear targeting signal in the human androgen receptor. *J. Biol. Chem.* 269, 13115 1994.
- Zacharewski T. (1996). A review of *in vitro* bioassays for assessing estrogenic substances. *Environmental Science and Technology* In Press:.
- Zacharewski T., Berhane K., Gillesby B. and Burnison B.K. (1995). Evidence for the presence of estrogen receptor and Ah receptor ligands in pulp and paper mill black liquor. *Environmental Science and Technology* 29:2140-2146.
- Zacharewski T.R., Bondy K.L., McDonell P. and Wu Z.F. (1994). Antiestrogenic effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on 17 beta-estradiol-induced pS2 expression. *Cancer Research* 54:2707-13.

II. Thyroid Sections

- Bhat, N. B., Shanker, G., Peringer, R. A. (1981) Investigations on myelination in vitro: regulation of 2',3'-cyclic nucleotide 3'-phosphohydrolase by thyroid hormone in cultures of dissociated brain cells from embryonic., *J. Neurochem.*, 37:695-701.
- Bhat, N. R., Sarlieve, L. L., Rao, G. S., al., e. (1979) Investigations on myelination in vitro: regulation by thyroid hormone in cultures of dissociated brain cells from embryonic micc., *J. Biol Chem.*, 254:9342-9344.
- Bradley, D. J., W. S. Young, I., Weinberger, C. (1989) Differential expression of alpha and beta thyroid hormone receptor genes in rat brain and pituitary., *Proc. Natl. Acad. Sci. USA*, 86:7250-7254.
- Brown, D. D., Wang, Z., Furlow, J. D., Kanamori, A., Schwartzman, R. A., Remo, B. F. and Pinder, A. (1996) The thyroid hormone-induced tail resorption program during *Xenopus laevis* metamorphosis, *Proc Natl Acad Sci USA*, 93: 1924-1929.
- Brown, D. D., Wang, Z., Kanamori, A., Eliceiri, B., Furlow, J. D. and Schwartzman, R. (1995) Amphibian metamorphosis: a complex program of gene expression changes controlled by the thyroid hormone, *Recent Prog Horm Res*, 50: 309-315.
- Carr, F. E., Fisher, C. U., Fein, H. G. and Smallridge, R. C. (1993) Thyrotropin-releasing hormone stimulates c-jun and c-fos messenger ribonucleic acid levels: implications for calcium mobilization and protein kinase-C activation., *Endocrinology*, 133: 1700-1707.

- Denver, R. J., Pavgi, S., and Shi, Y. B. (1997) Thyroid hormone-dependent gene expression program for *Xenopus* neural development, *J Biol Chem.*, 272: 8179-8188.
- Dussault, J. H. and Ruel, J. (1987) Thyroid hormones and brain development, *Annu Rev Physiol*, 49: 321-334.
- Escobar, G. M.d., Obregon, M. J., Rey, F. E.d. (1990) Contribution of maternal thyroxine to fetal thyroxine pools in normal rats near term, *Endocrinology*, 126: 2765-2767.
- Escobar, G. M.d., Obregon, M.J., Rey, F. E.d. (1987) Fetal and maternal thyroid hormones, *Hormone Res*, 26: 12-27.
- Escobar, G. M.d., Obregon, M. J., Rey, F. E.d. (1988) Transfer of thyroid hormones from the mother of the fetus. In Delang F. Fisher D. A., Glinoe D. (Eds), *Research in Congenital Hypothyroidism* Plenum Press: New York. 15-28.
- Farsotti, A., Mitsubashi, T., Desvergne, B., Robbins, J., Nikodem, V. M. (1991) Molecular basis of thyroid hormone regulation of myelin basic protein gene expression in rodent brain., *J. Boil. Chem.*, 266: 23226-23232.
- Fawcett, D. W., *Bloom and Fawcett: Textbook of Histology*, 11th ed. Philadelphia: W.B. Saunders Company. p. 973.
- Figueiredo. B. C., Almazan, G., Ma, Y., Tetzlaff, W. (1993) Gene expression in the developing cerebellum during perinatal hypo- and hyperthyroidism, *Brain Res Mol Brain Res*, 17: 258-268.
- Forman, B. M. and Samuels, H. H. (1990) Interactions among a subfamily of nuclear hormone receptors: the regulatory zipper model, *Molec Endocrinol*, 4: 1293-1301.
- Franklyn, J. A., Wood, D. F., Balfour, N. J., Ramsden, D. B., Docherty, K., Chin, W. W. and Sheppard, M. C. (1987) Effect of hypothyroidism and thyroid hormone replacement *in vivo* on pituitary cytoplasmic concentrations of thyrotropin- β and alpha-subunit messenger ribonucleic acids., *Endocrinol.*, 120: 2279-2288.
- Furlow, J. D., Berry, D. L., Wang, Z. and Brown, D. D. (1997) A set of novel tadpole specific genes expressed only in the epidermis are down-regulated by thyroid hormone during *Xenopus laevis* metamorphosis, *Dev Biol*, 182: 284-298.
- Gaitan, E. and Cooksey, R. C. (1989) General Concepts of Environmental Goitrogenesis, in Gaitan E, (ed): *Environmental Goitrogenesis*, CRC Press, Inc.: Boca Raton, p. 3-14.
- Gaitan, E., Lindsay, R. H. and Cooksey, R. C. (1989) Goiter endemias attributed to chemical and bacterial pollution of water supplies, in Gaitan E, (ed): *Environmental Goitrogenesis*, CRC Press, Inc.: Boca Raton, p. 207-232.
- Goldey, E. S., Kehn, L. S., Lau, C., Rehnberg, G. L and Crofton, K. M. (1995) Developmental exposure to polychlorinated biphenyls (Aroclor 1254) reduces circulating thyroid hormone concentrations and causes hearing deficits in rats, *Toxicol Appl Pharmacol*, 135: 77-88.

