

**Additional References on the Developmental Toxicity of Chlorpyrifos Provided to the Developmental and Reproductive Toxicant Identification Committee (DARTIC), Which Were Not Cited in OEHHA (2008), US EPA (2014) or US EPA (2016)<sup>1</sup>**

**August 2017  
(Rev September 8, 2017)**

Bailey J, Oliveri A and Levin ED (2013). Zebrafish model systems for developmental neurobehavioral toxicology. *Birth Defects Res. Part C-Embryo Today-Rev.* **99**(1): 14-23.

Barr DB, Ananth CV, Yan X, Lashley S, Smulian JC, Ledoux TA, Hore P and Robson MG (2010). Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey. *Sci Total Environ* **408**(4): 790-795.

Buratti FM, De Angelis G, Ricceri L, Venerosi A, Calamandrei G and Testai E (2011). Foetal and neonatal exposure to chlorpyrifos: biochemical and metabolic alterations in the mouse liver at different developmental stages. *Toxicology* **280**(3): 98-108.

Carr RL, Armstrong NH, Buchanan AT, Eells JB, Mohammed AN, Ross MK and Nail CA (2017). Decreased anxiety in juvenile rats following exposure to low levels of chlorpyrifos during development. *Neurotoxicology* **59**: 183-190.

Chen XP, Chao YS, Chen WZ and Dong JY (2017). Mother gestational exposure to organophosphorus pesticide induces neuron and glia loss in daughter adult brain. *J Environ Sci Health B* **52**(2): 77-83.

Chen XP, Chen WF and Wang DW (2014). Prenatal organophosphates exposure alternates the cleavage plane orientation of apical neural progenitor in developing neocortex. *PLoS One* **9**(4): e95343.

Christen V, Rusconi M, Crettaz P and Fent K (2017). Developmental neurotoxicity of different pesticides in PC-12 cells in vitro. *Toxicol Appl Pharmacol* **325**: 25-36.

Cole TB, Li WF, Co AL, Hay AM, MacDonald JW, Bammler TK, Farin FM, Costa LG and Furlong CE (2014). Repeated gestational exposure of mice to chlorpyrifos oxon is

---

<sup>1</sup> The references provided are not cited in sections on developmental toxicity excerpted from: Office of Environmental Health Hazard Assessment (2008). Evidence on the Reproductive and Developmental Toxicity of Chlorpyrifos. September 2008.  
US Environmental Protection Agency (US EPA, 2014). Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review.  
US EPA (2016). Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review. Available at (<https://oehha.ca.gov/proposition-65/crn/hazard-identification-materials-consideration-developmental-toxicity>)

associated with paraoxonase 1 (PON1) modulated effects in maternal and fetal tissues. *Toxicol Sci* **141**(2): 409-422.

Cole TB, Walter BJ, Shih DM, Tward AD, Lusi AJ, Timchalk C, Richter RJ, Costa LG and Furlong CE (2005). Toxicity of chlorpyrifos and chlorpyrifos oxon in a transgenic mouse model of the human paraoxonase (PON1) Q192R polymorphism. *Pharmacogenet Genomics* **15**(8): 589-598.

Condette CJ, Bach V, Mayeur C, Gay-Quéheillard J and Khorsi-Cauet H (2015). Chlorpyrifos Exposure During Perinatal Period Affects Intestinal Microbiota Associated With Delay of Maturation of Digestive Tract in Rats. *J Pediatr Gastroenterol Nutr* **61**(1): 30-40.

Darwiche W, Delanaud S, Dupont S, Ghamlouch H, Ramadan W, Joumaa W, Bach V, Gay-Quéheillard J (2017). Impact of prenatal and postnatal exposure to the pesticide chlorpyrifos on the contraction of rat ileal muscle strips: involvement of an inducible nitric oxide synthase-dependent pathway. *Neurogastroenterol Motil* **29**(2). DOI: 10.1111/nmo.12918

De Angelis S, Tassinari R, Maranghi F, Eusepi A, Di Virgilio A, Chiarotti F, Ricceri L, Venerosi Pesciolini A, Gilardi E, Moracci G, Calamandrei G, Olivieri A and Mantovani A (2009). Developmental exposure to chlorpyrifos induces alterations in thyroid and thyroid hormone levels without other toxicity signs in CD-1 mice. *Toxicol Sci* **108**(2): 311-319.

