



POLICY & ACTION FROM CONSUMER REPORTS

September 2, 2015

Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Woodcock,

Consumers Union (CU), the public policy and advocacy arm of Consumer Reports,¹ urges the Food and Drug Administration (FDA) to ban the use of lindane as a treatment for lice, their eggs, and scabies. Lindane is an organochlorine insecticide known to cause serious human health effects and to be very environmentally persistent. Recent studies have shown that lindane is a human carcinogen. Based on these recent studies and given that there are adequate and safer alternatives for treatments for lice, their eggs, and scabies, we urge FDA in this letter to ban any human topical uses of lindane. We intend to reiterate this request in a forthcoming citizen petition to the agency.

Background

Gamma-hexachlorocyclohexane (γ -HCH), commonly known as lindane, is an environmentally persistent organochlorine pesticide that has been manufactured since the 1940s and has been used for both agricultural and pharmaceutical purposes. Since lindane is fat soluble, it is very persistent in both the human body and in the environment. Lindane has been registered as a pharmaceutical product for treatment for lice, their eggs, and scabies, since 1951. As a result of lindane's human toxicity and environmental persistence, use of lindane for agricultural purposes has dramatically declined in the U.S. and worldwide. In 1976, production of lindane in the U.S. was terminated, while lindane continued to be imported for agricultural seed treatments and for treatment of lice and scabies.² In 2006, the U.S. Environmental

¹ Consumers Union is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers and to empower consumers to protect themselves. It conducts this work in the areas of food and product safety, telecommunications reform, health reform, financial reform, and other areas. Consumer Reports is the world's largest independent product-testing organization. Using its more than 50 labs, auto test center, and survey research center, the nonprofit organization rates thousands of products and services annually. Founded in 1936, Consumer Reports has over 8 million subscribers to its magazine, website, and other publications.

² Centers for Disease Control and Prevention (CDC) Agency for Toxic Substances and Disease Registry (ATSDR). 2005. Toxicological profile for Alpha-, Beta-, Gamma-, and Delta-Hexachlorocyclohexane, August 2005. At: www.atsdr.cdc.gov/Toxprofiles/tp43.pdf.

Protection Agency (EPA) cancelled all agricultural uses of lindane.³ In 2009, over 160 nations agreed to target lindane for elimination under the Stockholm Convention on Persistent Organic Pollutants.⁴ This agreement listed one “specific exemption” for the use of lindane as a second-line pharmaceutical product to control lice and scabies, but that exemption expired in 2014.

When used to treat lice, their eggs, and scabies, acute exposure to lindane has been reported to cause skin irritation, dizziness, headaches, diarrhea, nausea, vomiting, convulsions and death.⁵ Reports to FDA’s adverse events database have included 17 deaths, of which three have been confirmed, with 70% of the reported neurological events including seizure, dizziness, headache, and paresthesia.⁶ These effects are of concern since lindane is still being used for lice and scabies treatment. In 2014, there were 37,760 prescriptions issued in the U.S. for lindane, with 23,083 prescriptions for scabies and 14,677 for lice.⁷

The Agency for Toxic Substances and Disease Registry at the Centers for Disease Control and Prevention (CDC) has stated that lindane causes liver and kidney effects and that in laboratory rats it has “been reported to result in liver cancer.”⁸ The EPA classifies lindane as a possible human carcinogen (Group B2/C),⁹ and has prioritized it for review under the Endocrine Disruptor Screening Program.¹⁰

In 2002, California banned the use of lindane as a pharmaceutical treatment, in the forms of creams and lotion, for lice, their eggs, and scabies due to concerns of water quality, since lindane treatments for lice and scabies are rinsed down the drain. Wastewater treatment plants do not remove lindane, so it passes through to downstream lakes, rivers, and oceans. Since

³ U.S. Environmental Protection Agency (EPA). 2006. Lindane; Cancellation Order. Fed. Reg. 71:74905-74907. At: www.gpo.gov/fdsys/pkg/FR-2006-12-13/pdf/E6-21101.pdf.

⁴ The United States has not ratified this convention. Stockholm Convention Report. 2009. Report of the Conference of the Parties of the Stockholm Convention on Persistent Organic Pollutants on the work of its fourth meeting. Convention on Persistent Organic Pollutants. Fourth meeting, Geneva, 4–8 May 2009. At: chm.pops.int/Portals/0/Repository/COP4/UNEP-POPS-COP.4-38.English.pdf.

