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June 11, 2010

VIA CERTIFIED MAIL

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

CITIZEN PETITION

The Natural Resources Defense Council ("NRDC") and the undersigned ten supporting organizations submit this petition under § 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §355(e), ("FFDCA") and pursuant to 21 C.F.R. §§ 10.25(a), 10.30, and 10.33. Through this petition, NRDC and our partners request that the Commissioner of the Food and Drug Administration ("FDA") establish a regulation prohibiting the use of lindane as a pharmaceutical treatment for lice and scabies and act to ban lindane, revoking all approvals and existing regulations permitting these uses. Lindane is known to cause serious human health effects, and FDA's continued approval of lindane as a treatment for head lice and scabies not only places patients' health at risk, but also violates federal law.

I. BACKGROUND

Gamma-hexachlorocyclohexane, commonly known as lindane, is an "environmentally persistent organochlorine insecticide" that has been used both as a pharmaceutical to treat head

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lice and scabies, and in agriculture as a pesticide.¹ Out of recognition of its toxicity to humans and its environmental persistence, most countries, including the U.S., have stopped producing lindane.² In 2009, over 160 nations agreed to designate lindane for elimination under the Stockholm Convention on Persistent Organic Pollutants. The U.S. Environmental Protection Agency (“EPA”) withdrew registration for agricultural uses of lindane in 2006, and California has prohibited the use of lindane pharmaceutical products since 2002.³ Several other states within the U.S. have taken steps to severely restrict or move toward a ban of lindane pharmaceutical products as well.⁴

Despite clear scientific evidence of lindane’s toxicity to humans and the potentially severe health consequences of exposure, the U.S. FDA continues to allow the pharmaceutical use of lindane as a treatment for head lice and scabies. In addition to the risks of serious side effects from treatment (including death), lindane is one of the least effective methods for treating head lice and scabies as compared to alternative treatments. FDA must reexamine its ongoing approval of lindane. The FFDCA requires that lindane be safe and effective, and in the context of the many recent state, national and international actions to eliminate uses of lindane, FDA must act immediately to ban lindane as a treatment option for head lice and scabies to protect the public.

Petitioner NRDC is a national, non-profit environmental and public health membership organization with more than 565,000 members nationwide. Neither NRDC nor any of the supporting petitioners have a financial interest in lindane or any alternative products. NRDC’s

¹ Elizabeth H. Humphreys, et.al, *Outcomes of the California Ban on Pharmaceutical Lindane: Clinical and Ecological Impacts*, 116 ENVTL. HEALTH PERSPECTIVES 3, 297 (2008).

² *Id.* at 301 (It is thought that only India and China still have lindane production sites).

³ *Id.*

⁴ See, e.g., H.B. 4402, 95th Leg., Reg. Sess. (Mich. 2009).

members and the members of supporting petitioners are at risk of harm from exposure to lindane both as a drug and in the environment.

II. ACTION REQUESTED

NRDC and our partners petition the Commissioner to take the following actions:

- 1) Immediately withdraw approval of lindane as a treatment option for head lice and scabies pursuant to 21 U.S.C. § 355(e) and 21 C.F.R. §§ 314.150, 314.162.
- 2) In the alternative, require that lindane distributors immediately withdraw their products from the U.S. market pursuant to 21 C.F.R. § 314.150(d).
- 3) In conjunction with 1) and/or 2), institute recall procedures for all lindane currently available on the U.S. market through the procedures outlined in 21 C.F.R. §§ 7.40-7.59.

A. Statement of Grounds.

Lindane is currently approved by FDA as a “second line” treatment option for patients with pediculosis (commonly known as head lice) or scabies. “Second line” therapy is used when either “the patient cannot tolerate the first-line drug of choice or the patient has used the first-line drug of choice as instructed and the treatment has failed.”⁵ Lindane has been registered as a pharmaceutical since 1951, but in 1995, in response to a petition filed by Public Citizen, a citizen advocacy group, FDA restricted the use of lindane to second line therapy only. In 2003, FDA, again acting to guard against the risks of lindane use, updated the warning label on lindane prescription packaging to state that lindane pharmaceutical products are neurotoxic, even when used correctly.⁶ As a result, lindane products now carry FDA’s strongest warning label, the so-

⁵ U.S. FDA, *FDA Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Lice*, available at <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm110845.htm> (last visited May 5, 2010) (hereinafter “FDA public health advisory”).

⁶ U.S. FDA, *Warning on Lindane for Scabies and Lice*, available at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/prnter.cfm?id=133> (last visited May 19, 2010).

called “black box” warning label that indicates a drug carries a significant risk of serious or life-threatening adverse effects.

In light of the dangers associated with the use of lindane, FDA’s continued approval of lindane products for use as a treatment for head lice and scabies violates the Federal Food, Drug, and Cosmetic Act. FDA should take action to immediately withdraw lindane pharmaceutical products from the market.

1. Legal Standard.

The Federal Food, Drug, and Cosmetic Act has an extensive process for the approval of new drugs. After a drug is approved, the Act also provides a process for the withdrawal of approval of drugs that are no longer found to be safe or effective. FDA itself notes that the withdrawal calculus evaluates how “the drug’s benefit and risk balance compares with treatment alternatives.”⁷ Further, when “FDA believes that a drug’s benefits no longer outweigh its risks, the agency will ask the manufacturer to withdraw the drug.”⁸ Withdrawals of approval are based on safety and/or efficacy, and are governed by 21 U.S.C. § 355(e).⁹ Sections 355(e)(1) and 355(e)(2) address the safety of drugs that have been previously approved by FDA. Under § 355(e)(1), the Secretary analyzes safety based on data available at the time the drug was approved, and under § 355(e)(2), analyzes safety based on new information provided to the agency regarding already approved applications. Section § 355(e)(3) looks to efficacy of drugs,

⁷ U.S. FDA, *An FDA Guide to Drug Safety Terms*, available at <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107970.htm#removal> (last visited May 17, 2010).