- Gorbman, A., Dickhoff, W. W., Vigna, S. R., Clark, N. B. and Ralph, C. L., *Comparative Endocrinology*, New York: John Wiley & Sons.
- Green, W. L. (1996) Antithyroid Compounds, in Braverman L. E. and Utiger R. D., (ed): Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text, Lippincott-Raven: Philadelphia, p. 266-267.
- Greer, M. A., Sato, N., Wang, X., Greer, S. E. and McAdams, S. (1993) Evidence that the major physiological role of TRH in the hypothalamic paraventricular nuclei may be to regulate the set-point for thyroid hormone negative feedback on the pituitary thyrotroph, *Neuroendocrinol*, 57: 69-575.
- Hollenberg, A. N., Monden, T., Flynn, T. R., Boers, M.-E., Cohen, O. and Wondisford, F. E. (1995) The human thyrotropin-releasing hormone gene is regulated by thyroid hormone through two distinct classes of negative thyroid hormone response elements, *Molecular Endocrinology*, 9: 540-550.
- Iniguez, M., Rodriguez-Pena, A., Ibarrola, N., Aguilera, M., Escobar, G. M.d. and Bernal, J. (1993) Thyroid hormone regulation of RC3, a brain-specific gene encoding a protein kinase-C substrate, *Endocrinology*, 133: 467-473.
- Kanamori, A. and Brown, D. D. (1996) The analysis of complex developmental programmes: amphibian metamorphosis, *Genes Cell*, 1: 429-435.
- Kliwer, S. A., Umesono, K., Mangelsdorf, D. J., and Evans, R. M. (1992) Retinoid X receptor interacts with nuclear receptors in retinoic acid, thyroid hormone and vitamin D3 signalling, *Nature*, 355: 446-449.
- Koller, K. J., Wolff, R. S., Warden, M. K. and Zoeller, R. T. (1987) Thyroid hormones regulate levels of thyrotropin-releasing hormone mRNA in the paraventricular nucleus, *Proc Natl Acad Sci USA*, 84: 7329-7333.
- Lazar, M. A. (1993) Thyroid hormone receptors: multiple forms, multiple possibilities, *Endocrine Rev*, 14: 184-193.
- Lazar, M. A. (1994) Thyroid hormone receptors: Update 1994, *Endocrine Reviews Monographs*, 3: 280-283.
- Leatherland, J. F. (1994) Reflections on the thyroidology of fishes: from molecules to humankind, *Guelph Ichthyology Reviews*, 2: 1-67.
- Mano, H., Mori, R., Ozawa, T., Takeyama, K., Yoshizawa, Y., Kojima, R., Arao, Y., Masushige, S., and Kato, S. (1994) Positive and negative regulation of retinoid X receptor gene expression by thyroid hormone in the rat, *J Biol Chem*, 269: 1591-1594.
- Mirell, C. J., Yanagisawa, M., Lau, R., Pekary, A. E., Chin, W. W. and Hershman, J. M. (1987) Influence of thyroidal status on pituitary content of thyrotropin β - and alpha-subunit, growth hormone, and prolactin messenger ribonucleic acids, *Mol Endocrinol*, 1: 408-412.

- Mitsuhashi, T., Tennyson, G. E. and Nikodem, V. M. (1988) Alternative splicing generates messages encoding rat c-erbA proteins that do not bind thyroid hormone, *Proc Natl Acad Sci USA*, 85: 5804-5808.
- Morley, J. E. (1981) Neuroendocrine control of thyrotropin secretion, *Endocrine Rev.*, 2: 396-436.
- Myant, N. B. (1971). The role of thyroid hormone in the fetal and postnatal development of mammals. In Hamburgh M. Barrington EJ (Eds), *Hormones in Development* Appleton-Century-Crofts: New York.
- Oppenheimer, J. H., Schwartz, H. L., Strait, K. A. (1994) Thyroid hormone action 1994: the plot thickens., *Eur J Endocrinol*, 130: 15-24.
- Porterfield, S. P. (1994) Vulnerability of the developing brain to thyroid abnormalities: environmental insults to the thyroid system, *Environmental Health Perspectives*, 102 Suppl 2: 125-130.
- Porterfield, S. P., Hendrich, C. E. (1992) Tissue iodothyroidine levels in fetuses of control and hypothyroid rats at 13 and 16 days gestation, *Endocrinol*, 131: 195-106.
- Porterfield, S. P. and Hendrich, C. E. (1993) The role of thyroid hormones in prenatal neonatal neurological development-current perspectives, *Endocrine Rev*, 14: 94-106.
- Porterfield, S. P. and Stein, S. A. (1994) Thyroid hormones and neurological development: update 1994, *Endocrine Rev*, 3: 357-363.
- Rodriguez-Pena, A., Ibarrola, N., Iniguez, M. A., Munoz, A., Bernal, J. (1993) Neonatal hypothyroidism affects the timely expression of myelin-associated glycoprotein in the rat brain, *J. Clin Invest.*, 91: 812-818.
- Schreiber, G. and Richardson, S. J. (1997) The evolution of gene expression, structure and function of transthyretin, *Comp Biochem Physiol B Biochem Mol Biol*, 116: 137-160.
- Schwartz, H. L. (1983), in Oppenheimer J.H., and Samuels H. H., (ed): *Molecular Basis of Thyroid Hormone Action*, Academic Press: New York, p. 413-444.
- Shanker, G., Campagnoni, A. T., Pieringer, R. A. (1987) Investigations on myelinogenesis *in vivo*; Developmental expression of myelin basic protein mRNA and its regulation by thyroid hormone in primary cerebral cell cultures from embryonic mice., *J. Neurosci. Res.*, 17: 220-224.
- Shupnik, M. A. and Ridgway, E. C. (1987) Thyroid hormone control of thyrotropin gene expression in rat anterior pituitary cells., *Endocrinol*, 121: 619-624.
- Song, M.-K. H., Dozin, B., Grieco, D., Rall, J. E. and Nikodem, V. M. (1986) Transcriptional activation and stabilization of malic enzyme mRNA precursor by thyroid hormone., *J. Biol. Chem.*, 263: 17970-17974.