⁵ Thomson Micromedex. 2006. Lindane topical. In: Volume 1: Drug Information for the Healthcare Professional. 26th edition. Greenwood Village, CO: Thomson Micromedex

⁶ Food and Drug Administration (FDA) Center for Drug Evaluation and Research. 2003. Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Head Lice. At: www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm110845.htm.

⁷ IMS Health data. 2015.

⁸ ATSDR. Public Health Statement for Hexachlorocyclohexane. At: www.atsdr.cdc.gov/phs/phs.asp?id=752&tid=138.

⁹ EPA. 2000. Lindane (Gamma-Hexachlorocyclohexane). At: www.epa.gov/ttnatw01/hlthef/lindane.html.

¹⁰ EPA. 2014. Endocrine Disruptor Screening Program: Revised Second List of Chemicals for Tier 1 Screening. At: www.epa.gov/endo/pubs/prioritysetting/revlist2.htm.

California banned lindane, there has been a significant decline in lindane concentrations at wastewater treatment plants.¹¹

Over time, FDA has increasingly moved to restrict pharmaceutical uses of lindane. In 1981, CU submitted a citizen petition urging FDA to ban lindane for lice control and to develop a warning label for its use to control scabies. Although FDA did not take action in response to CU's petition, it did take action on a petition filed by Public Citizen in 1995. That year, FDA restricted pharmaceutical use of lindane to a second-line therapy, meaning that it is only to be used when either the patient "cannot tolerate the first-line drug of choice" or "has used the first-line drug of choice as instructed and the treatment has failed."¹² In 2003, FDA updated the warning label to state that lindane pharmaceutical products are neurotoxic even when used correctly.¹³ This "black box" warning label is FDA's strongest, which indicates that a drug carries a significant risk of serious or life-threatening adverse effects. In 2010, the Natural Resources Defense Council (NRDC) and ten other groups petitioned FDA to ban all pharmaceutical uses of lindane.¹⁴ In 2012, FDA denied the NRDC-led petition.

Due to concerns over the human health implications and decreased efficacy of lindane, the American Academy of Pediatrics (AAP) stopped recommending its use as a lice treatment—even as a second-line treatment—in 2009.¹⁵

CDC, while noting that lindane is to only be used as a second-line treatment for lice and scabies, points out just how dangerous its use can be: "Overuse, misuse, or accidentally swallowing lindane can be toxic to the brain and other parts of the nervous system ... Lindane should not be used to treat premature infants, persons with HIV, a seizure disorder, women who are pregnant or breast-feeding, persons who have irritated skin or sores where the lindane will be applied, infants, children, the elderly, and persons who weigh less than 110 pounds. Retreatment should be avoided."¹⁶

New studies

¹¹ Humphreys EH, Janssen S, Heil A, Hiatt P, Solomon G and MD Miller. 2008. Outcomes of the California ban on pharmaceutical lindane: Clinical and ecologic impacts. *Environmental Health Perspectives*, 116(3): 297-302. At: www.ncbi.nlm.nih.gov/pmc/articles/PMC2265033/pdf/ehp0116-000297.pdf.

¹² FDA. 1995. FDA Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Lice. At: www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm110845.htm.

¹³ FDA. 2003. Warning on Lindane for Scabies and Lice. At: www.headlice.org/news/2003/fda-lindane.htm.

¹⁴ Natural Resources Defense Council et al. 2010. Citizen Petition to FDA. Docket No. FDA-2010-P-0312.

¹⁵ Frankowski BL, Bocchini JA, and the Council on School Health and Committee on Infectious Diseases. 2010. Clinical Report—Head lice. *Pediatrics*, 126: 392-403. At: pediatrics.aappublications.org/content/126/2/392.full.pdf.

¹⁶ CDC. 2013. Parasites – Lice – Head Lice. At: www.cdc.gov/parasites/lice/head/treatment.html.