⁸ *Id.*

⁹ *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 134 (2000) (“If the FDA discovers after approval that a drug is unsafe or ineffective, it “shall, after due notice and opportunity for hearing to the applicant, withdraw approval” of the drug. 21 U.S.C. §§ 355(e)(1)-(3).”).

and requires that the drug work as it was approved to work.¹⁰ Specifically, 21 U.S.C. § 355(e) provides, in part, that:

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof.

First, as to § 355(e)(1) and (2)'s safety showings, updated information on lindane shows it is not safe "for use under the conditions of use upon the basis of which the application was approved." Second, the FFDCA compels withdrawal of approval under § 355(e)(3)'s efficacy requirement. The section requires a showing of a "lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested." "Substantial evidence" is defined in the act as:

evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed

21 U.S.C. § 355(d). This definition highlights that the "substantial evidence" standard for determining effectiveness is a scientific inquiry. Though efficacy itself is not defined in the act,

¹⁰ *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 609, 630 (1973) ("The Act requires the Commissioner to disapprove any application when there is a lack of "substantial evidence" that the applicant's drug is effective. § 505 (d), 21 U. S. C. § 355 (d). Similarly, he may withdraw approval for any drug if he subsequently determines that there is a lack of such evidence. § 505 (e), 21 U. S. C. § 355 (e).").

courts have consistently noted that the “effectiveness” requirement “necessarily entails a showing of some benefit to the patient.” *Warner-Lambert Co. v. Heckler*, 787 F.2d 147, 156 (3d. Cir. 1986).

FDA actions withdrawing other drugs from the market illuminate the factors considered when FDA decides to withdraw approval of a drug under the FFDCA. The 2007 withdrawal of the gastro-intestinal drug Zelnorm provides a parallel to the lindane case. In the press release announcing Zelnorm’s withdrawal, then-deputy director for the Center for Drug Evaluation and Research (“CDER”), Douglas Throckmorton, was quoted stating that the “decision reflects the FDA’s commitment to continuously monitor approved drugs throughout their marketing life, and take action when we believe the risks exceed the benefits,” and that “a potential risk of very serious harm to patients who have this non-life-threatening condition was recently identified, making this action necessary.”¹¹ Explicit weight here was given to the fact that the drug treated a non-life-threatening condition, where serious side effects were not worth any marginal benefits to continued approval. Similarly, head lice is not life threatening, and the side effects of lindane use, including neurological problems and the risk of death, outweigh the benefit of lindane use to eradicate lice or scabies.

Even in the case of more serious diseases, for example Parkinson’s disease, FDA looks to available alternatives when significant risks of approved drugs become apparent. In one case, FDA asked the manufacturers of pergolide drug products to voluntarily withdraw their products from the market, when there were “alternative therapies available for Parkinson’s disease,” and the removal was “not expected to adversely affect patient care because of the alternative

¹¹ U.S. FDA, *FDA Announces Discontinued Marketing of GI Drug, Zelnorm, for Safety Reasons*, March 30, 2007, available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108879.htm> (last visited May 19, 2010).

therapies available.”¹² Again, the deputy director of CDER noted in withdrawing pergolide drugs that “[t]he FDA’s increased evaluation of post-market safety is benefiting the public because, in this case, as new data about the product became available, we were able to remove a less safe drug from the market.”¹³ These and many other drug withdrawals highlight that the FDA must continue to reevaluate approved drugs. In particular, FDA looks at the context of the underlying medical condition to be treated, drug side effects, and ongoing safety and efficacy as compared to alternative treatments.¹⁴

FDA should also institute a recall under 21 C.F.R. § 7.40 *et seq.*, which allows either the Commissioner of Food and Drugs or the drug company itself to initiate action to recall drugs on the determination that, among other things, a recall would protect “the public health and well-being.” A recall paired with a withdrawal of the drug pursuant to 21 U.S.C. § 355 will expedite the long-overdue process of removing lindane from the market and protecting consumers. Recall of a drug requires three determinations: “(1) That a product that has been distributed presents a risk of illness or injury or gross consumer deception [;] (2) [t]hat the firm has not initiated a recall of the product [; and] (3) [t]hat an agency action is necessary to protect the public health and welfare.”¹⁵ Recall processes aid in alerting the public to FDA actions and would complement withdrawal of approval of lindane products.

¹² U.S. FDA, *FDA Announces Voluntary Withdrawal of Pergolide Products*, March 29, 2007, available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108877.htm> (last visited May 19, 2010).

¹³ *Id.*

¹⁴ See, e.g., Christine D. Galbraith, *Dying to Know: A Demand for Genuine Public Access to Clinical Trial Results Data*, 78 Miss. L.J. 705, 729 (2009) (“On September 30, 2004, Merck withdrew its pain medication Vioxx from the market due to clinical trial data that demonstrated a significant risk of cardiovascular incidents such as heart attacks and stroke. This represented the largest prescription-drug recall in history, as more than eighty million patients had formerly utilized this medication with annual sales for Merck estimated at more than \$2.5 billion dollars.”)

¹⁵ 21 C.F.R. § 7.45(a).

