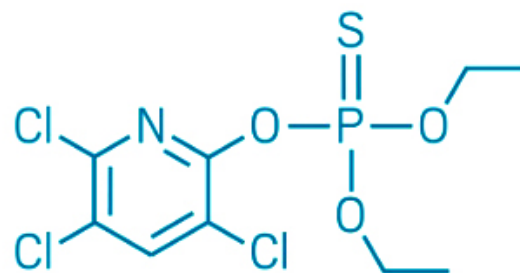




# Chlorpyrifos and

# Developmental Neurotoxic Effects in Children

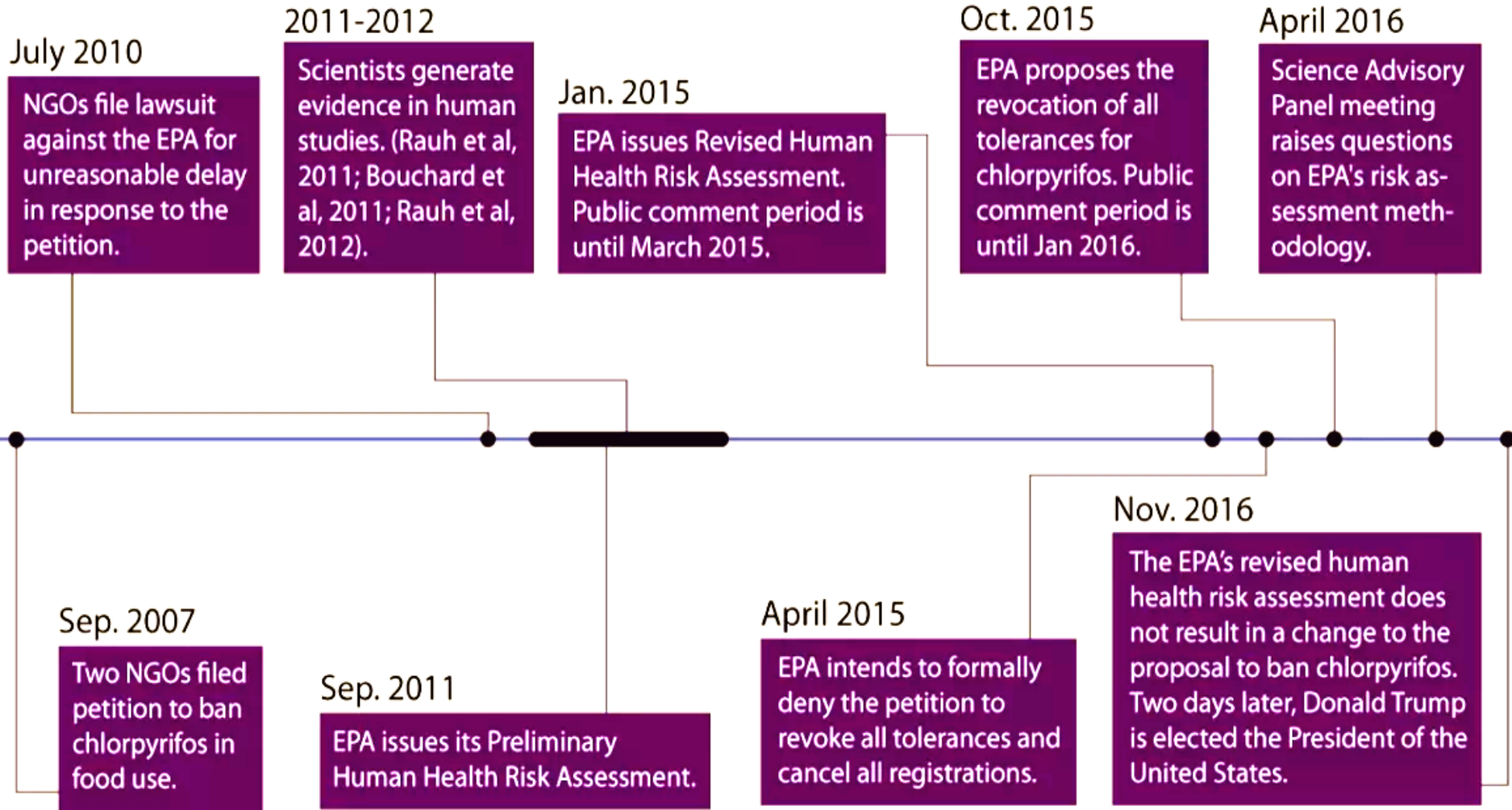


**Chlorpyrifos**

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# Chlorpyrifos Review



- In November 2016, **EPA released a revised human health risk assessment for chlorpyrifos** that confirmed that there are **no safe uses for the pesticide**. EPA found that:
  - All food exposures exceed safe levels, with children ages 1–2 exposed to levels of chlorpyrifos that are 140 times what EPA deems safe.
  - There is no safe level of chlorpyrifos in drinking water.
  - Pesticide drift reaches unsafe levels at 300 feet from the field’s edge.
  - Chlorpyrifos is found at unsafe levels in the air at schools, homes, and communities in agricultural areas.
  - All workers who mix and apply chlorpyrifos are exposed to unsafe levels of the pesticide even with maximum personal protective equipment and engineering controls.
  - Field workers are allowed to re-enter fields within 1–5 days after pesticide spraying, but unsafe exposures continue on average 18 days after applications.

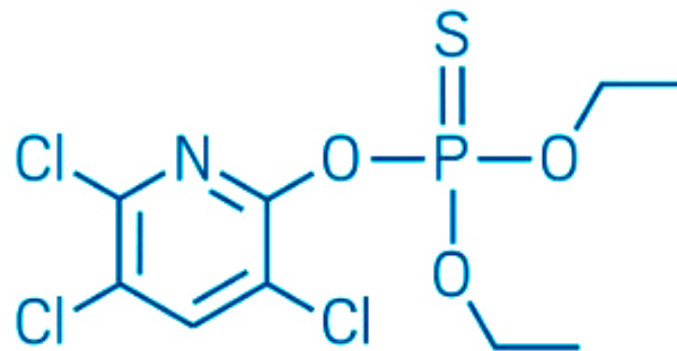
# Court orders EPA to ban chlorpyrifos

9th Circuit Court of Appeals directs agency to finalize Obama-era proposal

by **Britt E. Erickson**

AUGUST 10, 2018

**I**n a win for environmentalists and farmworkers, the U.S. Court of Appeals for the Ninth Circuit has ordered the Environmental Protection Agency to finalize a proposed ban on the organophosphate insecticide chlorpyrifos. The **Aug. 9 ruling** gives EPA 60 days to revoke all allowable limits in food and cancel all approved uses for the pesticide, which is linked to neurodevelopmental disorders in children.