New research has more strongly linked lindane to cancer, particularly non-Hodgkin's lymphoma. Last year, the U.S. Agricultural Health Study (AHS), a large prospective cohort study of licensed private pesticide applicators as well as commercial private applicators, reported statistically significant increases in non-Hodgkin's lymphoma with increasing use of lindane.¹⁷ In June 2015, the International Agency for Research on Cancer (IARC) concluded that lindane was "carcinogenic to humans" (Group 1).¹⁸ IARC stated that the epidemiological evidence—including the AHS study as well as population-based case-control studies in the Midwestern U.S. and Canada, which reported consistently positive association between exposure to lindane and non-Hodgkin's lymphoma—was sufficient evidence for carcinogenicity in humans. IARC also stated that there was sufficient evidence for carcinogenicity from several animal feeding studies, which found that lindane consistently increased the incidence of benign or malignant liver tumours. Finally, IARC noted there was strong evidence that lindane causes immunosuppressive effects in humans.

Lindane not effective—and alternatives exist

Given that lindane has been used to treat lice, their eggs, and scabies since 1951, many lice have evolved resistance to lindane, thereby decreasing its efficacy. A study published in 2002 found lindane to be the least effective pharmaceutical treatment for head lice when compared *in vitro* with pyrethroids, malathion, or synergized pyrethrins.¹⁹ A single-blinded, randomized controlled trial comparing the efficacy of a single treatment of lindane 1% shampoo and permethrin 1% cream rinse found that after 14 days, 99% of patients treated with permethrin were lice free, compared to 85% for lindane.²⁰ Another study found an outbreak of lindane-resistant scabies that was successfully treated by permethrin.²¹

There is also evidence for overdiagnosis and misdiagnosis of head lice. A prospective cohort study conducted in Atlanta elementary schools and published in 2001 found that only 18% of children with nits only (e.g., no live lice) had live lice two weeks later.²² In addition, there were more than twice as many children with nits but not lice compared to those with live lice. A study from Harvard School of Public Health researchers found that only one in ten

¹⁷ Alavanja MCR, Hofmann JN, Lynch CF et al. 2014. Non-Hodgkin lymphoma risk and insecticide, fungicide and fumigant used in the Agricultural Health Study. *PLoS One*, 9(10): e109332. At: www.ncbi.nlm.nih.gov/pmc/articles/PMC4206281/pdf/pone.0109332.pdf.

¹⁸ Loomis D, Guyton K, Grosse Y et al. 2015. Carcinogenicity of lindane, DDT, and 2,4-dichlorophenoxyacetic acid. *Lancet Oncology*, 16: 891-892. At: [www.lancet.com/pdfs/journals/lanonc/PIIS1470-2045\(15\)00081-9.pdf](http://www.lancet.com/pdfs/journals/lanonc/PIIS1470-2045(15)00081-9.pdf).

¹⁹ Meinking TL, Serrano L, Hard B, Entzel P, Lemard G, Rivera E et al. 2002. Comparative *in vitro* pediculicidal efficacy of treatments in a resistant head lice population in the United States. *Archives of Dermatology*, 38(2): 220-224. At: archderm.jamanetwork.com/article.aspx?articleid=478698.

²⁰ Brandenburg K, Deinard AS, DiNapoli J et al. 1% permethrin cream rinse vs 1% lindane shampoo in treating pediculosis capitis. 1986. *Am. J. Dis. Child*, 140: 894-896.

²¹ Purvis RS and SK Tying. 1991. An outbreak of lindane resistant scabies treated successfully with permethrin 5% cream. *Journal of American Academy of Dermatology*, 25: 1015-1016.

²² Williams LK, Reichert A, MacKenzie WR, Hightower AW, and PA Blake, 2001. Lice, nits, and school policy. *Pediatrics* 107(5): 1011-1015. At: www.ncbi.nlm.nih.gov/pubmed/11331679.

samples of supposed evidence from diagnosed cases of head lice actually contained lice; nurses fared better than the general public with almost a third (32%) of their cases actually having lice.²³ Thus, nurses were twice as likely to be wrong about a diagnosis of head lice as they were to be correct when interpreting evidence of an active infestation. This is evidence that there is a potentially significant problem with overdiagnosis and consequent mismanagement, including through overuse of prescriptions for head lice pesticidal products.

