Maine Board of Pesticides Control

Miscellaneous Pesticides Articles November 2014

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HONEY BEE BEST MANAGEMENT PRACTICES FOR CALIFORNIA ALMONDS

WHY SHOULD GROWERS AND OTHERS INVOLVED IN ALMOND POLLINATION CARE?

Honey bees are essential for successful pollination of almonds and the long-term health of the California Almond industry. Why should almond growers — and all parties involved in almond pollination — care about healthy, strong bees? First, bees are a valuable resource and almond production input, and the time they spend in almonds impacts hive health throughout the year, from the time they leave almond orchards until they return the next season. Second, although almonds are only one of more than 90 foods that rely on pollination by bees, because of its size and number of bees needed, the California Almond industry is increasingly being watched by the public on matters related to the health and stability of honey bee populations.

Of particular concern at this time is how to manage the use of pest control materials in ways that minimize their possible impact on honey bees. It is important that growers of all crops implement best management practices to support bee health, and for those whose crops rely on honey bee pollination, to consider honey bee health not only during the pollination season, but during the entire year.

The following pages outline the management practices that research supported by the Almond Board of California, and others, have determined will promote the health of honey bees and protect them from environmental factors that could be detrimental in the almond orchard. While many of these practices are generally applicable across all crops, some are almond specific.

This document covers precautions to follow to protect honey bees during the almond pollination season. Four key precautions are:

1. Maintain clear communication among all parties involved, particularly on the specifics of pesticide application.
2. If it is necessary to spray the orchard, for instance with fungicides, do so in the late afternoon or evening.
3. Until more is known, avoid tank-mixing products during bloom.
4. Avoid applying insecticides during bloom until more is known about the effects on honey bees, particularly to young, developing bees in the hive. Fortunately, there are several insecticide application timing options other than bloom time treatments.

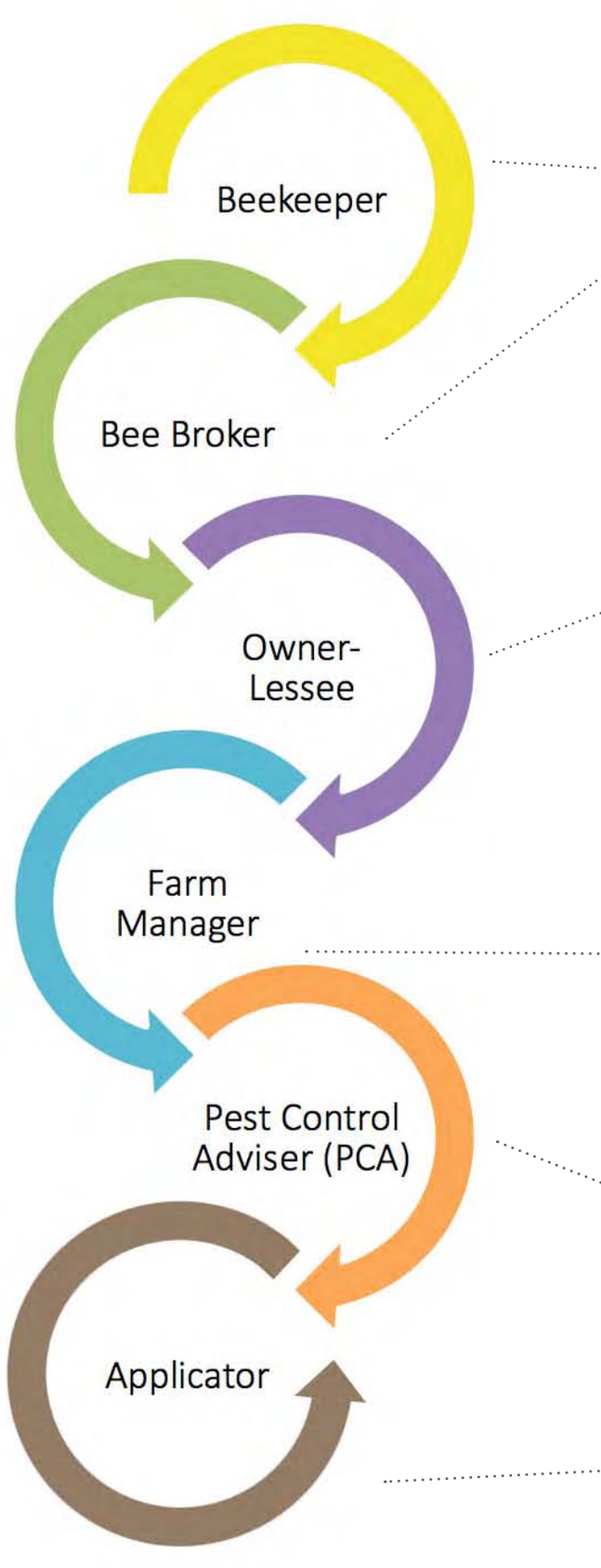
California Almond growers and others involved in the pollination process should follow these important best management practices to preserve the health of honey bees in California Almond orchards.

THE COMMUNICATION CHAIN

Establishing a clear chain of communication among all parties involved in pollination and pest management during almond bloom will help ensure that responsibilities are met and information is reported appropriately.

The parties can be simply a beekeeper and a grower, but depending on the scale and organization of the grower operation, can also involve a bee broker, owner-lessee, farm manager, pest control adviser (PCA) and pesticide applicator.

The California county agricultural commissioners are also a vital link in the communication chain. Each year, beekeepers in California are required to initially register their hive locations with county agricultural commissioners and should notify commissioners of subsequent movement to receive voluntary notifications for pesticide applications. This gives growers a resource to contact to determine if there are any honey bee hives within 1 mile of their location. This is important even outside the almond bloom period, particularly when applying insecticides. Even so, it is important to note that a 1-mile buffer will not protect honey bee colonies under all conditions, as bees will forage up to 4 miles to collect food and find water when resources are scarce.[1]



[1]Eckert, J.E. 1933. *The flight range of the honey-bee.* J. of Agri. Res. 47(8):257–285.

HONEY BEE BMP COMMUNICATION CHAIN FOR CALIFORNIA ALMONDS

- Engage in agreements with growers.
- Register hives with county agricultural commissioner by Jan. 1 each year or upon arrival in California.
- Request optional notification from county agricultural commissioner each year upon registration and with any hive movement.
- Immediately report any suspected pesticide-related bee incidents to owner-lessee/county agricultural commissioner at almond bloom and throughout the year.

- Engage in agreements with beekeepers/bee brokers.
- Communicate details and specifications of agreements to stakeholders down the chain (farm manager, PCA, applicator).
- Follow the *Honey Bee Best Management Practices Quick Guide for Almonds* and, if applying pesticides, follow the *Applicator/Driver Honey Bee Best Management Practices Quick Guide for Almonds.*
- If applying pesticides, contact local county agricultural commissioner to notify beekeepers with nearby managed hives before making applications any time of year. This is mandatory for "toxic to bees" label statements* and recommended for other applications, particularly during almond bloom.
- Immediately report any suspected pesticide-related bee incidents to beekeeper/county agricultural commissioner at almond bloom and throughout the year.

- Communicate details and specifications of pesticide application agreement to the PCA and applicator.
- Follow the *Honey Bee Best Management Practices Quick Guide for Almonds* and, if applying pesticides, follow the *Applicator/Driver Honey Bee Best Management Practices Quick Guide for Almonds.*
- If applying pesticides, contact local county agricultural commissioner to notify beekeepers with nearby managed hives before making applications any time of year. This is mandatory for "toxic to bees" label statements* and recommended for other applications, particularly during almond bloom.
- Immediately report suspected pesticide-related bee incidents to beekeeper/county agricultural commissioner at almond bloom and throughout the year.

- Communicate details and specifications of pesticide application agreement to applicator.
- Follow the *Honey Bee Best Management Practices Quick Guide for Almonds.*
- Immediately report suspected pesticide-related bee incidents to grower/beekeeper/county agricultural commissioner at almond bloom and throughout the year.

- Follow the *Applicator/Driver Honey Bee Best Management Practices Quick Guide for Almonds* and relay messages to the spray-rig driver.
- Before applying pesticides, contact local county agricultural commissioner to notify beekeepers with nearby managed hives before making applications any time of year. This is mandatory for "toxic to bees" label statements* and recommended for other applications, particularly during bloom.
- Immediately report suspected pesticide-related bee incidents to farm manager/owner-lessee/beekeeper/county agricultural commissioner.

- Collect and map locations of managed bees throughout the county based on information provided by registered beekeepers.
- Provide pesticide applicators the contact information for beekeepers with hives within a 1-mile radius of the application location.
- Investigate reports of suspected pesticide-related bee incidents.

**When a pesticide to be applied bears "toxic to bees" label statements, beekeepers with hives within 1 mile of the application must be notified (if they have requested notification) by the applicator at least 48 hours before the planned application.*

GROWER-BEEKEEPER COMMUNICATION PRIOR TO ALMOND BLOOM

The first step toward a successful almond pollination season is communication to ensure expectations between the beekeeper and grower/owner are fully understood. Growers should contact beekeepers as early as possible before the pollination season to discuss their requirements. Growers who do not have an established relationship with a beekeeper can refer to the Pollination Directory on the Almond Board of California website Almonds.com/PollinationDirectory. This database includes both beekeepers and bee brokers.

Growers and their beekeepers should outline and mutually agree on expectations of each other to avoid misunderstandings. Communication on pesticide use during bloom, for instance, should be a fundamental consideration. This could mean outlining a pesticide plan that specifies which pest control materials might be used. Grower and beekeeper should agree on which products can be applied if a treatment is deemed necessary. During bloom, when applications are imminent, establish a line of communication throughout the chain of all parties involved in pollinating almonds and/or applying pesticides to orchards so they are informed in advance.

By registering with the county agricultural commissioner and providing the location of colonies, beekeepers can request an advance notice of applications of pesticides labeled as toxic to bees within a mile of the colonies.

Beyond pesticides, other elements that should be agreed upon prior to bloom are the responsibilities of the grower and the responsibilities of the beekeeper in these areas:

- The number of frames of honey bees, including an average and minimum frame count;
- Date and location of placement in orchard;
- Ambient temperature and time of day at inspection site in the field;
- Payment amount, terms, deposit, progress payment and final payment;
- Accessibility of colonies to beekeeper; and
- When bees are to be removed from the orchard.

A sample of an almond pollination agreement template can be accessed at ProjectApism.org under the BMP menu (For Almond Growers); this template can be customized to meet individual needs and requirements.

For successful pollination and safeguarding of honey bees, growers should contact beekeepers early and follow through with an agreement that outlines the expectations of each.