De Felice A, Greco A, Calamandrei G and Minghetti L (2016). Prenatal exposure to the organophosphate insecticide chlorpyrifos enhances brain oxidative stress and prostaglandin E2 synthesis in a mouse model of idiopathic autism. *J Neuroinflammation* **13**(1): 149. DOI 10.1186/s12974-016-0617-4

De Felice A, Scattoni ML, Ricceri L and Calamandrei G (2015). Prenatal exposure to a common organophosphate insecticide delays motor development in a mouse model of idiopathic autism. *PLoS One* **10**(3): e0121663.

De Felice A, Venerosi A, Ricceri L, Sabbioni M, Scattoni ML, Chiarotti F and Calamandrei G (2014). Sex-dimorphic effects of gestational exposure to the organophosphate insecticide chlorpyrifos on social investigation in mice. *Neurotoxicol. Teratol.* **46**: 32-39.

Del Pino J, Moyano P, Anadon MJ, Garcia JM, Diaz MJ, Gomez G, Garcia J and Frejo MT (2016). SN56 basal forebrain cholinergic neuronal loss after acute and long-term chlorpyrifos exposure through oxidative stress generation; P75(NTR) and alpha7-nAChRs alterations mediated partially by AChE variants disruption. *Toxicology* **353-354**: 48-57.

Dishaw LV, Hunter DL, Padnos B, Padilla S and Stapleton HM (2014). Developmental exposure to organophosphate flame retardants elicits overt toxicity and alters behavior in early life stage zebrafish (*Danio rerio*). *Toxicol Sci* **142**(2): 445-454.

Ducharme NA, Reif DM, Gustafsson JA and Bondesson M (2015). Comparison of toxicity values across zebrafish early life stages and mammalian studies: Implications for chemical testing. *Reprod Toxicol* **55**: 3-10.

Espinoza M, Osimani VR, Sánchez V and Guiñazú N (2016). B-esterase determination and organophosphate insecticide inhibitory effects in JEG-3 trophoblasts. *Toxicol In Vitro* **32**(2): 190-197.

Estevan C, Fuster E, Del Río E, Pamies D, Vilanova E and Sogorb MA (2014). Organophosphorus pesticide chlorpyrifos and its metabolites alter the expression of biomarker genes of differentiation in D3 mouse embryonic stem cells in a comparable way to other model neurodevelopmental toxicants. *Chem Res Toxicol* **27**(9): 1487-1495.

Fluegge KR, Nishioka M and Wilkins JR, 3rd (2016). Effects of simultaneous prenatal exposures to organophosphate and synthetic pyrethroid insecticides on infant neurodevelopment at three months of age. *J Environ Toxicol Public Health* **1**: 60-73.

Fortin MC, Aleksunes LM and Richardson JR (2013). Alteration of the Expression of Pesticide-Metabolizing Enzymes in Pregnant Mice: Potential Role in the Increased Vulnerability of the Developing Brain. *Drug Metab. Dispos.* **41**(2): 326-331.

Furlong CE, Marsillach J, Jarvik GP and Costa LG (2016). Paraoxonases-1,-2 and-3: What are their functions? *Chem Biol Interact* **259**: 51-62.

Gao J, Naughton SX, Beck WD, Hernandez CM, Wu G, Wei Z, Yang X, Bartlett MG and Terry AV, Jr. (2017). Chlorpyrifos and chlorpyrifos oxon impair the transport of membrane bound organelles in rat cortical axons. *Neurotoxicology* **62**: 111-123.

Gomez-Gimenez B, Llansola M, Hernandez-Rabaza V, Cabrera-Pastor A, Malaguarnera M, Agusti A and Felipe V (2017). Sex-dependent effects of developmental exposure to different pesticides on spatial learning. The role of induced neuroinflammation in the hippocampus. *Food Chem Toxicol* **99**(4): 135-148.

Grabovska S and Salyha Y (2015). ADHD-like behaviour in the offspring of female rats exposed to low chlorpyrifos doses before pregnancy. *Arh Hig Rada Toksikol* **66**(2): 121-127.

Guiñazú N, Rena V, Genti-Raimondi S, Rivero V and Magnarelli G (2012). Effects of the organophosphate insecticides phosmet and chlorpyrifos on trophoblast JEG-3 cell death, proliferation and inflammatory molecule production. *Toxicol In Vitro* **26**(3): 406-413.