- Strait, K. A., Schwartz, H. L., Perez-Castillo, A., Oppenheimer, J. H. (1990) Relationship of c-erbA content to tissue triiodothyronine nuclear binding capacity and function in developing and adult rats, *J. Boil. Chem.*, 265: 10514-10521.
- Tata, J. R. (1994) Hormonal regulation of programmed cell death during amphibian metamorphosis, *Biochem Cell Biol*, 72: 581-588.
- Taylor, T., Wondisford, F. E., Blaine, T. and Weintraub, B. D. (1990) The paraventricular nucleus of the hypothalamus has a major role in thyroid hormone feedback regulation of thyrotropin synthesis and secretion., *Endocrinol.*, 126: 317-324.
- Thompson, C. C. (1996) Thyroid hormone-responsive genes in developing cerebellum include a novel synaptotagmin and a hairless homolog, *J. Neurosci.*, 16: 7832-7840.
- Timiras, P. S. and Nzekwe, E. U. (1989) Thyroid hormones and nervous system development, *Biol Neonate*, 55: 376-385.
- Tsai, S. Y. and Tsai, M. J. (1997) Chick ovalbumin upstream promoter-transcription factors (COUP-TFs): coming of age., *Endocr Rev*, 18: 229-240.
- Wondisford, F. E., Magner, J. A. and Weintraub, B. D. (1996) Thyrotropin, in Braverman L. E. and Utiger R. D., (ed): Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text, Lippincott-Raven: Philadelphia, p. 190-206.
- Yu, V. C., Delsert, C., Andersen, B., Holloway, J. M., Devary, O. V., Näär, A. M., Kim, S. Y., Boutin, J.-M., Glass, C. K. and Rosenfeld, M. G. (1991) RXR β : A coregulator that enhances binding of retinoic acid, thyroid hormone, and vitamin D receptors to their cognate response elements, *Cell*, 67: 1251-1266.
- Zhang, X., Hoffman, B., Tran, B.-V., Graupner, G. and Pfahl, M. (1992) Retinoid X receptor is an auxiliary protein for thyroid hormone and retinoic acid receptors, *Nature*, 335: 441-446.
- Zoeller, R. T., Kabeer, N. and Albers, H. E. (1993) Molecular mechanisms of signal integration in hypothalamic neurons., *Amer. Zool.*, 33: 244-254.

III. Frog Metamorphosis Assay

- Fort, D. J. and E. I. Stover. 1997. "Development of Short-Term, Whole-Embryo Assays to Evaluate Detrimental Effects on Amphibian Limb Development and Metamorphosis Using *Xenopus laevis*," Environmental Toxicology and Risk Assessment: Modeling and Risk Assessment (Sixth Volume), ASTM STP 1317, F. J. Dwyer, T. R. Doane, and Mark I. Hinman, Eds., American Society for Testing and Materials, Philadelphia, PA. pp, 376-390.
- Gustafsson, J.-A. 1996. Characteristics and function of a novel estrogen receptor β . Steroid Receptor Superfamily Symposium, University of Wisconsin, Madison, WI September 27-29, 1996.
- Hayes, T. B. 1997a. Amphian metamorphosis: An integrative approach. *Amer. Zool.*

37:121-123.

Hayes, T. B. 1997b. Steroids as potential modulators of thyroid hormone activity in anuran metamorphosis. *Amer. Zool.* 37:185-194.

Petit, F., Y. Valotaire and F. Pakdel. 1995. Differential functional activities of rainbow trout and human estrogen receptors expressed in the yeast *Saccharomyces cerevisiae*. *Eur. J. Biochem.* 223:584-592.

IV. Fish Gonadal Recrudescence Assay

Arcand-Hoy, L.D. and W.H. Benson. (1998) Fish reproduction: An ecologically relevant indicator of endocrine disruption. *Environ. Toxicol. Chem.* 17(1):49-57.

Gustafsson, J.-A. 1996. Characteristics and function of a novel estrogen receptor β . Steroid Receptor Superfamily Symposium, University of Wisconsin, Madison, WI September 27-29, 1996.

Nimrod, A.C. and W.H. Benson. (1996). Estrogenic responses to xenobiotics in channel catfish (*Ictalurus punctatus*). *Marine Environ. Res.* 42(1-4):155-160.

Nimrod, A.C. and W.H. Benson. (1998). Reproduction and development of Japanese medaka following early life stage exposure to xenoestrogens. *Aquatic Toxicol.* In press.