PREPARING FOR ARRIVAL

For pollination in mature almond orchards, it is common practice to place an average of two hives per acre having an average of eight frames of bees, with six-frame minimum hive strength.[2] There are a number of variables involved in any local situation, and pollination requirements will vary. Hives should be placed:

- Where they are accessible and convenient at all hours for servicing and removal;
- If possible, near flowering forage before bloom and after bloom;
- With eastern and southern exposures for hive openings to encourage honey bee flight;
- Away from areas prone to shade or flooding;
- For orchards of 40 acres or fewer, hives can be placed outside of the orchard;
- For orchards larger than 40 acres, hives should be placed at no more than quarter-mile intervals, which in larger acreages may be within orchards; and
- Research has shown that it is possible to place bees around the perimeter of orchard blocks of up to 70 acres if they are no more than a quarter-mile wide. However, to provide uniform bee activity in trees throughout the orchard, colonies should be clustered in greater numbers near the middle of the long sides of the orchard (Fig. 1).[3]

Fig. 1. Example distribution of honey bee colonies for orchards larger than 40 acres. The green box represents the orchard and the numbers outside the box represent the distribution and density of hives at the perimeter of the orchard. Note the concentration of colonies along the middle of the long sides of the orchard. (Diagram adapted from Almond Production Manual, University of California Division of Agriculture and Natural Resources; page 136, 22.7)

Hives should be placed near forage that is flowering before, during and after almond bloom, if possible, as an alternative source of food. (Photo courtesy Project Apis m.)

Hive placement depends on orchard size. Larger acreages may need to have hives placed within the orchard.

[2]Mueller, Shannon. 2012. "Colony Strength Evaluation." Presented at The Almond Conference.
[3]Thorp, Robbin. 1996. Bee Management for Pollination. Almond Production Manual, Publication 3364, University of California Division of Agriculture and Natural Resources. pp. 132–138.

Growers should provide a clear area for bee drop-off, and keep access roads free of obstructions and maintained at all times.

Choose locations that have appropriate buffers between pesticide-treated areas and colonies. Provide abundant, potable water, free from contamination, for bees to drink. This will ensure that more time is spent pollinating the crop than searching for water. Water should be checked and refilled throughout the time that the bees are in the orchard. Landings such as burlap or screens over containers make water accessible and prevent bee drowning. Either cover or remove water sources before a pest control treatment, or supply clean water after treatment is made.

Moving the hives into the orchard at about 10% bloom is recommended by the University of California.[4] At this point, there is enough bloom to hold bees in the orchard so they don't seek blooms elsewhere. However, until blooms from at least one additional compatible variety are available, cross-pollination, and thus fertilization, will not take place.

Almond growers should provide a clear and convenient place for beekeepers for bee drop-off.

Provide potable water sources for bees with a burlap landing. (Photo by Gordon Wardell, Paramount Farming Company)

The University of California recommends moving hives into the orchard at about 10% bloom.

[4]Mussen, E. 2014. *When to leave almond orchards.* UC Apiaries newsletter, Mar./Apr. 2014.

ASSESSING HIVE STRENGTH AND QUALITY

Hives should be inspected as they arrive in the orchard, either by an objective third-party apiary inspector or by the beekeeper, who is observed by the grower. They should inspect for colony strength (see Preparing for Arrival, page 7), and for other parameters as agreed upon.

An inspection will find if the agreed-upon terms are being met. Typically, only a representative sample of hives will be inspected. Growers should notify the beekeeper of the inspection so they can assist in handling the hives.

Colony strength evaluations not only help ensure growers get what they pay for, inspections also help ensure that beekeepers are compensated for additional expenses in providing quality hives. Comprehensive guidelines for all parties can be found in the learning course "Honey Bees and Colony Strength Evaluation," which can be accessed at class.ucanr.edu.

This online education and training course provides protocols for assessing the strength of honey bees and colonies, and can also help growers become better informed when renting hives from beekeepers and hiring apiary inspectors. The course covers basic bee biology and colony organization; different inspection procedures and standards; and how to recognize some parasites, diseases and other potential problems.

Growers can further monitor colony strength by walking orchards daily during bee flight hours to observe activity levels. Record hives that are weak or inactive, and report them to the beekeeper. This is also an opportunity to observe whether pollination is taking place. If the foraging bees are not collecting and carrying pollen on their legs, there is little to no pollination taking place.

Hives should be inspected by an apiary inspector or the beekeeper as soon as bees arrive in the orchard.

A hive inspection includes an evaluation of colony strength. (Photo courtesy Project Apis m.)

When walking orchards during bee flight hours, look for bees carrying pollen on their legs, which confirms that pollination is taking place. (Photo courtesy Project Apis m.)

PROTECTING HONEY BEES AT BLOOM

Despite efforts to protect honey bees from parasitic mites such as Varroa mite, loss of natural forage, diseases, and the possible effects of some pesticides, beekeepers are losing large numbers of colonies.[5] Research into the causes of these losses and how to prevent them is ongoing.

Pesticides (and their methods of application) under investigation include usage within the hive for mite and disease control as well as usage on crops. Honey bees are vulnerable to many of the pesticides used to control insects, disease and weeds. California Almond growers must maintain a delicate balance between protecting their crops from disease, insects and weeds, while at the same time protecting honey bees from potentially harmful insecticides, fungicides and other pest control materials.

Insecticide residues have been detected in pollen, including almond, brought back to the hive to feed bee brood. (Photo courtesy Project Apis m.)

HONEY BEES AND INSECTICIDES

All parties involved in almond pollination and/or applying pesticides should follow the precaution of not applying insecticides during bloom. Bee losses appear to have occurred in almonds as a result of tank-mixing insecticides with bloom-time fungicides. While the losses could have other causes, there is a scientific basis for concern; this is based on field experience that is being substantiated with controlled studies.[6,7] Currently, most bee label warnings are only based on adult acute toxicity studies; however, recent information indicates some may be harmful to young developing bees in the hive (bee brood). Until recently, the U.S. EPA has not required data for possible effects on bee brood. Foragers bring back pollen to the hive, which is fed to the bee brood. Insecticide residues have been detected in this pollen. The term 'insecticide' includes insect growth regulators, also known as IGRs.

[5]Spleen, A.M., E.J. Lengerich, K. Rennich, et al. 2013. Bee Informed Partnership. *A national survey of managed honey bee (2011–12) winter colony losses in the United States: results from the Bee Informed Partnership.* J. Apic. Res. 52(2):44–53.
[6]Mussen, Eric. 2013. *Problems with almond bloom sprays.* UC Apiaries newsletter, Jan./Feb. 2013.
[7]Johnson, R.M., E.G. Purcell. 2013. "Effect of 'Bee-Safe' Insecticides and Fungicides on Honey Bee Queen Development and Survival." Poster presented at 2nd International Conference on Pollinator Biology, Health and Policy, Aug. 14–17, 2013, Pennsylvania State University.

Furthermore, controlled studies[7] are demonstrating that some insecticides are known to synergize with some fungicides, and when an insecticide and a fungicide are tank-mixed, the spray can be more toxic to bees than either chemical used alone. This synergy has not been documented under field conditions, but until more is known, avoid tank-mixing an insecticide with a fungicide during the almond pollination season.

It is important to note that tank mixing of a number of these insecticides and fungicides is not a label violation. The U.S. EPA and California Department of Pesticide Regulation are evaluating information with an eye toward including warnings on product labels. However, until more is known about the effect of insecticides on bee brood, for their protection, avoid applying any insecticide during almond bloom; instead, rely on other effective timing options outside of the bloom period, such as delayed dormancy or post bloom. The UC Statewide Integrated Pest Management Guidelines for almonds provide insecticide and timing options (see ipm.ucdavis.edu and choose Agricultural Pests, then Almond).

Delayed dormancy is the period from the resumption of growth after dormancy, indicated by bud swell, until green tip, which occurs about Feb. 1, depending on region, variety and weather. **Post bloom** begins after petal fall, typically late March, but also may vary according to region, variety and weather.

Before making insecticide applications during the delayed-dormant or post-bloom period, contact the county agricultural commissioner to determine if there are any bees within a mile, and if there are, notify the beekeeper of the impending spray.

Another valuable resource is “How to Reduce Bee Poisoning from Pesticides,” a Pacific Northwest Extension publication, PNW 591. A free downloadable version is available at Almonds.com/Honey-Bee-Protection (under Additional Resources). It is important to note that toxicity ratings in this publication focus on acute toxicity to adult foraging bees, and additional risks to bee brood in the hive may occur and are not reflected in the toxicity category information given in this booklet.

“How to Reduce Bee Poisoning from Pesticides,” PNW 591, is a valuable resource available in downloadable format at Almonds.com/Honey-Bee-Protection under Additional Resources.

HONEY BEES AND FUNGICIDES

All parties involved in almond pollination and/or applying pesticides should follow the precaution of applying any fungicide deemed necessary during bloom in the late afternoon or evening, when bees and pollen are not present.

Disease protection during almond bloom is important, and fungicide applications are needed in many situations. However, fungicides may negatively impact pollination.

It has also been shown that some fungicides, while fairly safe for use around adult honey bees, may contribute to brood losses in larval and pupal stages.[8]

For some time, the University of California has recommended avoiding the use of fungicides containing iprodione, captan and/or ziram during almond bloom. Research performed in response to field observations of brood effects has confirmed that these fungicides can affect brood development. These compounds provide effective fungal control outside of bloom.

In addition, as noted previously, controlled studies[7] have demonstrated that some insecticides are known to synergize with some fungicides, and when an insecticide and a fungicide are tank-mixed, the spray can be more toxic to bees than either chemical used alone. This synergy has not been documented under field conditions, but until more is known, avoid tank-mixing an insecticide with a fungicide during the almond pollination season.

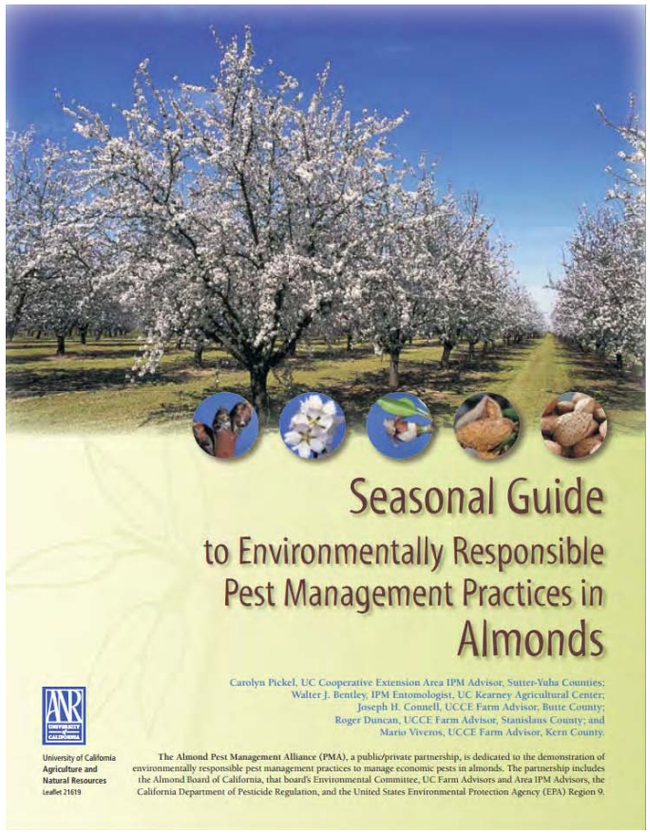
To protect honey bees from fungicides, apply in the late afternoon or evening, when bees and pollen are not present.