2. The Scientific Evidence Shows that Lindane Is Not Safe.

As noted above, the Federal Food, Drug, and Cosmetic Act provides for the withdrawal of approval of drugs that are no longer found to be safe or effective. *See supra*, requirements of 21 U.S.C. § 355, 21 C.F.R § 314.150. Recent studies of lindane indicate serious concerns over safety. First, safety studies by FDA and other federal agencies highlight the dangers of lindane use. In its public health advisory on lindane, FDA itself notes that serious adverse effects can result from use, including “skin irritation, dizziness, headaches, diarrhea, nausea, vomiting, and, in some instances, convulsions and death.”¹⁶ Though FDA notes that “[m]ost serious adverse events reported in association with Lindane products have been due to misuse...there have been rare case reports of serious reactions with apparently normal use.”¹⁷ The warning also notes that there have been three confirmed deaths from lindane use, and 14 other deaths reported to have been associated with lindane use.¹⁸

Further, the Agency for Toxic Substances and Disease Registry (“ATSDR”), in its public health statement on lindane and other isomers of hexachlorocyclohexane (“HCH”), provides a laundry list of serious health concerns relating to lindane. The statement notes that lindane causes liver and kidney effects, and in laboratory rats lindane has “been reported to result in liver cancer.”¹⁹ Additionally, “[t]he Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans” and “[t]he International Agency for Research on Cancer (IARC) has classified HCH (all isomers)

¹⁶ Humphreys, et al., *supra* note 1, at 297.

¹⁷ FDA public health advisory, *supra* note 3.

¹⁸ *Id.* (Regarding the three confirmed deaths, “[l]indane toxicity was confirmed by autopsy in a child, and was diagnosed in an adult. The third death occurred in an adult who ingested Lindane for suicide purposes.” As to the remaining 14 deaths, the FDA website notes that the group was made up of “4 children, 9 adults, and 1 patient of unknown age.” Further, of the 14 unconfirmed deaths, “[i]n 9 cases, use was not in accordance with the label (exceeded label use - 7, oral administration - 1, use was contraindicated - 2”).

¹⁹ Agency for Toxic Substances and Disease Registry, Public Health Statement: Hexachlorocyclohexane, *available at* <http://www.atsdr.cdc.gov/toxprofiles/tp43-c1-b.pdf> (last visited May 10, 2010).

as possibly carcinogenic to humans.”²⁰ Specifically, lindane exposure has been associated with leukemia, and more generally, has been identified as a hormone disruptor, which means that it “therefore may be a more potent carcinogen when exposures occur during early-life stages.”²¹

Lastly, FDA notes that the risks associated with lindane use are exacerbated in young children.²² As such, the FDA warning notes that lindane “should be used with extreme caution in children and in individuals weighing less than 50 kg (110 lbs).” Further, “[a]nimal studies have demonstrated that younger animals are more susceptible to the neurologic side effects seen with [l]indane use.”²³ Since infestations of lice and scabies are often found in large institutions such as schools, it is very likely that a large part of the potential U.S. population of patients treated with lindane is comprised of children weighing less than 110 lbs. The continued approval of lindane for use as a treatment for lice and scabies is of even greater concern if a large percentage of patients using the treatment are those very same patients identified by the FDA as particularly susceptible to the most serious side effects from the chemical.

3. The Scientific Evidence Shows that Lindane Is Not Effective.

Recent comparison studies of head lice and scabies treatments have found lindane treatments to be ineffective and expensive. A 2008 study notes that “[w]hereas lindane was once an inexpensive and effective treatment, it is now more expensive than many alternatives and has been associated with widespread resistance throughout the world.”²⁴ The evidence that lice and scabies have become resistant to lindane is not surprising, because “[m]ost chemical treatments

²⁰ *Id.* at 3; International Agency for Research on Cancer, *Summaries and Evaluations: Hexachlorocyclohexanes*, available at <http://www.inchem.org/documents/iarc/suppl7/hexachlorocyclohexanes.html> (last visited May 17, 2010).

²¹ Comments of NRDC, Assessment of Lindane and other HCH Isomers, EPA Doc. No. EPA-HQ-OPP-2006-0034-0022, at 11 (Apr. 10, 2006).

²² FDA public health advisory, *supra* note 3.

²³ *Id.*

²⁴ Humphreys, et al., *supra* note 1, at 300 (citing West, 2004; Heukelbach and Feldmeier 2006; Ko and Elston, 2004).

for pediculosis will result in resistance over time.”²⁵ Specifically, lindane is defined as having “low ovicidal activity (30% to 50% of eggs are not killed), and resistance has been reported worldwide for many years.”²⁶ In fact, in a study comparing a number of available treatments for head lice and scabies, lindane placed last in a list of five products in terms of efficacy.²⁷ Moreover, the difference between efficacy findings of lindane in the study as compared to lindane efficacy studies completed in prior years “supports the argument that some head lice in the United States have become resistant to these treatments.”²⁸

Alternatively, several recent studies have examined entirely nonchemical approaches, including suffocation, desiccation, and wet combing of the hair, and have found these treatments to be extremely effective.²⁹ Further, these “methods are preferable because they are not toxic to humans or the environment and are not susceptible to the development of resistance.”³⁰ Bans of lindane have similarly not affected doctors’ ability to treat head lice and scabies. The California ban, discussed in detail below, did not hinder physicians’ ability to treat lice or scabies. Also, a total ban in Mexico, where scabies can be a serious problem, has been successful.³¹ In fact, though scabies is one of the top ten leading causes of disease in indigenous communities in Mexico, the country has phased out the use of lindane under the terms of the North American

²⁵ *Id.*, citing Downs 2004.