Petit, F., Y. Valotaire and F. Pakdel. (1995). Differential functional activities of rainbow trout and human estrogen receptors expressed in the yeast *Saccharomyces cerevisiae*. *Eur. J. Biochem.* 223:584-592.

V. Uterotrophic Assay (intraperitoneal)

O'Connor, JC, et al. 1996. An *in vivo* battery for identifying endocrine modulators that are estrogenic or dopamine regulators. *Fund. Appl. Toxicol.* 33: 182-195.

VI. 14-Day Intact Adult Male Assay

Cook, JC, et al. 1997. Development of a tier I screening battery for detecting endocrine-active compounds. *Regul. Toxicol. Pharmacol.* 26: 60-68.

VII. Alternative Mammalian Reproduction Test

Gray LE Jr, Ostby J, Simong R, Ferrell J, Rehnberg G, Linder R, Cooper R, Goldman J, and Laskey J. 1988. The development of a protocol to assess reproductive effects of toxicants in the rat. *Reproductive Toxicology* 2, 281-287.

Zenick H, Clegg ED, Perreault SD, Klinefelter GR and Gray LE. 1994. Assessment of Male Reproductive Toxicity. In: Principles and Methods of Toxicology, Third Edition, Chapter 27 (ed A W Hayes). Raven Press, Ltd, NY. pp 937-988.

VIII. Avian Reproduction (EPA OPPTS 850.2300;OECD 206)

Baxter, W.L., Linder, R.L., and Dahlgren, R.B. (1969). Dieldrin Effects in Two Generations of Pinned Hen Pheasants. *J. Wildl. Mgmt.* 33(1):96-102.

Bellabarba, D., Belisle, S., Gallo-Payet, N. and Lehoux, J-G. (1988). Mechanism of Action of Thyroid Hormones During Chick Embryogenesis. *Amer. Zool.* 28:389-399.

Cruickhank, J.J. and Sim, J.S. (1986). Morphometric and Radiographic Characteristics Of Tibia Bone of Broiler Chickens with Twisted Leg Disorders. *Avian Diseases* 30(4):699-708.

Dahlgren, R.B. and Linder, R.L. (1971). Effects Of Polychlorinated Biphenyls On Pheasant Reproduction, Behavior and Survival. *J. Wildl. Mgmt.* 35(2):315-319.

Dvorak J., J.L. Halvorsen, P. Gulick, K.A. Rauen U.K. Abbott, B.J. Kelly, and F.T. Schultz. 1992. cDNA cloning of a Z- and W- linked gene in gallinaceous birds. **J. Heredity** 83:22-55.

Emlen, Jr., J.T. (1963). Determinants of Cliff Edge and Escape Responses In Herring Gull Chicks in Nature. *Behaviour* 22:1-15.

Fleming, W.J., Heinz, G.H., and Schuler, C.A. (1985a). Lethal and Behavioral Effects of Chlordimeform in Bobwhite. *Toxicology* 36:37-47.

Fleming, W.J., Heinz, G.H., Franson, J.C., and Rattner, B.A. (1985b). Toxicity of Abate 4E (Temephos) in Mallard Ducklings and the Influence of Cold. *Environ.Toxicol. Chem.* 4:193-199.

Fox, G.A. (1976). Eggshell Quality: It's Ecological and Physiological Significance In a DDE-Contaminated Common Tern Colony. *Wilson Bull.* 88(3):459-477.

Fox, G.A., Gilman, A.P., Peakall, D.B. and Anderka, F.W. (1978). Behavioural Abnormalities of Nesting Lake Ontario Herring Gulls. *J. Wildl. Mgmt.* 42:477-483.

Freeman, B.M., and Vince, M.A. (1974). Development of the Avian Embryo. A Behavioral and Physiological Study. John Wiley and Sons, New York 362 pp.

Halvorsen, J.L. 1990 Avian sex identification by recombinant DNA technology. pages 84-90 in Proceedings of the Annual Meeting of the Association of Avian Veterinarians, Phoenix, AZ, U.S.A.

Hoffman, D.J. and W.C. Eastin Jr. 1981. Effects of Malathion, Diazinon, and Parathion on Mallard Embryo Development and Cholinesterase Activity. *Environ. Res.* 15:100-107.

Hoffman, D.J. and P.H. Albers. 1984. Evaluation of Potential Embryotoxicity and Teratogenicity of 42 Herbicides, Insecticides and Petroleum Contaminants to Mallard Eggs. *Arch. Environ. Contam. Toxicol.* 13:15-27.

Hoffman, D.J. (1990). Embryotoxicity and Teratogenicity of Environmental Contaminants to Bird Eggs. *Rev. Environ. Contam. Toxicol.* 115:39-89.

Hoffman, D.J., Smith, G.J. and Rattner, B.A. (1993). Biomarkers of Contaminant Exposure in Common Terns and Black-Crowned Night Herons in the Great Lakes. *Environ. Toxicol. Chem.* 12:1095-1103.

Hoffman, D.J., Melancon, M.J., Klien, P.N., Rice, C.P., Eisemann, J.D., Hines, R.K., Spann, J.W., and Pendleton, G.W. (1996). Developmental Toxicity of PCB 126 (3,3',4,4',5-Pentachlorobiphenyl) in Nestling American Kestrels (*Falco sparverius*). *Fund. Appl. Toxicol.* 34:188-200.