Jeon HJ, Lee YH, Kim MJ, Choi SD, Park BJ and Lee SE (2016). Integrated biomarkers induced by chlorpyrifos in two different life stages of zebrafish (*Danio rerio*) for environmental risk assessment. *Environ Toxicol Pharmacol* **43**: 166-174.

Jin Y, Liu Z, Peng T and Fu Z (2015). The toxicity of chlorpyrifos on the early life stage of zebrafish: a survey on the endpoints at development, locomotor behavior, oxidative stress and immunotoxicity. *Fish Shellfish Immunol* **43**(2): 405-414.

Juberg DR, Gehen SC, Coady KK, LeBaron MJ, Kramer VJ, Lu H and Marty MS (2013). Chlorpyrifos: weight of evidence evaluation of potential interaction with the estrogen, androgen, or thyroid pathways. *Regul Toxicol Pharmacol* **66**(3): 249-263.

Kais B, Stengel D, Batel A and Braunbeck T (2015). Acetylcholinesterase in zebrafish embryos as a tool to identify neurotoxic effects in sediments. *Environ Sci Pollut Res Int* **22**(21): 16329-16339.

Kim HY, Wegner SH, Van Ness KP, Park JJ, Pacheco SE, Workman T, Hong S, Griffith W and Faustman EM (2016). Differential epigenetic effects of chlorpyrifos and arsenic in proliferating and differentiating human neural progenitor cells. *Reprod Toxicol* **65**: 212-223.

Lan A, Kalimian M, Amram B and Kofman O (2017). Prenatal chlorpyrifos leads to autism-like deficits in C57Bl6/J mice. *Environ Health* **16**(1): 43. DOI 10.1186/s12940-017-0251-3

Lee I, Eriksson P, Fredriksson A, Buratovic S and Viberg H (2015). Developmental neurotoxic effects of two pesticides: Behavior and biomolecular studies on chlorpyrifos and carbaryl. *Toxicol Appl Pharmacol* **288**(3): 429-438.

Lee YS, Lewis JA, Ippolito DL, Hussainzada N, Lein PJ, Jackson DA and Stallings JD (2016). Repeated exposure to neurotoxic levels of chlorpyrifos alters hippocampal expression of neurotrophins and neuropeptides. *Toxicology* **340**: 53-62.

Liu L, Xu Y, Xu L, Wang J, Wu W, Xu L and Yan Y (2015). Analysis of differentially expressed proteins in zebrafish (*Danio rerio*) embryos exposed to chlorpyrifos. *Comp Biochem Physiol C Toxicol Pharmacol* **167**: 183-189.

Mamczarz J, Pescrille JD, Gavrusenko L, Burke RD, Fawcett WP, DeTolla LJ, Jr., Chen H, Pereira EF and Albuquerque EX (2016). Spatial learning impairment in prepubertal guinea pigs prenatally exposed to the organophosphorus pesticide chlorpyrifos: Toxicological implications. *Neurotoxicology* **56**: 17-28.

Mansour SA and Gamet-Payraastre L (2016). Ameliorative effect of vitamin E to mouse dams and their pups following exposure of mothers to chlorpyrifos during gestation and lactation periods. *Toxicol Ind Health* **32**(7): 1179-1196.

Mullen BR, Ross B, Chou JW, Khankan R, Khialeeva E, Bui K and Carpenter EM (2016). A Complex Interaction Between Reduced Reelin Expression and Prenatal Organophosphate Exposure Alters Neuronal Cell Morphology. *ASN Neuro* **May-June**: 1-14.

Mullins RJ, Xu S, Pereira EF, Pescrille JD, Todd SW, Mamczarz J, Albuquerque EX and Gullapalli RP (2015). Prenatal exposure of guinea pigs to the organophosphorus pesticide chlorpyrifos disrupts the structural and functional integrity of the brain. *Neurotoxicology* **48**: 9-20.

Naseh M and Vatanparast J (2014). Enhanced expression of hypothalamic nitric oxide synthase in rats developmentally exposed to organophosphates. *Brain Res* **1579**: 10-19.

Oliveri AN, Bailey JM and Levin ED (2015). Developmental exposure to organophosphate flame retardants causes behavioral effects in larval and adult zebrafish. *Neurotoxicol Teratol* **52**(Pt B): 220-227.