A number of effective alternatives exist for treatment of lice²⁴ and scabies.²⁵ For scabies, a randomized trial found a single dose of ivermectin is as effective as a single application of 1% lindane.²⁶ Another randomized scabies trial found a single dose of ivermectin was more effective than a single application of 1% lindane.²⁷ A more recent randomized scabies trial found that a single dose of ivermectin was as effective as two applications of 1% lindane lotion.²⁸

Of particular interest are the studies that have found that relatively non-toxic methods of control have been effective for lice. Indeed, one study found that use of a small lice comb was four times more accurate in detecting current lice infestation compared to visual inspection.²⁹ A small single-blinded, randomized study comparing common pediculicides to wet combing with a fine-toothed comb found wet combing to be effective.³⁰ Uncontrolled studies have found that nonchemical treatments for head lice, relying on suffocation³¹ and desiccation,³² also show promise.

²³ Pollack RJ, Kiszewski AE, and A Speilman. 2000. Overdiagnosis and consequent mismanagement of head louse infestations in North America. *Pediatric Infectious Disease Journal* 19(8): 689-693. At: www.ncbi.nlm.nih.gov/pubmed/10959734.

²⁴ Devore CD, Schutze GE, and Council on School Health and Committee on Infectious Diseases. 2015. Head lice. *Pediatrics*, 135(5): e1355-e1365. At: pediatrics.aappublications.org/content/135/5/e1355.full.pdf.

²⁵ Goldstein BG and AO Goldstein. 2015. Scabies. UpToDate. At: www.uptodate.com/contents/scabies.

²⁶ Chouela EN, Abeldaño AM, Pellerano G et al. 1999. Equivalent therapeutic efficacy and safety of ivermectin and lindane in the treatment of human scabies. *Archives of Dermatology* 135: 651. At: archderm.jamanetwork.com/article.aspx?articleid=477887.

²⁷ Madan V, Jaskiran K, Gupta U, and DK Gupta. 2001. Oral ivermectin in scabies patients: a comparison with 1% topical lindane lotion. *Journal of Dermatology* 28: 481.

²⁸ Mohebbipour A, Saleh P, Goldust M, Amirmia M, Zadeh YJ, Mohamad RM, and E Resaee. 2013. Comparison of oral ivermectin vs. lindane lotion 1% for the treatment of scabies. *Clinical and Experimental Dermatology* 38(7): 719-723.

²⁹ Mumcuoglu KY, Friger M, Ioffe-Uspensky I, Ben-Ishai F, and J Miller. 2001. Louse comb versus direct visual examination for the diagnosis of head louse infestations. *Pediatric Dermatology* 18: 9-12.

³⁰ Hill N, Moor G, Butlin A, Preston S, Williamson MS, and C Bass. 2005. Single blind, randomized comparative study of the Bug Buster kit and the over the counter pediculicide treatments against head lice in the United Kingdom. *BMJ*, 331(7513): 384-387. At: www.bmj.com/content/331/7513/384.

³¹ Pearlman DL. 2004. A simple treatment for head lice: dry-on, suffocation-based pediculicide. *Pediatrics* 114(3): e275-279. At: www.researchgate.net/publication/8369531_A_Simple_Treatment_for_Head_Lice_Dry-On_Suffocation-Based_Pediculicide.

³² The Medical Letter. 2005. Drugs for head lice. *Medical Letters Drugs Therapy* 47(1215-1216): 68-70.

Conclusion

Lindane is clearly a very hazardous pesticide. EPA banned all agricultural uses in 2006. While not ratified by the U.S., there is also a global agreement that banned agricultural uses of lindane in 2009 and uses for lice and scabies treatment in 2014. California, with a population of more than 38 million people, banned pharmaceutical uses of lindane in 2002. Given, also, that the vast majority of cases of head lice occur in school-age children, that lindane is lipophilic and can be absorbed through the scalp, that there may be significant misdiagnosis of lice infestation, and that IARC has determined that lindane is a known human carcinogen—we are particularly concerned about the long-term health effects of treating children with lindane. Less-toxic alternatives to lindane exist for both lice and scabies infections. Although FDA turned down NRDC's petition to ban lindane, it did so before the new studies showing lindane leads to non-Hodgkin's lymphoma in humans and before IARC concluded that lindane is a known human carcinogen. Given the new studies, and the fact that less-toxic alternatives to lindane exist, we urge FDA to look at this issue again and ban any human topical uses of lindane.

Yours,

A handwritten signature in black ink that reads "Michael Hansen". The signature is written in a cursive style with a large, prominent "M" and "H".

Michael Hansen, Ph.D.
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Consumers Union