- Jefferies, D.L. & Parslow, J.L.F. (1976). Thyroid Changes in PCB-Dosed Guillemots and Their Indication of One of the Mechanisms of Action For These Materials. *Environ. Pollut.* 10:293-311.
- Maguire, C.C. and Williams, B.A. (1987). Response of Thermal Stressed Bobwhite to Organophosphorous Exposure. *Environ. Pollut.* 47:25-39.
- Martin, P.A. 1990. Effects of Carbofuran, Chlorpyrifos, and Deltamethrin on Hatchability, Deformity, Chick Size, and Incubation Time of Japanese Quail (*Coturnix japonica*) Eggs. *Environ. Toxicol. Chem.* 9:529-534.
- Martin, P.A. and Solomon, K.R. (1991). Acute Carbofuran Exposure and Cold Stress: Interactive effects in Mallard Ducklings. *Pesticide Biochemistry and Physiology* 40:117-127.
- McArthur, M.L.B., G.A. Fox, D.B. Peakall, and B.J.R. Philogene (1983). Ecological Significance of Behavioral and Hormonal Abnormalities in Breeding Ring Doves Fed an Organochlorine Chemical Mixture. *Arch Environm. Contam. Toxicol.* 12, 343-353.
- McNabb, F.M.A. (1988) Peripheral Thyroid Hormone Dynamics in Precocial and Altricial Avian Development. *Am Zool* 28:427-440.
- Moccia, R.D., Fox, G.A., and Britton, A. (1986). A Quantitative Assessment of Thyroid Histopathology Of Herring Gulls (*Larus Argentatus*) From the Great Lakes and A Hypothesis On the Causal Role Of Environmental Contaminants. *J. Wild. Dis.* 22(1)60-70.
- Ottinger, M.A. and M. Bakst. 1981. Peripheral androgen concentrations and testicular morphology in embryonic and young Japanese quail. **Gen. and Compare. Endocrinol.** 43:170-177.
- Ottinger, M.A. and H.J. Brinkley. 1978. Testosterone and sex-related behavior and morphology: Relationship during maturation in the adult Japanese quail. *Hormones and Behavior* 11; 175-182.
- Panzica, G.C., N. Aste, C. Viglietti-Panzica, and M.A. Ottinger. 1997. Structural sex differences in the brain: Influence of gonadal steroids and behavioral correlates. *Journal of Endocrinological Investigation* 18; 232-252.
- Rattner, B.A., Becker, J.M., and Nakatsugawa, T. (1987) Enhancement of Parathion Toxicity to Quail by Heat and Cold Exposure. *Pest. Biochem. Physiol.* 27:330-339.
- Rattner, B.A., Sileo, L. and C.G. Scanes. (1982). Hormonal Responses and Tolerance to Cold of Female Quail following Parathion Ingestion. *Pest. Biochem. Physiol.* 18:132-138.
- Sharp, P.J. 1975. A comparison of variations of plasma luteinizing hormone concentrations in male and female domestic chickens (*Gallus domesticus*) from hatch to sexual maturity. *J. Endocrinol.* 67:211-223.
- Somers, J.D., Moran Jr., E.T., and Reinhart, B.S. (1974). Effect of External Application of Pesticides to the Fertile Egg on Hatching Success and Early Chick Performance 3. Consequences of Combining 2,4-D with Picloram and Extremes in Contamination. *Bull. Environ. Contam. Toxicol.* 11(6)511-516.
- Summer, C.L., Giesy, J.P., Bursian, S.J., Render, J.A., Kubiak, T.J., Jones, P.D., Verbrugge, D.A., Aulerich, R.J. (1996). Effects Induced by Feeding Organochlorine-Contaminated Carp From Saginaw Bay, lake Huron, To Laying White Leghorn Hens. II. Embryonic and Teratogenic Effects. *J. Toxicol. Environ. Health* 49:409-438.
- Tori, G.M. and Mayer, L.P. (1981). Effects of Polychlorinated Biphenyls on the Metabolic Rates of Mourning Doves Exposed to Low Ambient Temperatures. *Bull. Environ. Contam. Toxicol.* 27:678-682.

XI. Nest Attentiveness/Incubation Behavior Test References To Be Used For Protocol Development And Standardization

- Fox, G.A., Gilman, A.P., Peakall, D.B. and Anderka, F.W. (1978). Behavioural Abnormalities of Nesting Lake Ontario Herring Gulls. *J. Wildl. Manage* 42:477-483.
- McArthur, M.L.B., Fox, G.A. Peakall, D.A. and Philogene, B.J.R. (1983). Ecological Significance Of Behavioral and Hormonal Abnormalities In Breeding Ring Doves Fed An Organochlorine Chemical Mixture. *Arch. Environ. Contam. Toxicol.* 12:343-353.
- Kubiak, T.J., Harris, H.J., Smith, L.M., Schwartz, T.R., Stalling, D.L., Trick, J.A., Sileo, L., Docherty, D.E., and Erdman, T.C. (1989). Microcontaminants and Reproductive Impairment of the Forster's Tern on Green Bay, Lake Michigan - 1983. *Arch. Environ. Contam. Toxicol.* 18:706-727.