[8]Mussen, E.C., J.E. Lopez, C.Y.S. Peng. 2004. *Effects of selected fungicides on growth and development of larval honey bees,* Apis mellifera L. Environ. Entomol. 33(5):1151–1154.

USE IPM STRATEGIES TO MINIMIZE AGRICULTURAL SPRAYS

Following a monitoring-based integrated pest management (IPM) program in every season enhances pest control, protects water and air quality, and minimizes exposure of bees and pollen to pesticide sprays. Sources of information on developing and conducting an IPM program in almonds include:

- Seasonal Guide to Environmentally Responsible Pest Management Practices in Almonds, University of California Agriculture and Natural Resources Leaflet 21619. This is available at Almonds.com/IPM under Additional Resources.
- UC IPM Pest Management Guidelines and Year-Round IPM Program for Almonds. These are available at ipm.ucdavis.edu by selecting Agricultural Pests and Almond.



"Seasonal Guide to Environmentally Responsible Pest Management Practices in Almonds" is available at Almonds.com/IPM under Additional Resources.

HONEY BEES AND SELF-COMPATIBLE ALMOND VARIETIES

Although using self-compatible (self-fertile) varieties will reduce reliance on bees, it will not eliminate them. A number of factors — genetic, environmental and the structure of the flower — determine self-pollination and set. Even with self-compatible varieties, honey bees can ensure maximum set because bees consistently transfer pollen within the same flower from the anthers to the stigma of the pistil, where fertilization is initiated (see Fig. 2, page 16). However, because pollen no longer needs to be transferred between different varieties, the number of hives required will be reduced.

The best practices for protecting honey bees at bloom apply equally to growers of self-compatible varieties. This is because bees foraging in surrounding orchards are likely to wander into orchards with self-compatible varieties and be exposed to any insecticide or fungicide sprays that have been applied there.

UC IPM online provides many resources to almond growers.

BEST MANAGEMENT PRACTICES FOR PEST CONTROL DURING ALMOND BLOOM

Following these precautions will help protect honey bees from pesticide applications:

- The first rule to follow when making pesticide applications at bloom time is to read labels carefully and follow directions.
- Do not use pesticides with cautions on the label that read “highly toxic to bees,” “toxic to bees” “residual times” or “extended residual toxicity.” Residual toxicity to bees varies greatly between pesticide products, and can range from hours to a week or more.
- Avoid applying insecticides during almond bloom until more is known. If treatment is necessary, apply only fungicides and avoid tank-mixing insecticides with fungicides.
- Apply fungicides in the late afternoon or evening, when bees and pollen are not present; this will help avoid contaminating pollen with spray materials such as fungicides. Pollen-collecting bees often remove the pollen and leave the almond blossoms by mid-afternoon. However, do not spray so late that the fungicide does not have time to dry before bees begin foraging the next day. See the next section, “Removing Honey Bees from the Orchard,” for guidelines to determine whether exposed pollen is present in flowers.
- Either remove or cover water sources before spraying, or supply clean water after a treatment is made.
- Do not directly spray hives with any pesticide. Ensure that the spray-rig driver turns off nozzles when near hives.
- Do not hit flying bees with spray applications. Bees that come in contact with agricultural sprays will not be able to fly because of the weight of spray droplets on their wings. Avoid pesticide application or drift to blooming weeds in or adjacent to the orchard if honey bees are present.
- Avoid applying a pesticide with a long residual (extended residual toxicity or systemic pesticides) prebloom. More information about residue toxicity time is available in the document “EPA Information on Residue Toxicity Times for Growers and Beekeepers,” which can be accessed at Almonds.com/Honey-Bee-Protection.

Remember to keep all parties informed of agricultural sprays according to the communication chain agreed upon, so that beekeepers are always aware of impending applications, and applicators are fully informed of the parameters required regarding materials, timing, location and method of application.

Pollen-collecting bees generally have removed pollen and left almond blossoms by mid-afternoon.

REMOVING HONEY BEES FROM THE ORCHARD

University of California recommends bee removal when 90% of the flowers on the latest blooming variety are at petal fall.[9] Past this point, no pollination is taking place, and bees that forage outside the orchard (up to 4 miles), seeking alternate food sources and water, will have a higher risk of coming in contact with insecticide-treated crops.

After blossoms open, they release pollen for about four days. When temperatures are above 55°F, pollen is released when the anthers split open, or dehisce. This happens in progression over this period, with not all anthers opening at once. Typically, the pollen that is released each day is collected by bees by mid-afternoon. The pollen-receiving structure, the stigma surface, is receptive to fertilization for about five days after a blossom opens. However, fertilization is most successful when pollination occurs during the first few days that a flower is open.

Bees, both pollen and nectar collectors, concentrate on recently opened blooms. In one study, about 90% of all bee visitations were confined to flowers that have pollen. With adequate weather and bee activity, essentially all pollen will be collected from individual flowers within about four days after they have opened. Conforming to this, past work shows that during favorable pollination weather, almond flowers remain receptive to cross-pollination up to about four to five days after opening. Cooler weather, below 55–60°F, will lengthen the period of pollen collection and flower receptivity, and will delay petal fall.

Petals normally remain on flowers past the receptive period for cross-pollination, but once the pollen is depleted, bee visitation to flowers drops off substantially, and the remaining few visitors concentrate on collecting nectar. Nectar collectors are not efficient pollinators. These bees typically descend on the petals, probe for nectar at the base of flowers, and rarely pick up or transfer pollen. In contrast, pollen-collecting bees descend on the top of anthers and transfer pollen to the stigma surface, which is necessary for fertilization.

Pollen-collecting bees land on the top of anthers and transfer pollen to the stigma surface, resulting in fertilization.

Both pollen and nectar collectors concentrate on recently opened blooms. After blossoms open, they release pollen for about four days.

[9]Mussen, E. 2014. *When to leave almond orchards.* UC Apiaries newsletter, Mar./Apr. 2014.

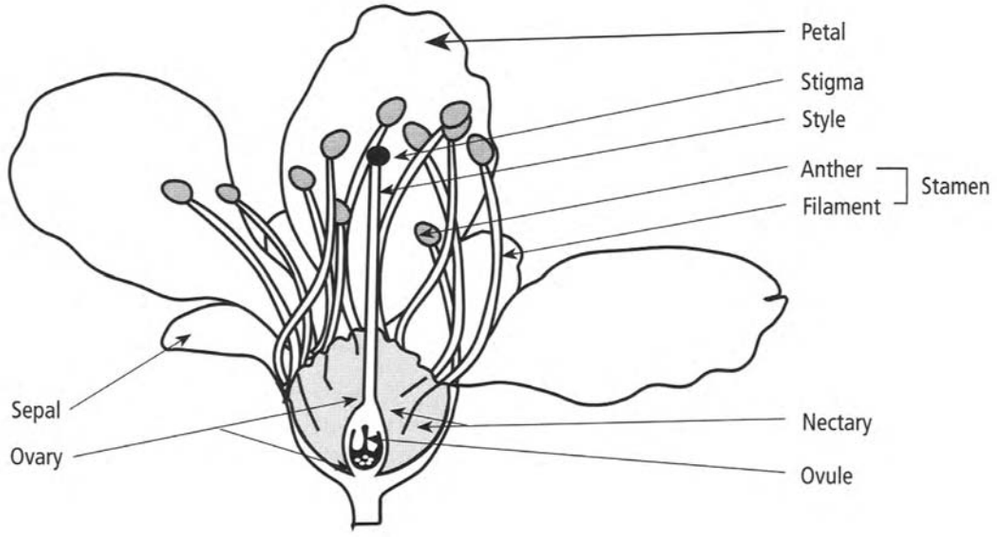


Fig. 2. Diagram of a Mission variety almond flower. For fertilization to be initiated, pollen from the anthers must be transferred to the stigma surface. When no anthers have pollen, the style turns from green to brown and the stigma and style are no longer receptive to pollination, and thus fertilization. (©1996 Regents of the University of California. Almond Production Manual, used by permission. Illustration adapted from USDA Agricultural Handbook 496 – S.E. McGregor).

It is fairly simple to determine if flowers have pollen and are receptive to cross-pollination. In newly opened flowers, most if not all anthers have not opened and are plump, yellow but not fuzzy. Anthers with pollen appear yellow and fuzzy, and for about four days, there will be a mixture of opened (dehisced) and unopened anthers. It is best to check for pollen in the morning before honey bees finish foraging all pollen available for that day. Older anthers without pollen are dry and light brown. Also in older flowers: When no anthers have pollen, the style (the tube below the stigma surface) turns from green to brown, and the stigma and style are no longer receptive to pollination.

When 90% of the flowers on the latest-blooming variety are at petal fall and no pollination is taking place, it is in the best interest of the bees to have beekeepers remove the colonies, regardless of the presence of petals or of nectar-foraging bees. Unfortunately, even if bee removal timing may be included in the pollination agreement, keep in mind that beekeepers can't always be available — or don't have an alternative location to move the bees to.

Once bees have been removed, it is still recommended to check with the county agricultural commissioner before making pesticide applications. Bees may still be foraging in neighboring orchards or in other crops nearby. Check with the county agricultural commissioner prior to the use of any insecticide.

ADDRESSING SUSPECTED PESTICIDE-RELATED HONEY BEE LOSSES

It is in the best interests of beekeepers and growers to immediately report suspected pesticide-related bee incidents to the local county agricultural commissioner's office. Here are some signs and symptoms to look for:

- Excessive numbers of dead and dying adult honey bees in front of hives;
- Dead brood at the hive entrance and dead newly emerged workers;
- Lack of foraging bees on a normally attractive blooming crop;
- Stupefaction (i.e., dazed, unconscious); paralysis; jerky, wobbly or rapid movements; spinning on the back;
- Disorientation and reduced efficiency of foraging bees;
- Immobile or lethargic bees unable to leave flowers;
- Bees unable to fly and crawling slowly as if chilled; and
- Queenless hives.