²⁶ Barbara L. Frankowski, MD, MPH, et al., *Head Lice*, 3 PEDIATRICS 110, 638-643 (2002).

²⁷ Terri L. Meinking, et al., *Comparative in vitro Pediculicidal Efficacy of Treatments in a Resistant Head Lice Population in the United States*, 2 Arch. Dermatol. 138, 220-224 (2002) (“The order of effectiveness from most to least effective was as follows: Ovide lotion, A-200 shampoo (a natural pyrethrin product synergized with piperonyl butoxide), undiluted Nix (1% permethrin), diluted Nix, RID (a natural pyrethrin product synergized with piperonyl butoxide), and 1% lindane shampoo.”).

²⁸ *Id.*

²⁹ Humphreys, et al., *supra* note 1, at 300 (citing Goates et al. 2006, The Medical Letter 2005, Pearlman 2004, and Hill et al. 2005).

³⁰ *Id.*

³¹ Commission for Environmental Cooperation of North America, *North American Regional Action Plan on Lindane: Background Document*, available at http://www.cec.org/Storage/48/4045_Background-Key_en.pdf (last visited May 25, 2010).

Regional Action Plan. Also, as a party to the Stockholm Convention, Mexico submitted the initial proposal to list lindane as a restricted chemical under the treaty.³²

Head lice is not a life-threatening condition, and rarely is scabies life-threatening. With other alternatives that are more effective, non-toxic, and less expensive, the continued approval of lindane as a treatment for head lice and scabies is unnecessarily dangerous. Under the standards elaborated in the FFDCA, and followed in the withdrawal of other drugs, lindane can no longer be shown to be safe or effective for the treatment of head lice and scabies. With many alternatives available, successful treatment of head lice and scabies would not be hindered by the absence of lindane as a therapeutic option.

4. Morton Grove's Misbehavior Shows that Lindane Cannot Be Safely Used.

In 2007 FDA sent a warning letter in 2007 to Morton Grove Pharmaceuticals, the sole U.S. manufacturer and distributor of Lindane products, reprimanding the company for its false claims about the safety and efficacy of lindane.³³ FDA asserts in its letter to Morton Grove that the company has attempted to hide the harms inherent to lindane, and notes that the company's

websites and newsletter are misleading in that they omit and/or minimize the most serious and important risk information associated with the use of Lindane Shampoo, particularly in pediatric patients; include a misleading dosing claim; and overstate the efficacy of Lindane Shampoo. In particular, Lindane Shampoo is plainly labeled as second line treatment, suitable only when other, safer treatments fail or are not tolerated. The materials convey little sense of this limitation and little about the magnitude and nature of the risks associated with the drug. The materials appear to represent an attempt

³² *Id.* at 7.

³³ See letter from Thomas W. Abrams, Director, Division of Drug Marketing, FDA, to Kurt Orlofski, CEO, Morton Grove Pharmaceuticals, Inc. (Dec. 13, 2007) (*available at* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/ucm054144.pdf>) (last visited May 4, 2010) [hereinafter Morton Grove Letter]; See also Steve Scholl-Buckwald, *FDA Slaps Morton Grove for Lindane Shampoo Advertising*, Pan North America Pesticide Action Network, *available at* <http://www.panna.org/newsroom/20080115> (last visited Apr. 30, 2010).

to downplay the significant risks associated with Lindane Shampoo use and encourage wider use, with less care, than is appropriate under approved labeling.³⁴

As the Morton Grove letter indicates, FDA recognizes that lindane as used to treat lice and scabies is an extremely toxic substance. This dangerous toxicity is exacerbated by the fact that the only distributor of Lindane products in this country has previously gone to great lengths, in violation of FDA regulations, to hide from patients the very information on toxicity and side effects that patients need to protect themselves.³⁵ Without adequate information on the correct application of lindane, misuse and serious side effects are more likely to occur. Inadequate information on risks associated with use provides another compelling reason for FDA to cancel the use of lindane as an approved second line treatment for head lice and scabies.

5. EPA's Regulation of Lindane as a Pesticide Shows that Lindane Is Not Safe and Has Serious Environmental Consequences.

In addition to pharmaceutical uses, lindane has in the past been used as an insecticide in the United States. EPA is charged with regulating insecticides, and their regulatory actions speak not only to the grave environmental consequences of lindane use, but also serve to highlight additional health analyses completed by and for EPA. Lindane was first registered for use as a pesticide in the 1940s, and starting in the 1980s, companies that used lindane began voluntarily cancelling their registrations of the chemical.³⁶ In 2006, the last 6 remaining EPA registrations, seed treatments for barley, oats, sorghum, corn, rye, and wheat, were voluntarily cancelled by the companies that registered those uses.³⁷ EPA made a contemporaneous decision that remaining uses of lindane were not eligible for reregistration, permanently cancelling use of

³⁴ Morton Grove Letter, *supra* note 33, at 1.

³⁵ *Morton Grove Pharms., Inc. v. Nat'l Pediculosis Ass'n*, 525 F. Supp. 2d 1039, 1041 (N.D. Ill. 2007) ("Presently M[orton Grove Pharmaceuticals] is the only United States manufacturer and distributor of Lindane") ("Lindane" here refers to Lindane lotion and shampoo, two products that have been manufactured and distributed by Morton Grove exclusively, it does not refer to the ingredient lindane.)

³⁶ U.S. EPA, *Lindane Voluntary Cancellation and RED Addendum Fact Sheet*, available at

http://www.epa.gov/opp00001/reregistration/REDs/factsheets/lindane_fs_addendum.htm (last visited May 5, 2010).