X. Visual Cliff Test References To Be Used For Protocol Development And Standardization

- Baxter, W.L., Linder, R.L., and Dahlgren, R.B. (1969). Dieldrin Effects in Two Generations of Pinned Hen Pheasants. *J. Wildl. Mgmt.* 33(1):96-102.
- Dahlgren, R.B. and Linder, R.L. (1971). Effects Of Polychlorinated Biphenyls On Pheasant Reproduction, Behavior and Survival. *J Wildl Mgmt* 35(2):315-319.
- Emlen, Jr., J.T. (1963). Determinants of Cliff Edge and Escape Responses In Herring Gull Chicks in Nature. *Behaviour* 22:1-15.
- Fleming, W.J., Heinz, G.H., and Schuler, C.A. (1985). Lethal and Behavioral Effects of Chlordimeform in Bobwhite. *Toxicology* 36:37-47.
- Fox, G.A. (1976). Eggshell Quality: It's Ecological and Physiological Significance In a DDE-Contaminated Common Tern Colony. *Wilson Bull* 88(3):459-477.

XI. Cold Stress References To Be Used For Protocol Development And Standardization

- Fleming, W.J., Heinz, G.H., Franson, J.C., and Rattner, B.A. (1985). Toxicity of Abate 4E (Temephos) in Mallard Ducklings and the Influence of Cold. *Environmental Toxicology and Chemistry* 4:193-199.
- Maguire, C.C. and Williams, B.A. (1987). Response of Thermal Stressed Bobwhite to Organophosphorous Exposure. *Environmental Pollution* 47:25-39.
- Martin, P.A. and Solomon, K.R. (1991). Acute Carbofuran Exposure and Cold Stress: Interactive effects in Mallard Ducklings. *Pesticide Biochemistry and Physiology* 40:117-127.
- Rattner, B.A., Becker, J.M., and Nakatsugawa, T. (1987) Enhancement of Parathion Toxicity to Quail by Heat and Cold Exposure. *Pesticide Biochemistry and Physiology* 27:330-339.
- Rattner, B.A., Sileo, L. and C.G. Scanes. (1982). Hormonal Responses and Tolerance to Cold of Female Quail following Parathion Ingestion. *Pesticide Biochemistry and Physiology* 18:132-138.
- Tori, G.M. and Mayer, L.P. (1981). Effects of Polychlorinated Biphenyls on the Metabolic Rates of Mourning Doves Exposed to Low Ambient Temperatures. *Bull. Environ. Contam. Toxicol.* 27:678-682.

XII. Fish Life Cycle Test

- Arcand-Hoy, L.D. and W.H. Benson. 1998. Fish reproduction: An ecologically relevant indicator of endocrine disruption. *Environ. Toxicol. Chem.* 17(1):49-57.
- Benoit, D.A. 1981. *User's Guide for Conducting Life-Cycle chronic Toxicity Tests with Fathead Minnows (Pimephales promelas)*. U. S. Environmental Protection Agency, Office of Research and Development. EPA-600/8-81-011.
- Benson, W.H., G. van der Kraak, C. Tyler, K.E. Brugger, G. Daston, M. Fry, S. Gimeno, F. Hunger, M. Kolossa, R. Länge, and P. Matthiessen. 1997. Strategies and approaches to in vivo screening and testing in identifying the hazards of endocrine modulating chemicals to wildlife. In L. Tattersfield, P. Matthiessen, P. Campbell, N. Grandy and R. Länge, eds., SETAC- Europe/OECD/EC Expert Workshop on Endocrine Modulators and Wildlife: Assessment and Testing. SETAC-Europe Publication, Brussels. pp. 59-78.
- Cyr, D.G. and J. G. Eales. 1996. Interrelationships between thyroidal and reproductive endocrine systems in fish. *Rev. Fish Biol.* 6:165-200.
- Ghosh, S. and P. Thomas. 1995. Antagonistic effects of xenobiotics on steroid-induced final maturation of Atlantic croaker oocytes in vitro. *Mar. Environm. Res.* 39:159-163.
- Hansen, D.J., Parrish, P.R., Schimmel, S.C., and Goodman, L.R. 1978. Toxicity Test Using Sheepshead Minnows (*Cyprinodon variegatus*). Bioassay Procedures for the Ocean Disposal Permit Program. EPA-600/9-78-010.
- Nimrod, A.C. and W.H. Benson. 1997. Assessment of estrogenic activity in fish. In: Chemically-Induced Alterations in the Functional Development and Reproduction of Fishes, R.M. Rolland, M. Gilbertson and R.E. Peterson (eds.) SETAC Press, Pensacola, FL. pp. 87-100.
- Tyler, C. R., B. van der Eerden, S. Jobling, G. H. Panter, and J. P. Sumpter. 1996. Measurement of vitellogenin, a biomarker for exposure to estrogenic chemicals, in a wide variety of cyprinid fish. *J. Comp. Physiol. B* 166:418-426.

XIII. Methods to Select the Target Doses for T2T

- Flaws, J.A., R.J. Sommer, E.K. Silbergeld, R.E. Peterson, and A.N. Hirshfield (1997). In Utero and Lactational Exposure to 2,3,7,8 - Tetrachlorodibenzo-*p*-dioxin (TCDD) Induces Gnital Dymorphogenesis in the Female Rat. *Toxicol. Appl. Pharmacol.* 147, 351-362.
- Gray, L.E. Jr., C. Wolf, P. Mann, and J.S. Ostby (1997). In Utero Exposure to Low Doses of 2,3,7,8 - Tetrachlorodibenzo-*p*-dioxin Alters Reproductive Development of Female Long Evans Hooded Rat Offspring. *Toxicol. Appl. Pharmacol.* 146, 237-244.