Perez J, Domingues I, Monteiro M, Soares AM and Loureiro S (2013). Synergistic effects caused by atrazine and terbuthylazine on chlorpyrifos toxicity to early-life stages of the zebrafish *Danio rerio*. *Environ Sci Pollut Res Int* **20**(7): 4671-4680.

Pinkas A, Turgeman G, Tayeb S and Yanai J (2015). An avian model for ascertaining the mechanisms of organophosphate neuroteratogenicity and its therapy with mesenchymal stem cell transplantation. *Neurotoxicol Teratol* **50**: 73-81.

Porreca I, D'Angelo F, De Franceschi L, Matte A, Ceccarelli M, Iolascon A, Zamo A, Russo F, Ravo M, Tarallo R, Scarfo M, Weisz A, De Felice M, Mallardo M and Ambrosino C (2016). Pesticide toxicogenomics across scales: in vitro transcriptome predicts mechanisms and outcomes of exposure in vivo. *Sci Rep* **6**: 11. DOI: 10.1038/srep38131

Reygner J, Lichtenberger L, Elmhiri G, Dou S, Bahi-Jaber N, Rhazi L, Depeint F, Bach V, Khorsi-Cauet H and Abdennebi-Najar L (2016). Inulin Supplementation Lowered the Metabolic Defects of Prolonged Exposure to Chlorpyrifos from Gestation to Young Adult Stage in Offspring Rats. *PLoS One* **11**(10): e0164614.

Richardson JR and Chambers JE (2004). Neurochemical effects of repeated gestational exposure to chlorpyrifos in developing rats. *Toxicol Sci* **77**(1): 83-90.

Richendrfer H and Creton R (2015). Chlorpyrifos and malathion have opposite effects on behaviors and brain size that are not correlated to changes in AChE activity. *Neurotoxicology* **49**: 50-58.

Ridano ME, Racca AC, Flores-Martin JB, Fretes R, Bandeira CL, Reyna L, Bevilacqua E, Genti-Raimondi S and Panzetta-Dutari GM (2017). Impact of chlorpyrifos on human villous trophoblasts and chorionic villi. *Toxicol Appl Pharmacol* **329**: 26-39.

Rodriguez-Fuentes G, Rubio-Escalante FJ, Norena-Barroso E, Escalante-Herrera KS and Schlenk D (2015). Impacts of oxidative stress on acetylcholinesterase transcription, and activity in embryos of zebrafish (*Danio rerio*) following Chlorpyrifos exposure. *Comp Biochem Physiol C Toxicol Pharmacol* **172-173**: 19-25.

Ruan QL, Ju JJ, Li YH, Li XB, Liu R, Liang GY, Zhang J, Pu YP, Wang DY and Yin LH (2012). Chlorpyrifos exposure reduces reproductive capacity owing to a damaging effect on gametogenesis in the nematode *Caenorhabditis elegans*. *J Appl Toxicol* **32(7)**: 527-535.

Rubin Y, Nyska A and Waner T (1987). Teratogenicity Study in the Rabbit. Makhteshim-Agan (America), Inc. 2 Park Avenue, New York, NY 10016.

Shin HS, Seo JH, Jeong SH, Park SW, Park Y, Son SW, Kim JS and Kang HG (2014). Exposure of pregnant mice to chlorpyrifos-methyl alters embryonic H19 gene methylation patterns. *Environ Toxicol* **29(8)**: 926-935.

Silva JG, Boareto AC, Schreiber AK, Redivo DD, Gambeta E, Vergara F, Morais H, Zanoveli JM and Dalsenter PR (2017). Chlorpyrifos induces anxiety-like behavior in offspring rats exposed during pregnancy. *Neurosci Lett* **641**: 94-100.

Silver MK, Shao J, Zhu B, Chen M, Xia Y, Kaciroti N, Lozoff B and Meeker JD (2017). Prenatal naled and chlorpyrifos exposure is associated with deficits in infant motor function in a cohort of Chinese infants. *Environ Int* **106**: 248-256.

Sledge D, Yen J, Morton T, Dishaw L, Petro A, Donerly S, Linney E and Levin E (2011). Critical Duration of Exposure for Developmental Chlorpyrifos-Induced Neurobehavioral Toxicity. *Neurotoxicol Teratol* **33(6)**: 742-751.