³⁷ *Id.*

lindane as a pesticide and finding that “the costs of continued lindane registration outweigh the benefits” and that “[c]ancellation of these uses is expected to result in no significant loss to U.S. agriculture due to the successful development and registration in recent years of safer alternative pesticides.”³⁸

EPA’s evaluation of the health and environmental costs and benefits associated with continued use of lindane as a pesticide is particularly striking as it relates to pharmaceutical uses of the chemical. In describing lindane’s toxicity, EPA notes:

[l]indane primarily affects the nervous system causing neurotoxic effects... [it] is recognized internationally as a toxic, persistent, and bio-accumulative pesticide...[and] [w]hen people are exposed to lindane through food, water, or the atmosphere, they will accumulate lindane residues in their fatty tissues, and these lindane residues will remain there for an undetermined amount of time.³⁹

All of the sources of lindane exposure within EPA’s purview (food, seed treatments, ambient levels in the environment) are much more attenuated than the acute exposure levels that FDA examines (direct application to the skin, often of children). Especially in this context, the statement that “FDA has determined that Lindane products have benefits that outweigh risks when used as directed,” as compared to EPA’s entirely opposite conclusion that the costs of indirect use as a pesticide outweigh the benefits, is particularly alarming.⁴⁰ As noted above, lindane use for the treatment of head lice and scabies is no more necessary than is its use as a pesticide, and, as with pesticidal lindane use, many more effective, safer, and less expensive alternatives are currently available for head lice and scabies control.

³⁸ *Id.*

³⁹ *Id.*

⁴⁰ U.S. FDA, *FDA Public Health Advisory: Safety of Topical Lindane Products for the Treatment of Scabies and Lice*, available at <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm110845.htm> (last visited May 5, 2010).

Further, EPA notes in its Reregistration Eligibility Decision (“RED”) on lindane, that the “[p]harmaceutical use of lindane for treatment of lice and scabies results in exposure to the treated individual, as well as exposure to the general population as a result of ‘down the drain’ release into drinking water.”⁴¹ More specifically, “lindane enters drinking water when individuals using the pharmaceutical products wash off their hands/bodies.”⁴² This “down the drain” aspect of drinking water contamination is of great concern, and has prompted states such as California to take action to ban the pharmaceutical use of lindane, as discussed below.

Further, the EPA RED notes that lindane’s persistence and bio-accumulation exacerbate the problem of general population exposure.⁴³ For example, significant concentrations of lindane are found in subsistence communities in the Arctic, where lindane is neither used nor manufactured, raising considerable environmental justice concerns, discussed in more detail below.

6. International Bans on Lindane Show that Lindane Is Not Safe.

In 2009, more than 160 countries agreed to designate lindane for global elimination under the Stockholm Convention on Persistent Organic Pollutants (POPs) because the chemical meets the treaty’s criteria for toxicity, bioaccumulation, persistence, and transport.⁴⁴ The treaty prohibits the production and use of lindane, allowing a limited exemption for use of existing stocks of pharmaceutical products in countries that specifically request it. This signal of overwhelming international consensus regarding lindane’s dangers highlights the importance of FDA prohibiting all pharmaceutical uses of lindane. The Stockholm Convention seeks to protect public health and the environment worldwide through a multilateral international treaty which

⁴¹ U.S. EPA, *Lindane Voluntary Cancellation and RED Addendum Fact Sheet*, available at http://www.epa.gov/opp00001/reregistration/REDs/factsheets/lindane_fs_addendum.htm (last visited May 5, 2010).

⁴² U.S. EPA, *Addendum to the 2002 Lindane Reregistration Eligibility Decision (RED)*, at 7, July 2006, available at http://www.epa.gov/opp00001/reregistration/REDs/lindane_red_addendum.pdf (last visited May 17, 2010).

⁴³ *Id.*

⁴⁴ Stockholm Convention on Persistent Organic Pollutants, decision SC-4/15, amending Annex A, May 22, 2001, 40 I.L.M. 531.

restricts use and production of listed POPs, while also providing mechanisms to encourage cleanup of the substances. The Stockholm Convention was adopted in 2001, and entered into force in 2004.⁴⁵ There are currently 170 parties to the treaty.⁴⁶ The initial Stockholm Convention focused on controlling the use and production of twelve particularly hazardous POPs known as the “dirty dozen.”⁴⁷ In May of 2009, at its fourth meeting, the Stockholm Convention’s Conference of the Parties (COP) voted to amend the convention to add nine additional chemicals as regulated POPs, among them lindane and other HCH isomers.⁴⁸ The treaty divides the POPs chemicals subject to regulation into three categories: Annexes A, B, and C. Annex C is the least stringent classification, requiring only that parties take certain measures to “reduce the total releases derived from anthropogenic sources of each of the chemicals listed.”⁴⁹ Annexes A and B require parties to eliminate (Annex A) or severely restrict (Annex B) the import, export, and production of the listed chemicals.⁵⁰

Lindane is listed as an “Annex A” chemical in the Stockholm Convention, the most severely restricted listing, indicating the highest level of concern for the chemical’s human health and environmental effects. The Annex A listing means that parties to the Convention must work to eliminate production and use of the chemical. There is one listed “specific exemption” under Annex A for the use of lindane as a pharmaceutical to control head lice and scabies that is only

⁴⁵ Stockholm Convention on Persistent Organic Pollutants, May 22, 2001, 40 I.L.M. 531 [hereinafter Stockholm Convention].

⁴⁶ *Id.* at art. 25(1).