XIV. Methods to Select the Target Doses for T2T

Flaws, J.A., R.J. Sommer, E.K. Silbergeld, R.E. Peterson, and A.N. Hirshfield (1997). In Utero and Lactational Exposure to 2,3,7,8 - Tetrachlorodibenzo-*p*-dioxin (TCDD) Induces Gnital Dymorphogenesis in the Female Rat. *Toxicol. Appl. Pharmacol.* 147, 351-362.

Gray, L.E. Jr., C. Wolf, P. Mann, and J.S. Ostby (1997). In Utero Exposure to Low Doses of 2,3,7,8 - Tetrachlorodibenzo-*p*-dioxin Alters Reproductive Development of Female Long Evans Hooded Rat Offspring. *Toxicol. Appl. Pharmacol.* 146, 237-244.

XV. “Low Dose Consideration for T2T”

Chamberlain, JG. Thalidomide and lack of teratogenesis in Long-Evans rats. *Teratology* 19(1):129, 1979.

Fraser FC. Thalidomide retrospective: what did we learn? *Teratology* 38(3):201-202, 1988.

Morrissey RE, George JD, Price CJ, et al. The Developmental Toxicity of Bisphenol A in Rats and Mice. *Fund Appl Tox* 8:571-582, 1987.

Nagel, Susan C., Frederick S. vom Saal, Kristina A. Thayer, Minati G. Dhar, Michael Boechler, and Wade V. Welshons. “Relative Binding Affinity-Serum Modified Access (RBA-SMA) Assay Predicts the Relative *in Vivo* Bioactivity of the Xenoestrogens Bisphenol A and Octylphenol.” *Environmental Health Perspectives*, Vol. 105, No. 1, pp. 70-76, January 1997.

Tilson HA, Jacobson JL, Rogan WJ. Polychlorinated Biphenyls and the Developing Nervous System: Cross-Species Comparisons. *Neurotox Teratol* 12:239-248, 1990.

vom Saal, F.S., Cooke, P.S., Buchanan, D.L., Palanza, P., Thayer, K.A., Nagel, S.C., Parmigiani, S. and Welshons, W.V. (1998). A physiologically based approach to the study of bisphenol A and other estrogenic chemicals on the size of the reproductive organs, daily sperm production and behavior. *Toxicol. Indus. Health* 14(1-2), 239-260.

XVI. Documents Distributed to Screening and Testing Work Group Members

During the course of their deliberations to evaluate all potentially relevant screening and test methods, the STWG utilized an extensive set of resource materials including peer-reviewed publications, workshop reports, and independent assessments by various international scientific groups and regulatory bodies. The following documents were of particular importance:

1. Endocrine Screening Methods Workshop: Meeting Report (July, 1996). Duke University Meeting.
2. Workshop on Screening Methods for Endocrine Disruptors in Wildlife: Draft Workshop Report. (March, 1997). Kansas City Meeting.
3. OECD Appraisal of Test Methods for Sex-Hormone Disrupting Chemicals. (1st Draft, October, 1996). Prepared by the MRC Institute for Environmental and Health.
4. Validation and Regulatory Acceptance of Toxicological Test Methods. A Report of the ad hoc Interagency Coordinating Committee on the Validation of Alternative Methods. NIEHS. (Draft Version, October 16, 1995).

In addition, the following documents were disseminated to the STWG members:

- Ankley, Gerald T., Johnson, Rodney D., Toth, Gregory, Folmar, Leroy C., Detenbeck, Naomi E., and Bradbury, Steven P. Development of a Research Strategy for Assessing the Ecological Risk of Endocrine Disrupters. In Press, *Rev. Toxicol.*
- Ashby, J., Oden, J. and Foster, J.R. Activity of Raloxifene in Immature and Ovariectomized Rat Uterotrophic Assays. May 22, 1997, Zenaca Central Toxicological Laboratory, Alderly Park, Macclesfield, Cheshire, UK.
- Ashby, J., Odum, J., Tinwell, H. and Lefevre, P.A. Jan. 30, 1997. Assessing the Risks of Adverse Endocrine-mediated Effects: Where to From Here? (submitted to *Reg. Tox Pharmacol.* as meeting overview).
- Cook, Jon. C., Kaplan, A. Michael, Davis, Leonard G., and O'Connor, John C. Development of a Tier 1 Screening Battery for Detecting Endocrine Active Compounds (EACs).
- Davis, Paul J., and Davis, Faith B. 1996. Nongenomic Actions of Thyroid Hormone. *Thyroid*, Vol. 6, No. 5: 497.
- DeGroot, M.D., Leslie J. 1996. Novel Actions of Thyroid Hormone. *Thyroid*, Vol. 6, No. 5: Final Report: NTP Workshop on Validation and Regulatory Acceptance of Alternative Toxicological Test Methods. December 11-12, 1995.
- Fingerman, Milton. 1997. Crustacean Endocrinology: A Retrospective, Prospective, and Introspective Analysis. *Physiological Zoology*, Vol. 70, No. 3: 257-269.
- Hajek, Richard A., Robertson, Audra D., Johnston, Dennis A., Van, Nguyen T., Tcholakian, Robert K., Wagner, Laura A., Conti, Claudio J., Meistrich, Marvin L., Contreras, Nancy, Edwards, Creighton L. and Jones, Lovell A. April, 1997. During Development, 17 β -Estradiol Is a Potent Estrogen and Carcinogen. *Environmental Health Perspectives*, Vol. 105, Supplement 2:
- The Health and Ecological Effects of Endocrine Disrupting Chemicals: A Framework for Planning. November 22, 1996. Committee on Environment and Natural Resources (CENR) of the National Science and Technology Council.

