November 13, 2017

Pesticide Re-evaluation Division
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

Re: Human health risks assessments for the following insecticides:
Permethrin, docket # EPA-HQ-OPP-2011-0039
Tau-Fluvalinate, docket # EPA-HQ-OPP-2010-0915
Pyrethrins, docket # EPA-HQ-OPP-2011-0885-0061

The Environmental Working Group, a nonprofit public health research and advocacy organization, is commenting on the Environmental Protection Agency's draft human health assessments for the insecticides permethrin, tau-fluvalinate and pyrethrins, as well as the EPA's overall approach to developmental neurotoxicity risks for the pyrethroid and pyrethrins family of insecticides.

EWG found that EPA's draft assessments for pyrethroid and pyrethrins insecticides have not incorporated new studies of American, Canadian and French children, which indicate that the insecticides can impair children's cognition and behavior. EWG considers these pesticides' risks during pregnancy and childhood to be unacceptable, and the EPA assessment flawed.

1. EPA must give full attention and respect to recent human data, which show the damage pyrethroids can cause to the nervous system, in order to ensure that children are not harmed by current exposures to these insecticides.

EPA has systematically waived the requirement for developmental neurotoxicity testing for the group of pyrethroid pesticides, and instead bases its safety assessment on short-term neurotoxicity in rodents. EWG strongly disagrees with this approach, because very recent epidemiology studies indicate a potential association with cognitive and behavioral changes in children at ambient levels of exposure.

Six recent epidemiology studies raise concerns that everyday exposures to American, Canadian and French children could cause subtle but lasting damages to brain development and behavior. This is a critical because Americans are universally exposed to pyrethroids through food residues and residential uses, and by living near or working in agriculture.

Data from the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) indicate that Americans' exposure to a number of different pyrethroids has been increasing since 2000. Examples of pyrethroids detected in people include 3-phenoxybenzoic acid, a metabolite of permethrin, cypermethrin and deltamethrin. The CDC data for the 2009 to 2010 sampling period show that children ages 6 to 11 had the greatest levels of 3-PBA compared to any other age group, and that median exposure levels increased by 50 percent between 2000 and 2010.[i] Similar exposures were reported for 3 to 5 year olds, in a pilot study published by the CDC in 2017.[ii]

Three draft human health assessments currently open for comment – for permethrin, tau-fluvalinate and pyrethrins – fail to address potential risks to the brain and behavior of a developing child. When reviewing the epidemiology research literature, the EPA's assessment has omitted all recent studies that found associations between low dose pyrethroid exposures and cognitive and behavioral changes. These studies must be included in the assessment if the EPA is serious about minimizing risks from pesticide exposure for young children.

The agency cannot move forward to assess risks of individual insecticides before it has considered new evidence on developmental neurotoxicity. These include several high quality studies EPA has already reviewed in its assessments for organophosphates (described more fully below). Furthermore, EPA must also ensure that cumulative exposures to pyrethroid and pyrethrins are safe for children.

2. The EPA should use a full tenfold safety factor as required by the Food Quality Protection Act of 1996 in order to protect children's health.

EWG found that the EPA has failed to use a full tenfold safety factor to account for children's sensitivity to pesticide toxicity. Instead, the Agency has only used a threefold factor, asserting that a smaller safety factor was sufficient.

EWG strongly disagrees with the position the Agency took in the draft human health risk assessment for these insecticides and urges the Agency to use the full tenfold safety factor. The EPA must pay attention to the known vulnerability of the fetal and juvenile nervous system to toxic chemicals that harm the nervous system and interfere with the brain and behavior. This is even more important given that the current health assessments are based on risks of acute rather than chronic exposure.

Below EWG lists human epidemiological studies that find a risk to children from exposure to pyrethroids. This body of research strongly supports the need for a tenfold children's health safety factor for the pyrethroid risk assessment, as well as more robust consideration of neurodevelopmental toxicity.

The French PELAGIE study found a statistically significant association between certain pyrethroid metabolites and cognitive and behavioral changes in children at 6 years. Exposure levels appear to be much lower than those measured in American children:

> Viel JF, Rouget F, Warembourg C, Monfort C, Limon G, Cordier S, Chevrier C. Behavioural disorders in 6-year-old children and pyrethroid insecticide exposure: the PELAGIE mother-child cohort. Occup Environ Med. 2017 Mar;74(4):275-281.
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> Viel JF, Warembourg C, Le Maner-Idrissi G, Lacroix A, Limon G, Rouget F, Monfort C, Durand G, Cordier S, Chevrier C. Pyrethroid insecticide exposure and cognitive developmental disabilities in children: The PELAGIE mother-child cohort. Environ Int. 2015 Sep;82:69-75.