⁴⁷ See, e.g., Pep Fuller & Thomas O. McGarity, *Beyond the Dirty Dozen: the Bush Administration’s Cautious Approach to Listing New Persistent Organic Pollutants and the Future of the Stockholm Convention*, 28 WM. & MARY ENVTL. L. & POL’Y REV. 1, 2 (2003) (“dirty dozen” chemicals include DDT, PCBs, aldrin, chlordane, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, and toxaphene).

⁴⁸ Stockholm Convention on Persistent Organic Pollutants, *What are POPs?: Nine New POPs*, <http://chm.pops.int/Convention/ThePOPs/tabid/673/language/en-US/Default.aspx> (last visited Apr. 30, 2010).

⁴⁹ Stockholm Convention, at art.3.

⁵⁰ *Id.*

available to parties that have applied for and registered to use the chemical in such a way.⁵¹

Most importantly, this specific exemption expires in 2014, permanently disallowing all uses of lindane by party-nations.⁵² Many party-nations opposed even this time-limited exemption, and advocated an outright ban, since the chemical was already entirely prohibited in over 50 countries.⁵³

Of critical importance to this petition is the fact that the United States delegation to the Stockholm Convention supported the addition of lindane under the treaty without an exemption for pharmaceutical uses. Though U.S. delegates could not formally participate at the meeting because the U.S. is not a party to the Convention, U.S. delegates attended the 2009 Conference of the Parties and publicly announced that the U.S. not only supported the international ban on lindane but also favored the ban without an exemption for pharmaceutical use of lindane.⁵⁴

This broad U.S. support is in line with prior national action regarding chemicals listed under the Stockholm Convention. Of the original “dirty dozen” chemicals listed under the POPs treaty, only one remains approved, for extremely limited uses, in the U.S., and 8 are flatly banned.⁵⁵ Further, five of the nine newly listed POPs are entirely prohibited in the U.S.⁵⁶ Of the remaining four, one is lindane, and two are byproducts of lindane manufacturing.⁵⁷

⁵¹ See, e.g., Paul E. Hagen & Michael P. Walls, *The Stockholm Convention on Persistent Organic Pollutants*, 19 NAT. RESOURCES & ENV'T. 51-2 (2005).

⁵² Stockholm Convention on Persistent Organic Pollutants, decision SC-4/15, amending Annex A, May 22, 2001, 40 I.L.M. 531.

⁵³ Conference of the Parties of the Stockholm Convention on Persistent Organic Pollutants, Geneva, Switz., May 4-8, 2009, ¶ 12, U.N. Doc UNEP/POPS/COP.4/38 (May 8, 2009).

⁵⁴ Kristin Schafer, *Global Chemical Treaty Adds Lindane to Ban List*, Pan North America Pesticide Action Network, available at: <http://www.panna.org/newsroom/20090511> (last visited Mar. 30, 2010).

⁵⁵ See, e.g., Agency for Toxic Substances and Disease Registry, ToxFAQs for Heptachlor available at <http://www.atsdr.cdc.gov/tfacts12.html> (last visited May 5, 2010) (Heptachlor is banned except for fire ant control in underground power transformers).

⁵⁶ See, e.g., Agency for Toxic Substances and Disease Registry, ToxFAQs for Chlordecone, available at <http://www.atsdr.cdc.gov/tfacts66.html> (last visited May 5, 2010) (has not been manufactured or used in the U.S. since 1978).

⁵⁷ See, e.g., Agency for Toxic Substances and Disease Registry, ToxFAQs for Alpha hexachlorocyclohexane, available at <http://www.atsdr.cdc.gov/tfacts43.html> (last visited May 5, 2010) (alpha and beta hexachlorocyclohexane are byproducts of lindane production.).

Lindane has also been addressed in other international treaties. It is listed under the Rotterdam Convention on Prior Informed Consent, and is restricted under the Convention on Long-Range Transboundary Air Pollution (“LRTAP”). Further, lindane is the subject of a North American Regional Action Plan (“NARAP”), a regional agreement between the U.S., Mexico, and Canada, under the United Nations Commission on Environmental Cooperation (“UNCEC”). The U.S. nominated lindane for a NARAP on January 15, 1999.⁵⁸ The NARAP was created through a regional task force that examined how lindane was used in the region, and the U.S., Mexico, and Canada all agreed to take certain national actions relating to lindane. Specifically, through the action plan, Mexico agreed to phase out all uses of lindane through a prioritized phase-out approach.⁵⁹ Like the U.S., the only remaining use of lindane in Canada is as a treatment for head lice and scabies. Canada agreed to, among other things, examine the risks associated with lindane use, and improve education on the risks of use.⁶⁰ Under the terms of the NARAP, the United States specifically agreed that the “U.S. Food and Drug Administration (FDA) will work proactively with pharmaceutical companies to facilitate the development of alternatives to lindane for the treatment of lice and scabies.”⁶¹ The U.S. also promised through the NARAP to educate the public and eliminate pesticidal use of lindane (accomplished by EPA in 2006). Both Canada and Mexico are now signatories to the Stockholm Convention, and Mexico nominated lindane for listing under the POPs treaty. Mexico and Canada have worked towards the stated goals of the NARAP both within their boundaries and through international agreements. While the U.S. has moved towards elimination of lindane through EPA and state

⁵⁸ Commission for Environmental Cooperation of North America, *Lindane*, March 2002, available at http://www.cec.org/Storage/36/2794_Lindane_Fact_Sheet.pdf (last visited May 25, 2010).

⁵⁹ Commission for Environmental Cooperation, *The North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane (HCH) Isomers*, at 26, Nov. 30, 2006, available at http://www.cec.org/Storage/36/2797_NARAP_on_Lindane_and_Other_Hexachlorocyclohexane_Isomers.pdf (last visited May 25, 2010).