- Hormone-Related Toxicants in the Environment; Proposal No. 95-CLS-056-01 of the National Academy of Science. September 1994. National Research Council, Commission on Life Sciences.
- Horwitz, Alan F. Integrins and Health. *Scientific American*, pp. 68-75, May 1997.
- Katzenellenbogen, Benita S., Montano, Monica M., le Goff, Pascale, Schodin, David J., Kraus, W. Lee, Bhardway, Bhavna and Fujimoto, Nariaki. 1995. Antiestrogens: Mechanisms and Actions in Target Cells. *J. Steroid Biochem. Molec. Biol.*, Vol. 53, No. 1-6: 387-393.
- Kavlock, et al. August, 1996. Research Needs for the Risk Assessment of Health and Environmental Effects of Endocrine Disrupters: A Report from the U.S. EPA-Sponsored Workshop. *Environmental Health Perspectives*, Vol. 104, Supplement 4:
- Kohn, Michael C., Sewall, Charles H., Lucier, George W. and Portier, Christopher J. 1996. A Mechanistic Model of Effects of Dioxin on Thyroid Hormones in the Rat. *Toxicology and Applied Pharmacology*, 165: 29-48.
- Leonard, Jack L., and Farwell, Alan P. 1997. Thyroid Hormone-Regulated Actin Polymerization in Brain. *Thyroid*, Vol. 7, No. 1: 147-151.
- Nagel, Susan C., vom Saal, Frederick S., Thayer, Kristina A., Dhar, Minati G., Boechler, Michael and Welshons, Wade V. January 1997. Relative Binding Affinity-Serum Modified Access (RBA-SMA) Assay Predicts the Relative *in Vivo* Bioactivity of the Xenoestrogens Bisphenol A and Octylphenol. *Environmental Health Perspectives*, Vol. 105, No. 1: 70-76.
- Nagel, Susan C., vom Saal, Frederick S. and Welshons, Wade V. The Effective Free Fraction of Estradiol and Xenoestrogens in Human Serum Measured By the Whole Cell Uptake Assays: Physiology of Delivery Modifies Estrogenic Activity. In Press, *Proc. Soc. Exp. Bio. Med.*
- O'Connor, John C., Cook, Jon C., Craven, Suzanne C., Van Pelt, Carolyn S. and Obourn, John D. 1996. An *in Vivo* Battery for Identifying Endocrine Modulators that are Estrogenic or Dopamine Regulators. *Fundamental and Applied Toxicology*. Vol. 3: 182-195.
- Odum, J., Lefevre, P.A., Tittensor, S., Paton, D., Routledge, E.J., Beresford, N.A., Sumpter, J.P. and Ashby, J. The Rodent Uterotrophic Assay: Critical Protocol Features, Studies With Nonylphenols, Comparison With a Yeast Estrogenicity Assay. In Press, *Reg. Tox. Pharmacol.* April Edition.
- Rudel, Ruthann. April, 1997. Predicting Health Effects of Exposure to Compounds With Estrogenic Activity. Silent Spring Institute, Newton, MA. *Environmental Health Perspectives*, Vol. 105, Supplement 3.
- Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis Document (Draft Version); EPA Risk Forum White Paper, November 28, 1996.

- Szelei, Jozsef, Jimenez, Jesus, Soto, Ana M., Luizzi, Maria F. and Sonnenschein, Carlos. 1997. Androgen-Induced Inhibition of Proliferation in Human Breast Cancer MCF7 Cells Transfected with Androgen Receptor. *Endocrinology*, Vol. 138, No. 4: 1406-1412.
- Tong, Weida, Xing, Li, Welsh, William J. and Sheehan, Daniel M. QSAR Models for Binding of Estrogenic Compounds to Estrogen Receptor α and β Subtypes. R.O.W. Sciences, Jefferson, Arkansas.
- Tong, Weida, Perkins, Roger, Strelitz, Richard, Collantes, Elizabeth R., Keenan, Susan, Welsh, William J., Branham, William S. and Sheehan, Daniel M. Quantitative Structure-Activity Relationships (QSARs) for Estrogen Binding to the Estrogen Receptor: Predictions Across Species. R.O.W. Sciences, Jefferson, Arkansas.
- Validation and Regulatory Acceptance of Toxicological Test Methods: A Report of the Ad Hoc Interagency Coordinating Committee on the Validation of Alternative Test Methods. NIEHS. Final Report, March, 1997.
- vom Saal, Frederick S., Timms, Barry G., Montano, Monica M., Palanza, Paola, Thayer, Kristina A., Nagel, Susan C., Dhar, Minati D., Ganjam, V.K., Parmigiani, Stefano and Welshons, Wade V. March 1997. Prostate Enlargement in Mice Due to Fetal Exposure to Low Doses of Estradiol or Diethylstilbestrol and Opposite Effects at High Doses. *Proc. Natl. Acad. Sci. USA*, Vol. 94: 2056-2061.
- vom Saal, Frederick S., Cooke, Paul S., Buchanan, David L., Palanza, Paola, Thayer, Kristina A., Nagel, Susan C., Parmigiani, Stefano and Welshons, Wade V. May 1997. A Physiologically Based Approach to the Study of Bisphenol A and Other Estrogenic Chemicals on the Size of Reproductive Organs, Daily Sperm Production and Behavior. *Journal of Toxicology and Industrial Health*.