In reporting a suspected incident to the local county agricultural commissioner's office, include notes describing the previous health of the colony, prevailing wind, EPA registration number from the suspected pesticide label, name of the suspected pesticide and, in your opinion, how the bees may have been exposed. Photos or videos can also be included.

Beekeepers should also report pesticide treatments that have been applied to the hives and other pertinent details.

Preserving at least 2 ounces of adult bees, brood, pollen, honey, nectar or wax by immediately freezing in labeled, clean containers may be helpful if the incident warrants lab analysis.

Do not disturb the hives or site, pending an investigation.

WHAT TO EXPECT IN AN INVESTIGATION

Suspected honey bee pesticide-related incidents are investigated by the local county agricultural commissioner, aided at times by the California Department of Pesticide Regulation, to determine if there were any problems associated with the use of a pesticide.

Evidence gathering will include pesticide use information to determine which pesticides were used in the orchard where the hives were placed. The surrounding area will be surveyed to consider pesticide applications to blooming crops and orchards or weeds where the bees may have been foraging. The beekeeper will be asked about any pesticide treatments made to the hives to protect against various hive pests. Samples of the bees and surfaces of the identified hives may be obtained for analysis of pesticide residues.

If a beekeeper expresses concern that their bees may have been affected by pesticides, a report needs to be submitted by the beekeeper and/or the grower or other involved parties listed on the Honey Bee BMP Communication Chain (on pages 4 and 5) to the county agricultural commissioner's office. Only if suspected bee incidences are properly investigated can accurate information and real data be obtained. Without an investigation, it becomes a matter of opinion and supposition.

The area surrounding affected hives will be inspected in cases of suspected honey bee pesticide-related incidents.

A digital version of this publication is available at Almonds.com/BeeBMPs

Also Available:
Honey Bee Best Management Practices Quick Guide for Almonds
Applicator/Driver Honey Bee Best Management Practices Quick Guide for Almonds (in English and Spanish)

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Almond Board adopts new rules for pesticide use

By John Holland

The Modesto BeeOctober 16, 2014 Updated 15 hours ago

Bees help pollinate blossoming trees south of Dinuba in this 2013 photo.

MARK CROSSE — Fresno Bee Staff Photo Buy Photo

The Almond Board of California announced a new push Thursday to keep pesticides from harming the bees that pollinate the nut trees.

The Modesto-based group released a detailed set of farming practices, many of them already in use, and said it would share them with growers in advance of the February start of pollination.

Chief among the practices is to avoid spraying when the bees are flying amid the blooming trees. If growers still need to use chemicals, such as those that protect the crop against fungi in winter, they should be applied in the late afternoon or evening.

“The chemicals are important, but you have to be very judicious in how you use them,” said Eric Mussen, a recently retired bee expert at UC Davis.

He took part in a media conference call with Richard Waycott, chief executive officer at the board, and Bob Curtis, its associate director for agricultural affairs.

The state produces about 80% of the world’s almonds, and demand is booming thanks to studies on the nuts’ health benefits and their many uses. The gross income to Stanislaus County growers surged to $1.13 billion last year, according to its agricultural commissioner. Merced and San Joaquin are big players, too.

None of that happens without the commercial colonies of European honeybees, trucked from many parts of the country to meet the pollination demand in February and March. Some beekeepers have struggled to maintain their numbers because of diseases, mites and other threats to the hives. Drought in California and other places has reduced the flowering plants that sustain the bees.

Experts have said more research is needed on whether pesticides are a major threat, but in the meantime, farmers can help by using them carefully.

The Almond Board drafted the new guide with the help of beekeepers, researchers, the pesticide industry and state and federal regulators. It stresses communication among the parties in every part of the process, including where to place the bee boxes in the orchard, how to do spraying that cannot be avoided, and how to report possible poisoning of bees.

An abridged version of the guide is in both English and Spanish.

Curtis said the pesticide guide meshes with the effort to get growers to plant wildflowers so bees have other food sources just before and after the almond bloom.

Beekeepers make some of their money from honey sales, but rental fees for pollination are a bigger source. Stanislaus County alone reported that this service brought $53.6million last year, most of it for almonds.

“We wouldn’t have an almond industry if we didn’t have bees,” Waycott said.

Mussen said the pesticide advice could apply to the many other U.S. crops that rely on these pollinators. They number about 90 and account for a third of the nation’s food supply, Waycott said.

Also this week, the Whole Foods Market chain announced an effort to avoid selling fruits, vegetables and flowers produced with harmful pesticides. The threat to bees is among the criteria cited by the Austin-based company, which does not have any stores in the northern San Joaquin Valley.

“Whole Foods is stepping up, and other retailers should follow suit,” said Paul Towers, spokesman for the Oakland-based Pesticide Action Network, in a news release. “The transparent program gives shoppers more choices about what’s on their food and how it’s grown, including purchasing fruits and vegetables that protect pollinators, farmworkers and children.”

Cascadian Farm, a Washington state-based producer of organic products, announced its own effort on behalf of the bees this week. It urges consumers to eat pesticide-free food, to sow wildflowers and to donate to bee research and conservation.

The Almond Board's farming practices:

Modesto Bee staff writer John Holland can be reached at jholland@modbee.com or (209) 578-2385.

Join The Conversation

EPA announces voluntary program aimed at curbing pesticide drift | AgriPulse

agri-pulse.com/EPA-announces-voluntary-program-aimed-at-curbing-pesticide-drift-10212014.asp

WASHINGTON, Oct. 22, 2014 - The Environmental Protection Agency today announced a voluntary program aimed at showing applicators which products should be used to promote drift reduction during pesticide application.

The Drift Reduction Technology (DRT) program will recognize products that can reduce drift by at least 25 percent. An EPA-assigned star-rating system will recognize the degree to which these products can reduce pesticide drift, up to four stars.

Jim Jones, EPA assistant administrator for the Office of Chemical Safety and Pollution Prevention, said state and local agencies receive “thousands” of drift-related complaints every year, and this program will be an easy way for farmers to recognize ways to keep their product on their fields.

“Our new star-rating system of products and technologies will help farmers reduce drift, protect neighbors and reduce costs by keeping more of the pesticide on the crop,” Jones said in an EPA release. “We hope the new voluntary DRT will encourage the manufacture, marketing and use of safer spray technology and equipment scientifically proven to reduce pesticide drift.”

EPA says between 1-10 percent of pesticides are lost every year to drift, which accounts for about 70 million pounds of pesticides valued up to $640 million. State agencies also use resources to investigate drift claims, so the total amount of money lost to drift annually could be much higher than $640 million in product loss.

DRT will be a voluntary program encouraging manufacturers to study products such as spray nozzles, spray shields, and drift reduction chemicals and test their potential for drift reduction. Questions remain about the testing of the products since EPA workers will be receiving company data rather than conducting the testing themselves, but the EPA does allude to testing protocols on its website.

Mike Leggett, CropLife America senior director of environmental policy, said he is “optimistic about the program” and says it is a way for companies to be recognized for work already being done to reduce drift.

“There has been a great deal of scientific investigation directed at understanding what factors are most influential in the off-target movement of spray applications, and many manufacturers are incorporating this knowledge to innovations in spray application technology that will minimize drift potential,” Leggett said in an email to *Agri-Pulse.* “The DRT program provides a means of recognizing the benefit from adoption of those technologies. It is an important milestone for EPA, and we hope that it will continue to evolve and

improve as the program matures."

American Retailers Association President and CEO Daren Coppock said the goal of this program is a one shared by ARA's members.

"EPA's Drift Reduction proposal has evolved and improved greatly from its beginning, and off-target spray drift is certainly something that our members want to prevent as much as possible," Coppock said in an email to *Agri-Pulse.* "Crop protection products perform an essential role in environmentally responsible food production, and our industry is always working to improve how we use them."

Coppock said "it will be interesting to see how EPA uses (DRT) in label negotiations with registrants." Although the voluntary program is meant to advise applicators of the safest products to avoid drift, Coppock said "the primary burden of complying with label requirements that are added because of DRT will fall directly on applicators."

ARA is hopeful the program will be able to analyze many products in each category. For instance, if the EPA gives a four-star rating to one brand of spray nozzle but fails to properly analyze and announce ratings for other brands, it could put those without a rating at a competitive disadvantage.

Drift occurs in virtually every pesticide application, according to the Clemson University Cooperative Extension service. The degree to which drift occurs depends on factors such as "the formulation of the material applied, how the material is applied, the volume used, prevailing weather conditions at the time of application, and the size of the application job," the service said on its website.

EPA says it hopes the program will "move the agricultural sector toward the widespread use of low-drift technologies" and that stars could appear on pesticide labels as early as fall 2015. Before ratings can be placed on labels, EPA needs to collect and analyze company data, assign a rating for those products, and inform the company of the rating so product packaging can be changed.

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Newsroom

News Releases By Date

EPA Proposes to Remove 72 Chemicals from Approved Pesticide Inert Ingredient List

Release Date: 10/23/2014
Contact Information: Cathy Milbourn Milbourn.cathy@epa.gov 202-564- 4355 202-564-4355

WASHINGTON - The U.S. Environmental Protection Agency (EPA) is requesting public comment on a proposal to remove 72 chemicals from its list of substances approved for use as inert ingredients in pesticide products.

“We are taking action to ensure that these ingredients are not added to any pesticide products unless they have been fully vetted by EPA,” said Jim Jones, Assistant Administrator for the Office of Chemical Safety and Pollution Prevention. “This is the first major step in our strategy to reduce risks from pesticides containing potentially hazardous inert ingredients.”

EPA is taking this action in response to petitions by the Center for Environmental Health, Beyond Pesticides, Physicians for Social Responsibility and others. These groups asked the agency to issue a rule requiring disclosure of 371 inert ingredients found in pesticide products. EPA developed an alternative strategy designed to reduce the risks posed by hazardous inert ingredients in pesticide products more effectively than by disclosure rulemaking. EPA outlined its strategy in a May 22, 2014 letter: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2014-0558-0003 to the petitioners.

Many of the 72 inert ingredients targeted for removal, are on the list of 371 inert ingredients identified by the petitioners as hazardous. The 72 chemicals are not currently being used as inert ingredients in any pesticide product. Chemicals such as, turpentine oil and nitrous oxide are listed as candidates for removal.

Most pesticide products contain a mixture of different ingredients. Ingredients that are directly responsible for controlling pests such as insects or weeds are called active ingredients. An inert ingredient is any substance that is intentionally included in a pesticide that is not an active ingredient.

For the list of 72 chemical substances and to receive information on how to provide comments, see the Federal Register Notice in docket # EPA-HQ-OPP-2014-0558. To access this notice, copy and paste the docket number into the search box at: http://regulations.gov. Comments are due November 21, 2014.