Slotkin TA, Card J, Infante A and Seidler FJ (2013a). Prenatal dexamethasone augments the sex-selective developmental neurotoxicity of chlorpyrifos: implications for vulnerability after pharmacotherapy for preterm labor. *Neurotoxicol Teratol* **37**: 1-12.

Slotkin TA, Card J and Seidler FJ (2013b). Adverse benzo[a]pyrene effects on neurodifferentiation are altered by other neurotoxicant coexposures: interactions with dexamethasone, chlorpyrifos, or nicotine in PC12 cells. *Environ Health Perspect* **121(7)**: 825-831.

Slotkin TA and Seidler FJ (2015). Prenatal nicotine alters the developmental neurotoxicity of postnatal chlorpyrifos directed toward cholinergic systems: better, worse, or just "different?". *Brain Res Bull* **110**: 54-67.

Slotkin TA, Skavicus S, Levin ED and Seidler FJ (2015a). Prenatal nicotine changes the response to postnatal chlorpyrifos: Interactions targeting serotonergic synaptic function and cognition. *Brain Res Bull* **111**: 84-96.

Slotkin TA, Skavicus S and Seidler FJ (2015b). Prenatal drug exposures sensitize noradrenergic circuits to subsequent disruption by chlorpyrifos. *Toxicology* **338**: 8-16.

Sogorb MA, Fuster E, Del Rio E, Estevez J and Vilanova E (2016a). Effects of mipafox, paraoxon, chlorpyrifos and its metabolite chlorpyrifos-oxon on the expression of biomarker genes of differentiation in D3 mouse embryonic stem cells. *Chem Biol Interact* **259**(Pt B): 368-373.

Sogorb MA, Pamies D, Estevan C, Estevez J and Vilanova E (2016b). Roles of NTE protein and encoding gene in development and neurodevelopmental toxicity. *Chem Biol Interact* **259**: 352-357.

Sun L, Xu W, Peng T, Chen H, Ren L, Tan H, Xiao D, Qian H and Fu Z (2016). Developmental exposure of zebrafish larvae to organophosphate flame retardants causes neurotoxicity. *Neurotoxicol Teratol* **55**: 16-22.

Tian J, Dai H, Deng Y, Zhang J, Li Y, Zhou J, Zhao M, Zhao M, Zhang C, Zhang Y, Wang P, Bing G and Zhao L (2015). The effect of HMGB1 on sub-toxic chlorpyrifos exposure-induced neuroinflammation in amygdala of neonatal rats. *Toxicology* **338**: 95-103.

Venerosi A, Ricceri L, Tait S and Calamandrei G (2012). Sex dimorphic behaviors as markers of neuroendocrine disruption by environmental chemicals: the case of chlorpyrifos. *Neurotoxicology* **33**(6): 1420-1426.

Venerosi A, Tait S, Stecca L, Chiarotti F, De Felice A, Cometa MF, Volpe MT, Calamandrei G and Ricceri L (2015). Effects of maternal chlorpyrifos diet on social investigation and brain neuroendocrine markers in the offspring - a mouse study. *Environ Health* **14**: 32. DOI 10.1186/s12940-015-0019-6

Williams AL and DeSesso JM (2014). Gestational/perinatal chlorpyrifos exposure is not associated with autistic-like behaviors in rodents. *Crit Rev Toxicol* **44**(6): 523-534.

Yu K, Li G, Feng W, Liu L, Zhang J, Wu W, Xu L and Yan Y (2015). Chlorpyrifos is estrogenic and alters embryonic hatching, cell proliferation and apoptosis in zebrafish. *Chem Biol Interact* **239**: 26-33.

Zarei MH, Soodi M, Qasemian-Lemraski M, Jafarzadeh E and Taha MF (2016). Study of the chlorpyrifos neurotoxicity using neural differentiation of adipose tissue-derived stem cells. *Environ Toxicol* **31**(11): 1510-1519.

Zhang J, Dai H, Deng Y, Tian J, Zhang C, Hu Z, Bing G and Zhao L (2015). Neonatal chlorpyrifos exposure induces loss of dopaminergic neurons in young adult rats. *Toxicology* **336**: 17-25.

Zhang X, Sui H, Li H, Zheng J, Wang F, Li B and Zhang Y (2014). Paraoxonase activity and genetic polymorphisms in northern Han Chinese workers exposed to organophosphate pesticides. *Exp. Biol. Med.* **239**(2): 232-239.