**Chlorpyrifos**

**EPA determined** in a 2015 human health risk assessment that combined exposure to chlorpyrifos from food and drinking water in the U.S. likely exceeds safe levels, particularly for children. The agency twice proposed to ban chlorpyrifos under the Obama administration, but the agency did not finalize either rule. In March 2017, then-EPA Administrator Scott Pruitt **delayed EPA's proposed ban** and put off any decision about chlorpyrifos until 2022.



## Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide

Virginia Rauh,<sup>1</sup> Srikesk Arunajadai,<sup>2</sup> Megan Horton,<sup>3,4</sup> Frederica Perera,<sup>4</sup> Lori Hoepner,<sup>4</sup> Dana B. Barr,<sup>5</sup> and Robin Whyatt<sup>4</sup>

<sup>1</sup>Heilbrunn Center for Population and Family Health, Mailman School of Public Health, <sup>2</sup>Department of Biostatistics, Mailman School of Public Health, <sup>3</sup>Sergievsky Center, and <sup>4</sup>Columbia Center for Children's Environmental Health, Mailman School of Public Health, Columbia University, New York, New York, USA; <sup>5</sup>Emory University, Atlanta, Georgia, USA

**BACKGROUND:** In a longitudinal birth cohort study of inner-city mothers and children (Columbia Center for Children's Environmental Health), we have previously reported that prenatal exposure to chlorpyrifos (CPF) was associated with neurodevelopmental problems at 3 years of age.