General information on inert ingredients can be found at: http://www2.epa.gov/pesticide-registration/inert-ingredients-overview-and-guidance.

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10/23/2014 EPA Invites Communities to Apply for Assistance to Build Resilience, Pursue Revitalization
10/23/2014 EPA Proposes to Remove 72 Chemicals from Approved Pesticide Inert Ingredient List
10/23/2014 FRIDAY: EPA Administrator to Give Keynote Address at Georgetown University Conference on Energy and the Environment

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National Water-Quality Assessment Program

An Overview Comparing Results from Two Decades of Monitoring for Pesticides in the Nation's Streams and Rivers, 1992–2001 and 2002–2011

Scientific Investigations Report 2014–5154

U.S. Department of the Interior
U.S. Geological Survey

An Overview Comparing Results from Two Decades of Monitoring for Pesticides in the Nation's Streams and Rivers, 1992–2001 and 2002–2011

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U.S. Department of the Interior
U.S. Geological Survey

U.S. Department of the Interior
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U.S. Geological Survey
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Conversion Factors and Abbreviations

SI to Inch/Pound

Multiply	By	To obtain
	Area	
square kilometer (km^2)	247.1	acre
square kilometer (km^2)	0.3861	square mile (mi^2)

Water year is the 12-month period of October 1, for any given year through September 30, of the following year. The water year is designated by the calendar year in which it ends and which includes 9 of the 12 months.

Abbreviations used in this report

ALB	Aquatic Life Benchmark
GCMS	gas chromatography/mass spectrometry
HHB	Human Health Benchmark
NASQAN	National Stream Quality Accounting Network
NAWQA	National Water-Quality Assessment
NLCD	National Land Cover Data
NLCD06	National Land Cover Data 2006
NLCDe	National Land Cover Data enhanced
NWQL	National Water Quality Laboratory
USGS	U.S. Geological Survey

An Overview Comparing Results from Two Decades of Monitoring for Pesticides in the Nation's Streams and Rivers, 1992–2001 and 2002–2011

By Wesley W. Stone, Robert J. Gilliom, and Jeffrey D. Martin

Abstract

This report provides an overview of the U.S. Geological Survey National Water-Quality Assessment program and National Stream Quality Accounting Network findings for pesticide occurrence in U.S. streams and rivers during 2002–11 and compares them to findings for the previous decade (1992–2001). In addition, pesticide stream concentrations were compared to Human Health Benchmarks (HHBs) and chronic Aquatic Life Benchmarks (ALBs). The comparisons between the decades were intended to be simple and descriptive. Trends over time are being evaluated separately in a series of studies involving rigorous trend analysis. During both decades, one or more pesticides or pesticide degradates were detected more than 90 percent of the time in streams across all types of land uses. For individual pesticides during 2002–11, atrazine (and degradate, deethylatrazine), carbaryl, fipronil (and degradates), metolachlor, prometon, and simazine were detected in streams more than 50 percent of the time. In contrast, alachlor, chlorpyrifos, cyanazine, diazinon, EPTC, Dacthal, and tebuthiuron were detected less frequently in streams during the second decade than during the first decade. During 2002–11, only one stream had an annual mean pesticide concentration that exceeded an HHB. In contrast, 17 percent of agriculture land-use streams and one mixed land-use stream had annual mean pesticide concentrations that exceeded HHBs during 1992–2001. The difference between the first and second decades in terms of percent of streams exceeding HHBs was attributed to regulatory changes. During 2002–11, nearly two-thirds of agriculture land-use streams and nearly one-half of mixed land-use streams exceeded chronic ALBs. For urban land use, 90 percent of the streams exceeded a chronic ALB. Fipronil, metolachlor, malathion, cis-permethrin, and dichlorvos exceeded chronic ALBs for more than 10 percent of the streams. For agriculture and mixed land-use streams, the overall percent of streams that exceeded a chronic ALB was very similar between the decades. For urban land-use streams, the percent of streams exceeding a chronic ALB during 2002–11 nearly doubled that seen during 1992–2001. The reason for this difference was the inclusion of fipronil monitoring during the second decade. Across all land-use streams, the percent of streams exceeding a chronic ALB for fipronil during 2002–11 was greater than all other insecticides during both decades. The percent of streams exceeding a chronic ALB for metolachlor, chlorpyrifos, diazinon, malathion, and carbaryl decreased from the first decade to the second decade. The results of the 2002–11 summary and comparison to 1992–2001 are consistent with the results from more rigorous trend analysis of pesticide stream concentrations for individual streams in various regions of the U.S.

Introduction

The U.S. Geological Survey (USGS) National Water-Quality Assessment (NAWQA) and National Stream Quality Accounting Network (NASQAN) are monitoring programs that collect and report data for national assessments of pesticide concentrations in the Nation's streams and rivers. Gilliom and others (2006) reported findings for the first decade (1992–2001) of the NAWQA program and found that pesticides or their degradates were present in one or more water samples from every stream included in the assessment; one or more pesticides were detected more than 90 percent of the time in agricultural, urban, and mixed land-use streams; and the most frequently detected pesticides also had the greatest use.

This report builds upon the 1992–2001 assessment of pesticides in the Nation's streams (Gilliom and others, 2006) by summarizing pesticide occurrence in streams during the second decade (2002–11) of NAWQA stream monitoring, including pesticide stream concentration data from the NASQAN program, and providing descriptive comparisons between the two decades of pesticide monitoring. Gilliom and others (2006) assessed the occurrence of 83 pesticides and degradates from 186 stream sites that represented agriculture, urban, mixed, and undeveloped land uses during 1992–2001.

Changes in the NAWQA program between the first and second decades reduced the number of monitored stream sites. The sampling design (number of samples to be collected and when they were to be collected) also changed between the decades. Specifically, the 1992–2001 sampling design was a mix of fixed-frequency sampling and high-flow sampling (to characterize times of expected higher stream pesticide concentrations); however, the 2002–11 sampling design was fixed-frequency with minimal high-flow sampling efforts. In addition, the number of pesticides and degradates that were monitored in streams sufficient for a national assessment nearly doubled during the second decade.

The changes in the NAWQA pesticide stream monitoring program from the first to second decade made it difficult to do simple, stream site to stream site comparisons between the decades and compare directly to the assessment by Gilliom and others (2006). In addition, this assessment differs from the previous assessment by Gilliom and others (2006) because (1) Human Health Benchmarks (HHBs) and chronic Aquatic Life Benchmarks (ALBs) have been updated; (2) some pesticides assessed during 1992–2001 were not sampled at enough sites to attain a reasonable national distribution during 2002–11; (3) land use ancillary data used to group sites have changed over time; (4) the stream-site selection process was revised; and (5) this assessment includes multiple years of data for sites, when available. The inclusion of multiple years of concentration data rather than a single year in the assessment, as was done by Gilliom and others (2006), was evaluated in terms of occurrence and percent of stream sites exceeding an HHB or chronic ALB for 1992–2001. The occurrence of pesticides in streams and the percent of stream sites that exceeded an HHB or chronic ALB for a single year compared to multiple years were all within 10 percent of each other for 1992–2001. Overall, the 1992–2001 results in this report are not markedly different than those reported by Gilliom and others (2006) except in cases where an ALB has been more recently established. For example, an ALB for metolachlor or *S*-metolachlor did not exist when Gilliom and others (2006) completed the initial assessment for 1992–2001; however, ALBs for *S*-metolachlor have been established and are used in this assessment. This report uses the most current HHBs and chronic ALBs for assessment of annual pesticide stream concentrations. Acute ALBs were not used in the comparisons between decades because the differences in sampling designs between them would likely bias the comparisons.

Purpose and Scope

The purpose of this report is to summarize pesticide occurrence in U.S. streams and rivers during 2002–11 in comparison to the previous decade, 1992–2001. This overview focuses on pesticide occurrence (percent of time detected) and pesticide concentrations in relation to HHBs and chronic ALBs. Although pesticide occurrence is compared between the decades for perspective, the comparisons are simple and descriptive, and are not meant as a rigorous trend analysis. Trends are being evaluated separately in a series of studies involving quantitative site-based trend models, including Corn-Belt streams (Sullivan and others, 2009) and urban streams (Ryberg and others, 2010).

Pesticide Monitoring Design

The national design for monitoring pesticides in streams and rivers has evolved from the combination of two USGS programs, NAWQA and NASQAN. NAWQA stream monitoring during 1992–2001 focused on assessing water-quality conditions in 51 of the Nation's river basins, referred to as "Study Units," on a rotational schedule—20 Study Units during 1992–95, 16 during 1996–98, and 15 during 1998–2001 (Gilliom and others, 2006). Pesticide samples generally were collected at each stream site by using a combination of fixed-frequency and high-flow sampling (Gilliom and others, 1995). Fixed-frequency sampling means that a given number of water-quality samples were allocated to each month (more samples for months with expected higher potential for pesticide runoff and fewer samples during months of lower expected potential for pesticide runoff), and the water samples were collected at regularly spaced intervals within each month. High-flow sampling was used to allocate additional water samples to characterize high-flow events during seasonal periods of high pesticide use and potential runoff. Changes to the design of the NAWQA program during 2002–2011 included reduction in the number of long-term stream-monitoring sites, an increased emphasis on regional assessments, and supplemental high-flow sampling was limited to special regional studies.

The NASQAN program was redesigned in 1995 to estimate the mass flux of pesticides and other constituents at 41 monitoring sites in four large river systems: the Mississippi, the Rio Grande, the Columbia, and the Colorado. Similar to the NAWQA program, water samples generally were collected at each stream site by using a combination of fixed-frequency and high-flow sampling (Hooper and others, 2001). Also similar to the NAWQA program, the frequency of water-quality sampling typically changed seasonally, with more frequent samples during the peak pesticide-runoff months. The NASQAN sampling strategy was revised in 2000 (U.S. Geological Survey, 2010), with reduced monitoring in the Columbia and Colorado River Basins.

Methods

This report summarizes pesticide stream concentration data from samples collected during 2002–11 and compares the results to findings from 1992–2001. Site selection was based on the number of years with data, watershed size, and frequency of sampling within each year. For a sampling site, all years of sampling that met the minimum sampling criteria were included in the summaries. The summaries for

both decades are based on the estimated amount of time a pesticide was detectable at a stream site and the number of times HHBs and chronic ALBs were exceeded. For summary purposes, sampling sites were grouped by dominant land-use classification.

Pesticides

During any given year more than 400 different pesticides are used in agricultural settings (Stone, 2013). The large number of pesticides in use and the phasing out and introduction of new pesticides make it not possible to monitor all pesticides because of budget and method constraints. This report includes a selected subset of pesticides in use over the last two decades that were sampled at enough sites to attain a reasonable national distribution during 2002–11.