⁶⁰ *Id.* at 25-26.

⁶¹ *Id.* at 28.

action, FDA should follow its stated aim to “work proactively” to move towards alternative treatments for head lice and scabies. In doing so, FDA should withdraw the approval of lindane.

The listing of lindane under the Stockholm Convention, along with the administration’s support of this listing without exemption, EPA’s pesticide cancellation, and the actions of states (discussed below), signal that at all levels of government within the U.S., significant action has been taken to align the U.S. with the global community in prohibiting all uses of lindane. FDA must take action, in line with EPA, states, and the governments of many other nations, to immediately ban the use of lindane to treat head lice and scabies.

7. U.S. Use of Lindane Has Environmental Justice Implications.

The fact that lindane is used but not produced in the U.S., see *supra*, raises significant environmental justice concerns. Three of the nine newly listed POPs under the Stockholm Convention are related to lindane production, which highlights that it is not only dangerous to health and the environment within the United States to use lindane, but also our nation’s continued use of the product has very significant and damaging health and environmental consequences for the rest of the world.⁶²

Not only do the two countries that manufacture lindane have high concentrations of this persistent chemical within their borders which may be threatening the public health, but also, areas of the world that neither use nor manufacture lindane exhibit high levels of the chemical. This presence is due to long-range transport of the chemical and lindane’s ability to bio-accumulate. Lindane’s presence in Arctic indigenous communities calls attention to this concern. EPA notes in its RED cancellation that:

[i]ndigenous populations are exposed to lindane via consumption of subsistence diets... indigenous populations rely heavily on animal fats and protein in their subsistence diets. For example, EPA reported high harvest amounts of walrus, seal and whale for Alaska

⁶² Humphreys, et al., *supra* note 1, at 301.

communities. Residues of lindane and other HCH isomers are present in these animals even though they are not in areas where lindane is manufactured or used ... [L]indane and other HCH isomers are mobile once released into the environment and can be transported long distances. Lindane and other HCH isomers tend to accumulate in colder climates, such as the arctic, and concentrate in the food chain. Thus any manufacture or use of lindane, or other HCH isomers, is a potential source of exposure to indigenous populations⁶³

This exposure to lindane in arctic subsistence communities is not trivial, and in fact, “HCH isomers are among the most abundant organochlorine contaminants in the Arctic Ocean,” with “[t]he highest known concentrations [] in the Beaufort Sea and the Canadian Archipelago; marine mammals in those regions have elevated residues of HCH isomers.”⁶⁴ Arctic subsistence communities that rely on marine mammals as their primary source of food have no way to control their lindane exposure. Nevertheless, “[i]t was estimated in 1995 that nearly half the lindane in the global environment was in the polar regions,” making this threat to health ever-present.⁶⁵

In recognizing and evaluating lindane’s persistence in subsistence communities and capacity for long-range transport throughout the globe, EPA noted that “costs of continued lindane registration far outweigh the benefits.”⁶⁶ EPA’s focus on health and environmental effects in the arctic is particularly striking in the context of FDA’s duties under §355(e). Under §§355(e)(1)-(3), FDA is required to withdraw drugs that are no longer safe or effective. The severe consequences to third party indigenous communities in Alaska and the Arctic provide the basis for EPA’s cancellation of pesticidal uses of lindane, and speak to the safety of lindane. The dangerous consequences of lindane use are not only limited to the patient using the product, as

⁶³ *Addendum to RED*, supra note 42, at 7.

⁶⁴ U.S. EPA, *Lindane and Other HCH Isomers – EPA Risk Assessment Fact Sheet*, February 8, 2006, available at http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm (last visited May 17, 2010).

⁶⁵ Kristin Schafer, *Lindane: Partial Ban in California Spurs Action in Other States*, Pan North American Pesticide Action Network, available at: http://www.panna.org/legacy/gpc/gpc_200408.14.2.06.dv.html (last visited March 30, 2010).

⁶⁶ *Addendum to RED*, supra note 42, at 17.

EPA's cancellation powerfully points out. FDA must examine not only the safety of lindane to individual patients, but also the health impacts on the nation as a whole. Along with harms to individual patients, harm to indigenous communities through bioaccumulation and long-range transport highlights that lindane is not safe under the terms of §355(e)

Since FDA's mission is targeted at protecting human health, the grave and disproportionate health risks borne by arctic subsistence communities, in Alaska and elsewhere, as a result of worldwide lindane use, should compel FDA to immediately withdraw lindane from the market. Data on bioaccumulation and high lindane concentrations in subsistence communities highlight the health risk and corresponding necessity to ban lindane.

8. State Actions to Ban Lindane Show that Lindane Is Not Safe.

In 2000, the California legislature unanimously passed a ban on the sale of lindane for pharmaceutical purposes, effective in 2002.⁶⁷ The ban was enacted both out of concern over the health consequences of lindane, described in detail above, and in an effort to control costs of wastewater treatment to remove lindane from water. Wastewater treatment is a serious issue for many regions, since certain treatment technologies are very expensive, and "may not be affordable for many municipalities."⁶⁸ California has very stringent water quality standards for lindane, and wastewater treatment engineers in urban areas noted that these standards were frequently exceeded. The engineers "calculated that a single treatment for head lice or scabies contain[ed] enough lindane to bring 6 million gallons of water above the California water quality standards."⁶⁹ The serious impact that only one lindane treatment could have on an entire municipality's compliance with water quality standards led to the unanimous enactment of California's ban on lindane in 2002.