**OBJECTIVE:** The goal of the study was to estimate the relationship between prenatal CPF exposure and neurodevelopment among cohort children at 7 years of age.

**METHODS:** In a sample of 265 children, participants in a prospective study of air pollution, we measured prenatal CPF exposure using umbilical cord blood plasma (picograms/gram plasma) and 7-year neurodevelopment using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV). Linear regression models were used to estimate associations, with covariate selection based on two alternate approaches.

**RESULTS:** On average, for each standard deviation increase in CPF exposure (4.61 pg/g), Full-Scale intelligence quotient (IQ) declined by 1.4% and Working Memory declined by 2.8%. Final covariates included maternal educational level, maternal IQ, and quality of the home environment. We found no significant interactions between CPF and any covariates, including the other chemical exposures measured during the prenatal period (environmental tobacco smoke and polycyclic aromatic hydrocarbons).

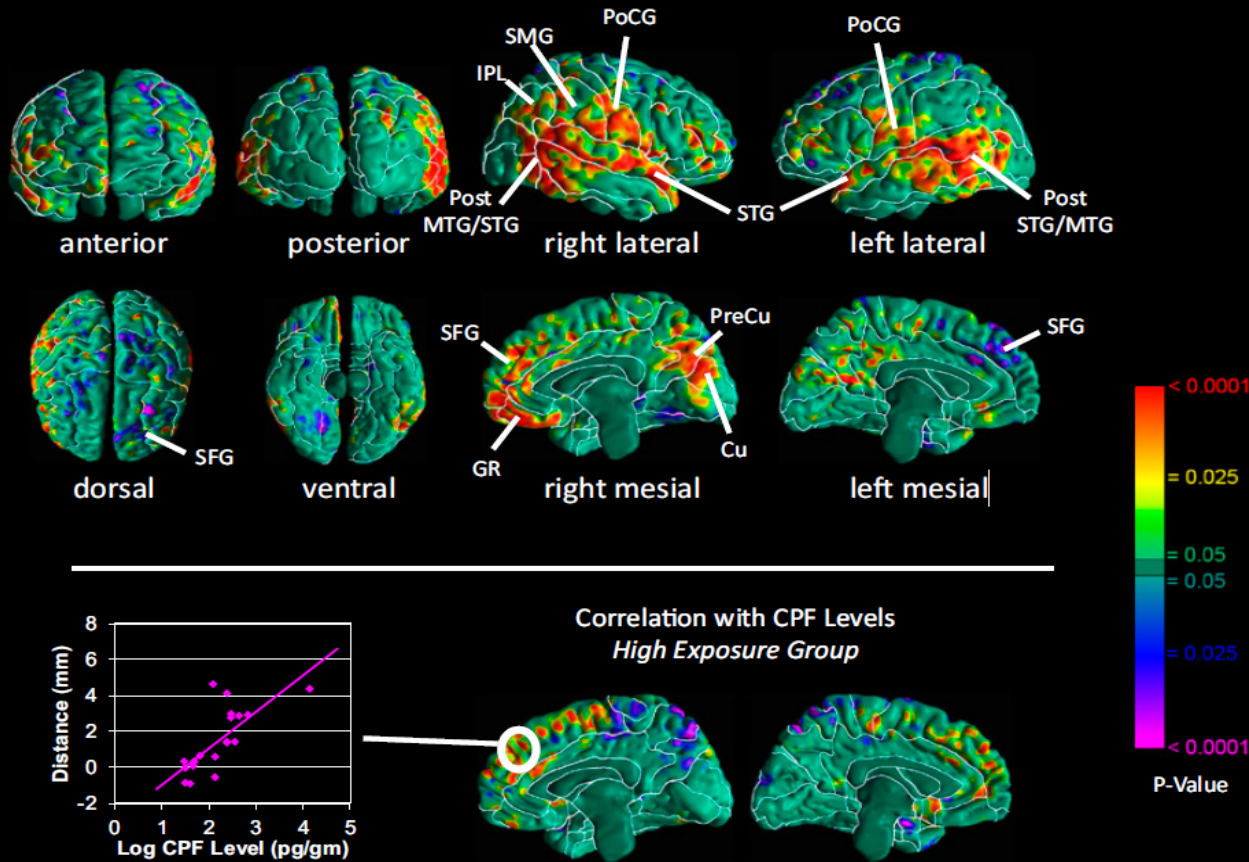
**CONCLUSIONS:** We report evidence of deficits in Working Memory Index and Full-Scale IQ as a function of prenatal CPF exposure at 7 years of age. These findings are important in light of continued widespread use of CPF in agricultural settings and possible longer-term educational implications of early cognitive deficits.