Pesticides included in this report are listed in appendix 1 (table 1–1). Martin (2009) determined that only pesticide data from a single laboratory and analytical method were sufficiently extensive in time and space for a national assessment across decades. Hence, only pesticides and pesticide data that were analyzed at the National Water-Quality Laboratory (NWQL) by a gas chromatography/mass spectrometry (GCMS) method were included in this report. The NAWQA and NASQAN programs periodically evaluate the full range of pesticides in use to prioritize monitoring to include the most important ones in relation to ecosystem and human health (Norman and others, 2012). This prioritization process also evaluates the likelihood that a pesticide will be found in surface water or sediment, based on chemical properties. During 2002–11, there were 123 pesticides and pesticide degradates with sufficient stream concentration data to include in this assessment. Gilliom and others (2006) included 83 pesticides in their assessment of 1992–2001; however, only 47 of these pesticides were sampled at enough sites during 2002–11 for a national-level comparison between the decades. The difference between the 47 pesticides assessed during the first decade and the 123 pesticides assessed during the second decade included 39 (or 51 percent) pesticide degradates; 21 (or 28 percent) insecticides; 8 (or 11 percent) fungicides; and the remaining were herbicides, nematicides, plant growth regulators, and defoliants.

Figure 1 shows an overview by one measure—amount used—of how pesticides included in this report relate to total national use and to selected pesticides or groups not included. A large portion of the difference between national total herbicide use and the proportion included in this report was the result of increased use of glyphosate that came with the rapid adoption of genetically modified crops resistant to glyphosate, beginning in the mid-1990s. Glyphosate is difficult and costly to measure, and efforts to assess glyphosate have been limited primarily to local or short-term studies. Other types of pesticides not comprehensively included in this report, such as fungicides and neonicotinoid insecticides, are not individually as prominent as glyphosate in terms of amounts applied, but may be environmentally important because of their greater toxicity. Finally, some hydrophobic pesticides, such as legacy organochlorines and pyrethroid insecticides, are important as contaminants of sediment and (or) tissues, but are not often found in filtered-water samples.

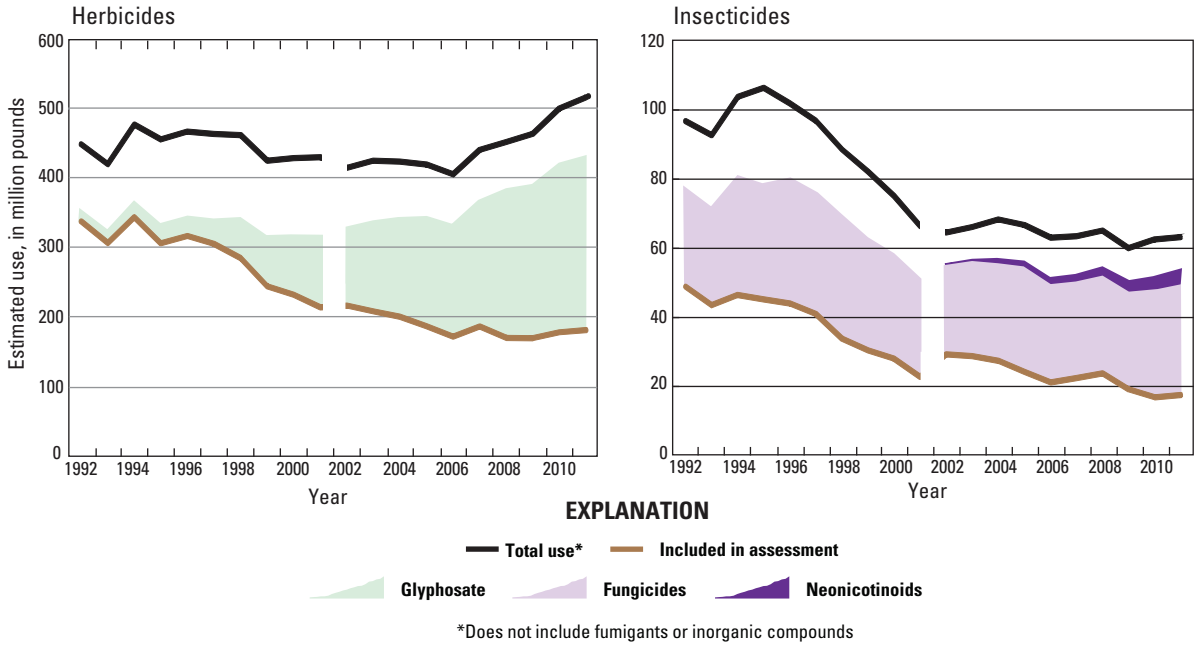

Figure 1. Estimated agricultural use of synthetic organic herbicides, insecticides, and fungicides in the conterminous U.S. during first (1992–2001) and second (2002–11) decades of stream monitoring. (GfK Kynetec, Inc., proprietary data, written commun., December 2011 and July 2013).

Stream-Site Selection

Stream-site selection was based on total number of samples each year, watershed size, and the number of samples during potentially high pesticide runoff months. A year was defined as the water year, beginning October 1 and ending September 30. Stream-site selection was based on modification of the criteria used in Stone and others (2013). The stream-site selection process began with an evaluation of the number of samples collected for the water year compared to minimums based on watershed size (table 1). Stream sites retained from the previous step were then evaluated to make sure there was at least one sample during the months of May, June, and July. These three months are typically the months of expected higher transport of pesticides to streams for the most heavily used pesticides (Stone and others, 2013). Stream sites retained to this point were then evaluated to ensure that samples were present during times when pesticides are less likely transported to streams in order to better represent their occurrence during the entire water year. Specifically, each stream site could not have a consecutive 3-month period without a sample. The stream-site selection process was done by individual pesticide because changing analysis schedules over time caused variations in sample numbers between pesticides for some years. The stream-site selection process also did not limit the selection to a single year; all years of sampling at a stream site that met the selection criteria were included in this summary. Stream sites selected for the summary are shown in figure 2 and listed in appendix 1 (table 1–2).

Table 1. Minimum samples, per water year, by watershed size.

[km^2, square kilometer; water year, the 12-month period of October 1, for any given year through September 30, of the following year. The water year is designated by the calendar year in which it ends and which includes 9 of the 12 months]

Watershed size (km^2)	Minimum number of samples
Less than 500	16
500 to 4,999	12
5,000 to 50,000	10
Greater than 50,000	8

Detection Frequency and Concentration Statistics

Time-weighted detection frequencies account for the more frequent sample collection during some months than in other months and provide an estimate of the percentage of time (throughout the water year) that a pesticide was detected. The weights were calculated as the amount of time extending from one-half the time interval between an observation and the preceding observation and one-half the time interval extending from the observation to the subsequent observation, divided by the total time in one year. Sample weights for a pesticide at a stream site sum to one for each year; therefore, the sum of the weights for samples with detections represent the percentage of time that pesticide was detected for that stream site and year. When there were multiple water years for a stream site and pesticide, the median percentage of time detected across the years was used for that stream site and pesticide. Both the mean and median were evaluated for sites and pesticides with multiple water years of data, and there was not a large difference between the two statistics for the sites and pesticides used in this summary.

Annual concentration statistics were calculated for each stream site and pesticide for comparison to HHBs (Toccalino and others, 2014) and chronic ALBs (U.S. Environmental Protection Agency Office of Pesticide Program, *http://www.epa.gov/oppefed1/ecorisk_ders/aquatic_life_benchmark.htm*, accessed July 2013). Specifically, the annual mean concentration for comparison to HHBs, the annual maximum 21-day moving-average concentration for comparison to the chronic invertebrate ALBs, and the annual maximum 60-day moving-average concentration for comparison to chronic fish and chronic aquatic community (atrazine) ALBs were calculated for this comparison.

Annual mean pesticide concentrations were calculated following the methods described in Larson and others (2004). Specifically, each observed concentration was weighted according to the amount of time it was used to represent the pesticide concentration in the stream. The weights were calculated as the amount of time extending from one-half the time interval between an observation and the preceding observation and one-half the time interval extending from the observation to the subsequent observation, divided by the total time in 1 year. Censored observations complicate the calculation of annual mean concentrations. As described in Larson and others (2004), if less than 10 percent of the weighted data for a site, pesticide, and year combination were censored, censored observations were replaced by one-half the censoring threshold reported by the laboratory. If more than 10 percent of the weighted data were censored, and there were at least 20 annual observations with at least 10 uncensored observations and at least 33 percent of the sample weights were represented by uncensored observations, then the log-regression method (Gilliom and Helsel, 1986; Helsel and Gilliom, 1986) was used to approximate the annual mean concentration. Otherwise, the annual mean concentration was considered to be censored at the censoring threshold reported by the laboratory. For stream sites and pesticides with multiple years of data, if an HHB was exceeded for a pesticide in any year during the first or second decade then the HHB was considered exceeded for that stream site and pesticide in the respective decade.

Annual maximum moving-average pesticide concentrations were calculated following the methods described in Stone and others (2008). Hourly pesticide concentrations were estimated for each stream site through linear interpolation of actual observations. Censored observations were assigned a value of zero for the process of linear interpolation. The hourly concentration estimates were averaged to obtain an