⁶⁷ Humphreys, et.al, *supra* note 1, at 298.

⁶⁸ *Id.* at 297.

⁶⁹ *Id.* at 298.

Prior to the ban, California wastewater concentrations of lindane from washing lindane off the body and down the drain was approximately 36 parts per thousand (ppt). This level was much higher than the California water quality standard for lindane, which is set at 19 ppt.⁷⁰ After the ban, a 2006 study observed that concentrations of lindane in wastewater had dropped to “almost undetectable concentrations in California,” as compared to a county outside California used as a control, where levels remained high.⁷¹ Further, physicians in California reported no problems in treating patients without the option of lindane, and there were many fewer calls to poison control centers in California regarding lindane exposure.⁷²

In addition to large savings on wastewater treatment and reduced exposure to lindane for residents of California, such a successful large-scale ban of lindane as a treatment for head lice and scabies highlights the ease with which FDA could ban the pharmaceutical use of lindane. The California ban proves that the risks of lindane far outweigh the benefits, and that head lice and scabies can be effectively treated without lindane, highlighting the need for FDA to reanalyze its approval of lindane. The American College of Preventive Medicine passed a resolution echoing the California ban that supports “efforts to curtail all pharmaceutical uses of lindane in the United States.”⁷³

Following the California ban, the Michigan House of Representatives passed legislation in 2009 restricting the use of lindane to doctor’s offices.⁷⁴ Other states, including New York and Minnesota, have also considered banning the substance within their states.⁷⁵

⁷⁰ *Id.* at 298-301.

⁷¹ *Id.* at 299.

⁷² *Id.* at 301.

⁷³ American College of Preventive Medicine, *ACPM Resolution for the Pharmaceutical Ban of Lindane*, attached.

⁷⁴ Kristin Schafer, *Lindane: Partial Ban in California Spurs Action in Other States*, Pesticide Action Network North America, available at: http://www.panna.org/legacy/gpc/gpc_200408.14.2.06.dv.html (last visited March 30, 2010).

⁷⁵ *Id.*

9. Summary of Information that May Be Unfavorable.

FDA's regulations require inclusion in this petition of representative information known to NRDC that may not support the actions requested herein. 21 C.F.R. § 10.30(b). To the extent that there is any information unfavorable to this petition, it is summarized by the FDA in its "Public Health Advisory" issued in 2003 in conjunction with new labeling requirements.⁷⁶ The Advisory describes many dangerous side effects from lindane use, and nonetheless concludes that the benefits of use outweigh the costs.

NRDC and our petitioning partners strongly disagree with FDA's conclusion that continued lindane use is of overall net benefit in the treatment of lice and scabies infestations. The toxic health effects of lindane are severe and potentially fatal, particularly for young children. Further, there are significant environmental and international health consequences to continued use of lindane, and there is broad consensus of hundreds of nations, including the U.S., that lindane is a toxic chemical that must be banned. Moreover, entirely nontoxic alternatives to lindane exist as treatments for head lice and scabies, neither of which is a life-threatening condition.

B. Environmental Impact.

This petition requests action to ban the use of a substance as a pharmaceutical option for the treatment of head lice and scabies and is therefore categorically excluded from the requirement to prepare an environmental assessment or environmental impact statement under 21 C.F.R. §§ 25.30 and 25.31.

⁷⁶ FDA Public Health Advisory, *supra* note 3.

C. Certification.

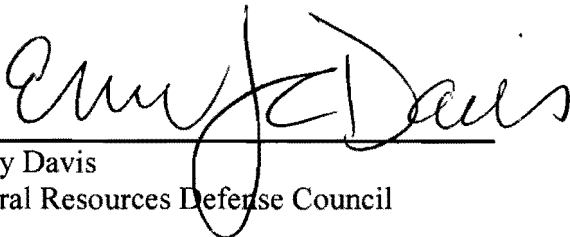
This petition includes all information and views on which the petition relies, and it includes representative data and information known to NRDC and our partners which may be unfavorable to the petition. NRDC attaches and incorporates by reference the comments and reports listed below, as well as copies of all studies cited in this petition. As required by 21 C.F.R. § 10.20(a), NRDC is submitting the original and four copies of this petition to the FDA Division of Dockets Management. NRDC reserves the right to supplement this petition pursuant to 21 C.F.R. § 10.30(g).

III. CONCLUSION

FDA must take immediate action to ban the pharmaceutical use of lindane for treatment of lice and scabies. Lindane was recently added to the Stockholm POPs treaty, highlighting significant and overwhelming international consensus that the environmental and human health costs of lindane far outweigh any perceived benefits from use. Further, the fact that only two countries manufacture lindane raises significant environmental justice concerns surrounding continued use. In addition to these serious concerns, lindane is an expensive and ineffective treatment for lice and scabies when compared to alternative treatments on the market. FDA's continued approval of lindane as a treatment for lice and scabies is out of line with current science and both national and international consensus. FDA, as an agency charged with protecting the public health by assuring that drugs are safe and effective, has an immediate and urgent responsibility to ban the pharmaceutical use of lindane and move towards safer and more effective treatments for head lice and scabies.

For the reasons presented above, as supported by the attached studies and reports, NRDC and our petitioning partners request that the FDA: (a) withdraw the approval of lindane as a pharmaceutical drug for the treatment of head lice and scabies, and (b) act immediately to recall lindane from the U.S. market.

Respectfully Submitted,



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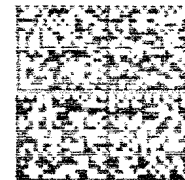
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