In California, the CHARGE study found an association between maternal residential proximity to agricultural fields with pyrethroid application and neurodevelopmental disorders, including autism:

> Shelton JF, Geraghty EM, Tancredi DJ, Delwiche LD, Schmidt RJ, Ritz B, Hansen RL, Hertz-Picciotto I. Neurodevelopmental disorders and prenatal residential proximity to agricultural pesticides: the CHARGE study. Environ Health Perspect. 2014 Oct;122(10):1103-9.

Canadian children with higher exposures to cis-DCCA, a metabolite of deltamethrin, were more likely to have parent-reported behavior problems relative to children with lower exposures:

> Oulhote Y, Bouchard MF. Urinary metabolites of organophosphate and pyrethroid pesticides and behavioral problems in Canadian children. Environ Health Perspect. 2013 NovDec;121(1112):137884.

The CHAMACOS study reports an association between child IQ and residential proximity to application of pyrethroids, neonicotinoids and manganese-based fungicides:

> Gunier RB, Bradman A, Harley KG, Kogut K, Eskenazi B. Prenatal Residential Proximity to Agricultural Pesticide Use and IQ in 7-Year-Old Children. Environ Health Perspect. 2017 May 25;125(5):057002.

Researchers report a statistical association between pyrethroid metabolites and parent-reported ADHD in the NHANES 2001 to 2002 study:

Wagner-Schuman M, Richardson JR, Auinger P, Braun JM, Lanphear BP, Epstein JN, Yolton K, Froehlich TE. Association of pyrethroid pesticide exposure with attention-deficit/hyperactivity disorder in a nationally representative sample of U.S. children. Environ Health. 2015 May 28;14:44.

Several recent laboratory studies concur with general effects observed in epidemiology studies that developmental exposures may be more damaging that acute exposures. EPA must review the results of recent animal studies examining the potential mechanisms of low-dose toxicity in rodents. For example these six studies:

Gómez-Giménez B, Felipo V, Cabrera Pastor A, Agustí A, Hernández Rabaza V, Llansola M. Developmental Exposure to Pesticides Alters Motor Activity and Coordination in Rats – Sex Differences and Underlying Mechanisms. Neurotox Res. 2017 Oct 3.

Lee I, Eriksson P, Fredriksson A, Buratovic S, Viberg H. Developmental neurotoxic effects of two pesticides: Behavior and neuroprotein studies on endosulfan and cypermethrin. Toxicology. 2015 Sep 1;335:1-10.

Richardson JR, Taylor MM, Shalat SL, Guillot TS 3rd, Caudle WM, Hossain MM, Mathews TA, Jones SR, Cory-Slechta DA, Miller GW. Developmental pesticide exposure reproduces features of attention deficit hyperactivity disorder. FASEB J. 2015 May;29(5):196072.

Syed F, John PJ, Soni I. Neurodevelopmental consequences of gestational and lactational exposure to pyrethroids in rats. Environ Toxicol. 2016 Dec;31(12):1761-1770.

Laugeray A, Herzine A, Perche O, Richard O, Montecot-Dubourg C, Menuet A, Mazaud-Guittot S, Lesné L, Jegou B, Mortaud S. In utero and lactational exposure to low-doses of the pyrethroid insecticide cypermethrin leads to neurodevelopmental defects in male mice-An ethological and transcriptomic study. PLoS One. 2017 Oct 11;12(10):e0184475.

Magby JP, Richardson JR. Developmental pyrethroid exposure causes long-term decreases of neuronal sodium channel expression. Neurotoxicology. 2017 May;60:274-279.

In conclusion, EWG finds that the draft human health risk assessments for pyrethroid insecticides must be updated and corrected by inclusion of recent epidemiological studies

and incorporation of a tenfold children's health safety factor. Without these corrections, the EPA's assessments would leave American children at risk of excessive exposures to harmful pesticides that could permanently alter their brains and behavior. We urge the Agency to remedy these concerns through an updated risk assessment.

Submitted on behalf of the Environmental Working Group,

Sonya Lunder, MPH, Senior Analyst

References:

[i] Centers for Disease Control and Prevention. 2017. Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, January 2017, Volume One. Available: https://www.cdc.gov/exposurereport/index.html

[ii] Antonia M. Calafat, Xiaoyun Ye, Liza Valentin-Blasini, Zheng Li, Mary E. Mortensen, Lee-Yang Wong. Co-exposure to non-persistent organic chemicals among American pre-school aged children: A pilot study. International Journal of Hygiene and Environmental Health 220 (2017) 55–63.