# Neurotoxicity in Children

## Brain anomalies in children exposed prenatally to a common organophosphate pesticide

Virginia A. Rauh<sup>a,b,1</sup>, Frederica P. Perera<sup>b,c</sup>, Megan K. Horton<sup>b,d</sup>, Robin M. Whyatt<sup>b,c</sup>, Ravi Bansal<sup>e</sup>, Xuejun Hao<sup>e</sup>, Jun Liu<sup>e</sup>, Dana Boyd Barr<sup>f</sup>, Theodore A. Slotkin<sup>g</sup>, and Bradley S. Peterson<sup>e,h</sup>

### Main Effects of Exposure on Surface Measures



Prenatal **chlorpyrifos** exposure, at levels observed with routine (non-occupational) use and below the threshold for any signs of acute exposure, has a measurable effect on brain structure in a sample of 40 children 5.9–11.2 y of age.

# Conclusion: Chlorpyrifos

## • Neurotoxicity in children:

- Rauh *et al.* 2011. seven-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. *Environ Health Perspect*; 119(8): 1196-201.
- Rauh *et al.* 2012. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. *PNAS USA.*;109(20):7871-6.
- Rohitrattana *et al.* 2014. Organophosphate pesticide exposure in school-aged children living in rice and aquacultural farming regions of Thailand. *J Agromedicine*; 19(4):406-16.
- Rauh *et al.* 2015. Prenatal exposure to the organophosphate pesticide chlorpyrifos and childhood tremor. *Neurotoxicology*; 51:80-6.
- Gunier *et al.* 2017. Prenatal residential proximity to agricultural pesticide use and IQ in 7-year-old children. *Environ Health Perspect*;125(5):057002.
- Curtis AC, Sattler B. 2018. Organophosphate insecticide exposure: A clinical consideration of chlorpyrifos regulation. *J Am Assoc Nurse Pract*; 30(5):299-304.

## • Neurotoxicity in animal and *in vitro* studies:

- Lee *et al.* 2015. Developmental neurotoxic effects of two pesticides: Behavior and neuroprotein studies on endosulfan and cypermethrin. *Toxicol Appl Pharmacol*; 335:1-10.
- del Pino *et al.* 2015. Acute and long-term exposure to chlorpyrifos induces cell death of basal forebrain cholinergic neurons through AChE variants alteration. *Toxicology*; 336:1-9.
- Guardia-Escote *et al.* 2018. Postnatal exposure to chlorpyrifos produces long-term effects on spatial memory and the cholinergic system in mice in a sex- and APOE genotype-dependent manner. *Food Chem Toxicol*;122:1-10.

# Conclusion: Chlorpyrifos

- **Immunotoxicity:**

- Wang *et al.* 2018. Evaluation of the effects of chlorpyrifos combined with lipopolysaccharide stress on neuroinflammation and spatial memory in neonatal rats. *Toxicology*; 410:106-115.
- Aroonvilairat *et al.* 2018. Effects of topical exposure to a mixture of chlorpyrifos, cypermethrin and captan on the hematological and immunological systems in male Wistar rats. *Environ Toxicol Pharmacol*; 59:53-60.

- **Cancer:**

- Lee *et al.* 2004. Cancer incidence among pesticide applicators exposed to chlorpyrifos in the agricultural health study. *J Natl Cancer Inst*; 96:1781–9.
- Suriyo *et al.* 2015. Chlorpyrifos promotes colorectal adenocarcinoma H508 cell growth through the activation of EGFR/ERK1/2 signaling pathway but not cholinergic pathway. *Toxicology*; 338:117-29.