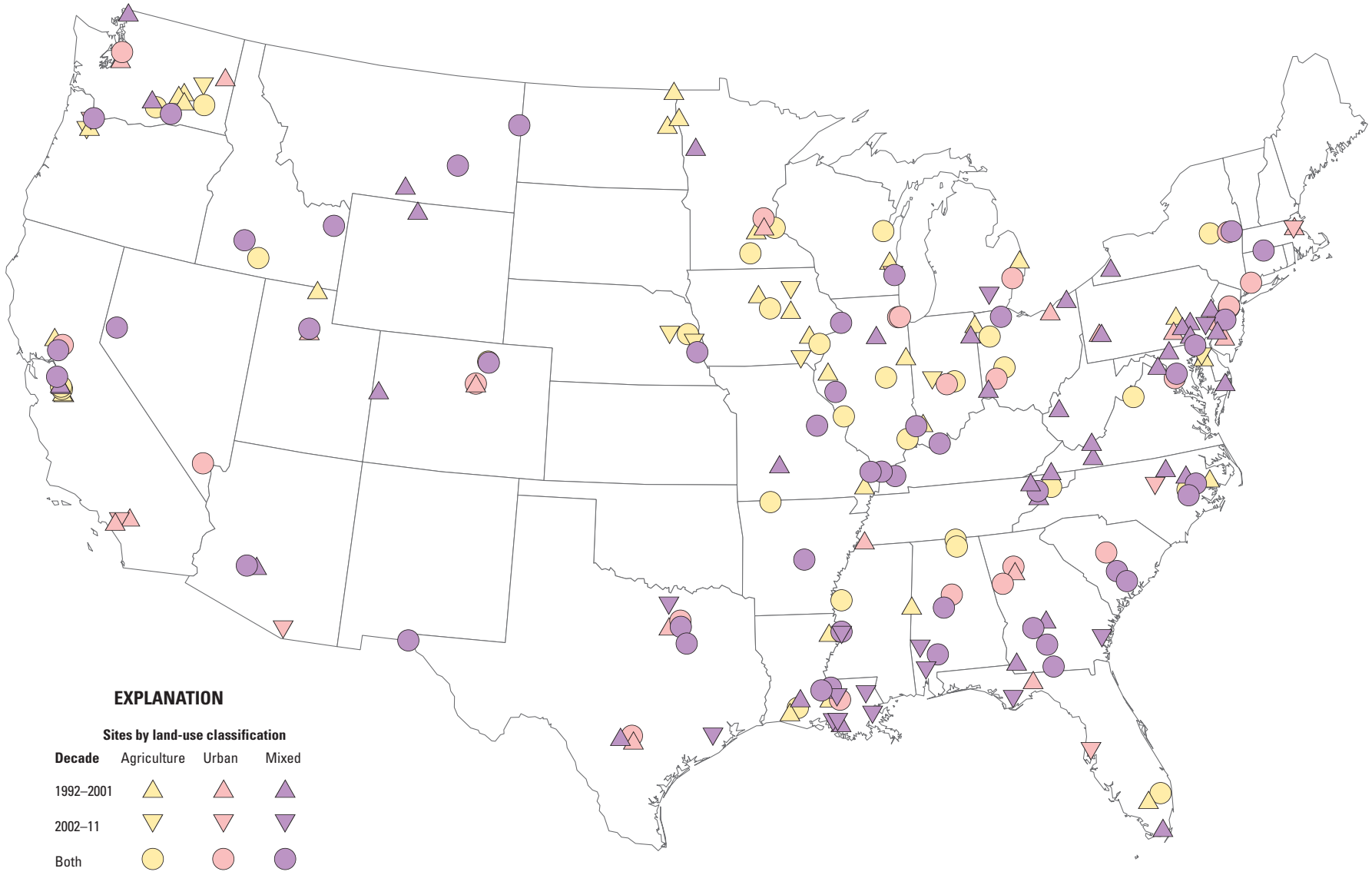

Figure 2. The national monitoring network for pesticides in streams and rivers included 182 sites during 1992–2001 and 125 sites during 2002–11, with 96 of the sites common to both decades.

estimated daily concentration. The hourly estimates facilitated computations for days with multiple samples but were not used for other purposes. Moving-average concentrations for the selected durations (21 and 60 days) were computed for each day. The annual maximum moving-average pesticide concentrations for each duration were then determined for each stream site/year combination meeting the selection criteria. In most cases, insufficient observations were available for stream sites to calculate moving-average concentrations (21- or 60-day durations) for the beginning of the selected year used in the summary. For example, if the selected year for a stream site was 1993, and there were no observations available prior to that year. To address this issue and estimate moving-average concentrations for the beginning of the selected year, the actual observations for the selected year for that stream site and pesticide were used as surrogate observations for the prior year. For stream sites and pesticides with multiple years of data, if a chronic ALB was exceeded for a pesticide in any year during the first or second decade then the chronic ALB was considered exceeded for that stream site and pesticide in the respective decade.

For discussion and illustration purposes, the percentage of time pesticides were detected in streams and percent of streams exceeding an HHB or chronic ALB were grouped by land-use classification, which is discussed in the subsequent section. The percentage of time a pesticide was detected in a stream for a land-use classification was normalized by the number of stream sites within that land-use classification to avoid one stream site having more influence than another in the summary.

Land-Use Classifications

The summaries and comparisons in this report group streams into three land-use classifications: agriculture, urban, and mixed. The land-use classifications and watershed land-use criteria are similar to those used in Gilliom and others (2006), with two modifications. First, the 2006 National Land Cover Data (NLCD06) was used to classify streams based on land use instead of the 1992 enhanced NLCD (NLCDe). Second, the amount of urban land use allowable in a watershed for the agriculture stream classification was increased from 5 to 10 percent because of the differences in methodology between NLCDe and NLCD06. In addition, Gilliom and others (2006) included streams with a land-use classification of undeveloped; however, this summary does not include streams with this land-use classification. The land-use classifications and watershed land-use criteria are shown in table 2. For some streams (fewer than 5 percent), the area within the watershed that contributed the majority of water to the stream was not reflective of the land use for the total watershed area. Differences between the total watershed area and the area contributing the majority of water to a stream can be caused by natural landscape variations and water-management practices. In these cases, the land-use classification for the stream was changed to reflect the land use for the area contributing the majority of water to the stream. The land-use classifications for each stream are shown in figure 2 and listed in appendix 1 (table 1–2). The number of stream sites by land-use classification is shown in table 3.

Table 2. Land-use classifications and watershed land-use criteria.

Land-use classification	Watershed land-use criteria
Agriculture	Greater than 50 percent agricultural land and less than or equal to 10 percent urban land
Urban	Greater than 25 percent urban land and less than or equal to 25 percent agricultural land
Undeveloped	Less than or equal to 5 percent urban land and less than or equal to 25 percent agriculture land
Mixed	All other combinations of agriculture, urban, and undeveloped land use

Table 3. Number of stream sites by land-use classification.

Land-use classification	Number of stream sites 1992–2001	Number of stream sites 2002–11	Number of common stream sites
Agriculture	59	36	28
Mixed	83	59	45
Urban	40	30	23
Total	182	125	96

Pesticide Occurrence

One or more pesticides or pesticide degradates were detectable more than 90 percent of the time in streams across all land uses during 2001–11 (table 4). As mentioned previously, the data from this second decade included analysis of nearly twice as many pesticides and pesticide degradates than the first decade; however, the overall percent of time they were detected in streams was nearly the same for both decades (table 4). Variations in percent of time pesticides and pesticide degradates were detected in streams was more evident for individual compounds.

Table 4. Percent of time one or more pesticides or pesticide degradates were detected in streams, by land-use classification.

Land-use classification	Percent of time detected for 1992–2001	Percent of time detected for 2002–11
Agriculture	98	95
Mixed	96	96
Urban	98	99

Figure 3 shows the percent of time individual compounds were detected in streams. For illustration purposes, only the top 20 most frequently detected pesticides and degradates by land-use classification and decade are shown. The top 20 most frequently detected are a composite of the top 10 most frequently detected from each land use/decade combination. Across all land-use classifications, the herbicides atrazine, deethylatrazine (atrazine degradate), metolachlor, and simazine were detected more than 50 percent of the time in streams during 2002–11 (fig. 3). The herbicide prometon was detected more than 50 percent of the time in mixed and urban land-use classification streams during 2002–11. The insecticides fipronil, fipronil sulfide (degradate), and carbaryl, were detected more than 50 percent of the time in urban land-use classification streams during 2002–11.

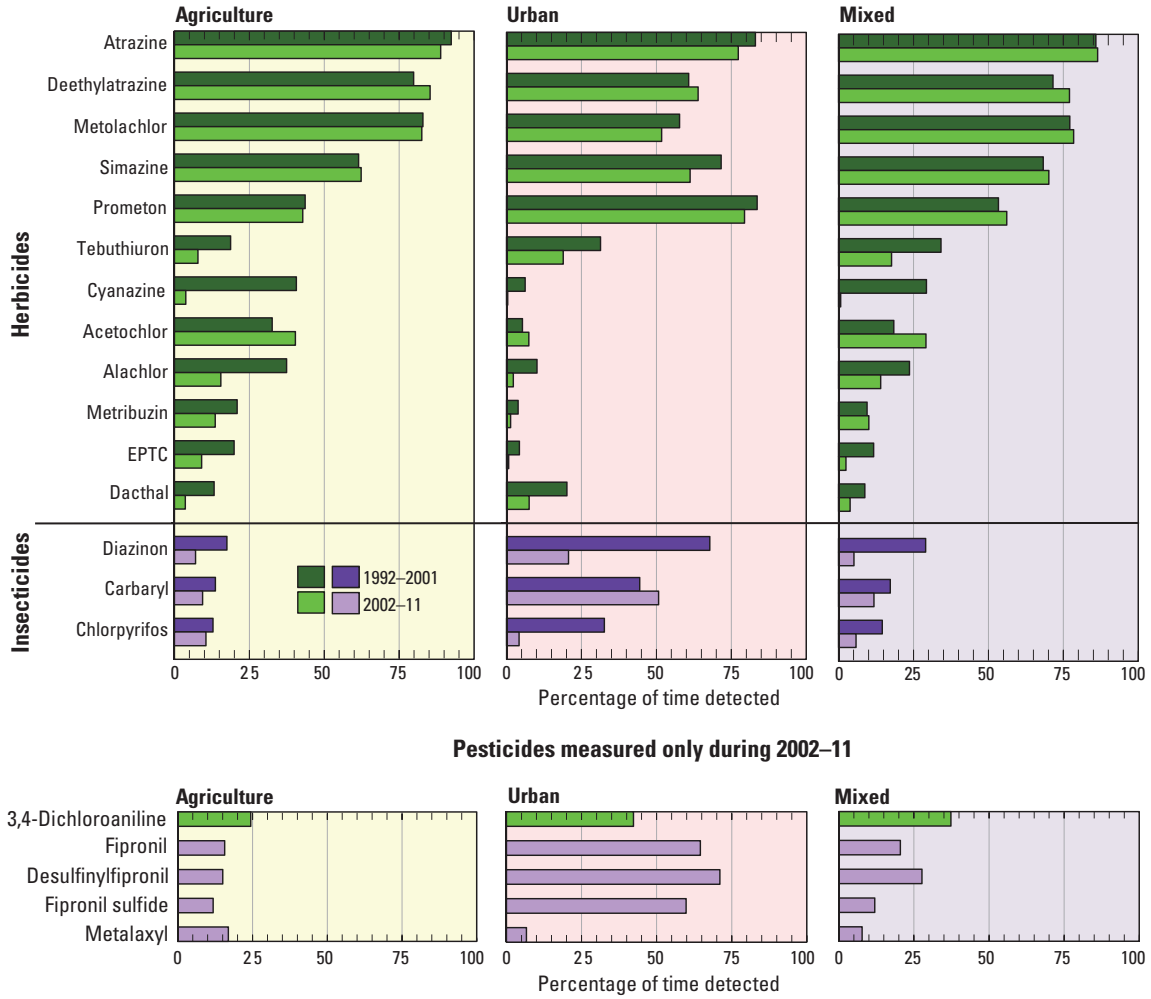

Figure 3. Percentage of time during a year that the most frequently detected pesticides were detected in streams and rivers in relation to land-use classification.

The herbicides alachlor, cyanazine, EPTC, Dacthal, and tebuthiuron were detected less frequently in streams (more than 10 percent change) during the second decade than during the first decade. Sullivan and others (2009) found generally decreasing stream concentration trends for alachlor, cyanazine, and EPTC at individual stream sites within the Corn Belt. The decrease in the amount of time these pesticides were detected in streams between decades may reflect use changes from pesticide-registration cancellations and increased use of other herbicides. For example, cyanazine registration was voluntarily cancelled in the mid-1990s, which was followed by a rapid decline in cyanazine use. Alachlor use steadily declined after the introduction of acetochlor in the mid-1990s, which was an expected result following the registration of acetochlor (de Guzman and others, 2005). In addition, the introduction of genetically modified crops that are resistant to the herbicide, glyphosate, has seen rapid adoption over the course of the last two decades with a corresponding decrease in other herbicides over the same time period (fig. 1).

The organophosphate insecticides chlorpyrifos and diazinon were detected less frequently in streams (more than 10 percent change) during the second decade than during the first decade (fig. 3). Sullivan and others (2009) and Ryberg and others (2010) found generally decreasing stream concentration trends for these two pesticides at individual stream sites in agricultural and urban land-use areas, respectively. The change in detection frequency between the two decades for these pesticides reflects registration changes and changes in pesticide-use patterns. Various uses of chlorpyrifos and diazinon, primarily residential, began being voluntarily cancelled during the late-1990s, and these regulatory changes continued into the early-2000s. In addition, fipronil was first registered for use in the United States in 1996 (Jackson and others, 2009) and was suggested as an alternative to organophosphate insecticides for residential and commercial turf applications during the early-2000s (U.S. Environmental Protection Agency, 2001).

Fipronil was detected in streams across all land-use classifications from 17 to 63 percent of the time during 2002–11 (fig. 3); however, fipronil was not included in the NAWQA and NASQAN efforts during 1992–2001 because it was not registered for use until 1996. Ryberg and others (2010) found a preponderance of increasing fipronil stream concentration trends for urban land-use streams from 2000 to 2008.

An important consideration when comparing detection frequencies over time is the possible impacts of analysis instrument changes. The assumption is that improvements in laboratory instrumentation could result in increased detection sensitivity over time. Alternatively, changes in instrumentation over time could possibly result in decreased sensitivity over time. Ryberg and others (2010) evaluated detections of trace concentrations in duplicate quality-control water samples collected from 1994 to 2005. They found that for most of the pesticides evaluated, improvements to instrumentation did not result in changes to detection sensitivities through time. However, instrumentation improvements did increase the detection sensitivity for tebuthiuron and carbaryl (Ryberg and others, 2010). As discussed previously, the amount of time tebuthiuron was detected in streams decreased from the first to the second decade (fig. 3); therefore, improvements to instrumentation was not a factor for this pesticide. For carbaryl, the differences in detection frequency between the first and second decades were less than 10 percent in all land-use classifications.

Concentrations And Benchmark Comparisons

Annual mean pesticide concentrations in streams were compared to HHBs to provide perspective; however, these comparisons are not appropriate for assessing compliance with drinking-water regulations, which are applied to treated water. The pesticide stream concentrations used in this report represent untreated water from sites that are not located at drinking-water intakes.

During 2002–11, one agriculture land-use stream had an annual mean pesticide concentration that exceeded an HHB (atrazine), and no urban or mixed land-use streams had annual mean pesticide concentrations that exceeded HHBs. In contrast, 17 percent of the agriculture land-use streams and 5 percent of mixed land-use streams exceeded HHBs during 1992–2001. During the previous decade, alpha-HCH (lindane), atrazine, cyanazine, molinate, dieldrin, and propargite annual mean concentrations exceeded HHBs in 10 agriculture and 4 mixed land-use streams. The differences in the percent of streams exceeding an HHB between the first and second decade are related to regulatory and use changes. Throughout the last three decades, various lindane uses were voluntarily cancelled by registrants; the last remaining uses were cancelled in 2006. Sullivan and others (2009) found downward trends in atrazine concentrations measured in agriculture streams of the Corn Belt. As mentioned previously, cyanazine registration was voluntarily cancelled in the mid-1990s, and cyanazine use sharply declined from the first to the second decade. During the early-2000s, molinate registration was voluntarily cancelled, and use sharply declined during 2002–11. Dieldrin registration was voluntarily cancelled during the late-1980s, and certain uses of propargite were voluntarily cancelled during the mid-1990s.

Pesticide concentrations in streams were compared to chronic ALBs. Acute ALBs were not used because the sampling frequencies do not adequately represent the highest concentrations that may be present in a stream during the year (Crawford, 2004). In addition, differences in sampling designs between the two decades limit comparisons between the decades based on the highest concentrations measured in streams. Specifically, sampling during the first decade included samples targeting high-flow events during the season when pesticides were expected to be transported to streams,

while sampling during the second decade maintained a fixed-frequency sampling design. Therefore, comparison of the highest pesticide stream concentrations between the two decades would be biased.

During 2002–11, nearly two-thirds of agriculture land-use classification streams and nearly one-half of mixed land-use classification streams exceeded a chronic ALB (table 5). For urban land-use classification streams, 90 percent exceeded a chronic ALB. The insecticide fipronil exceeded chronic ALBs for more than 20 percent of the streams across all land-use classifications (fig. 4). The herbicide metolachlor (chronic ALB for *S*-metolachlor) exceeded chronic ALBs for more than 10 percent of agriculture and mixed land-use streams. Similarly, the insecticide malathion exceeded chronic ALBs for more than 10 percent of agriculture and urban land-use streams. The insecticides cis-permethrin (chronic ALB for permethrin) and dichlorvos exceeded chronic ALBs for more than 10 percent of mixed and urban land-use streams, respectively.

Overall, the percent of streams with pesticides that exceeded a chronic ALB was very similar between the two decades for the agriculture and mixed land-use groups (table 5). In terms of pesticides that were evaluated during both decades, the percent of urban land-use streams that exceeded a chronic ALB during the second decade was about the same as that for the first decade. However the inclusion of fipronil and dichlorvos during the second decade nearly doubled the percent of urban land-use streams that exceeded a chronic ALB during the second decade in comparison to the first decade (table 5; fig. 4).

During 2002–11, there were 21 pesticides that exceeded chronic ALBs compared to 16 that exceeded chronic ALBs during 1992–2001. Figure 4 shows a subset of the pesticides that had annual concentration statistics that exceeded a chronic ALB (pesticides and degradates that exceeded a chronic ALB for more than 5 percent of the stream sites, by pesticide and land-use classification). The second decade had a lower percent of streams exceeding a chronic ALB for the herbicide metolachlor than the first decade for all land-use classifications. For the agriculture land-use streams, this difference was greater than 10 percent. During the last part of the first decade

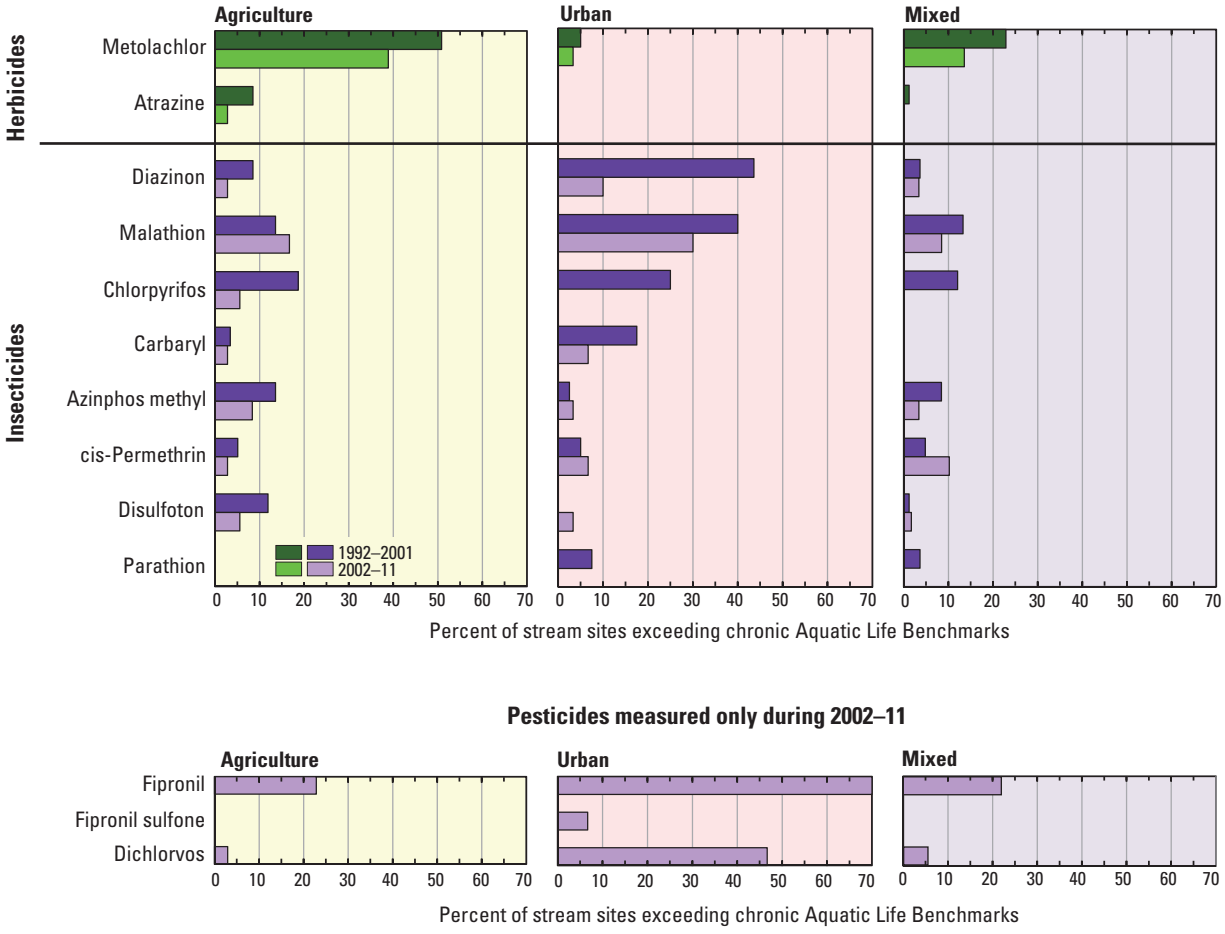

Figure 4. Pesticides that exceeded chronic Aquatic Life Benchmarks at more than 5 percent of stream sites and percent of streams by land-use classification.

Table 5. Percent of streams with one or more pesticide concentration statistics that exceeded a chronic Aquatic Life Benchmark (ALB), by land-use classification.

Land-use classification	Percent of streams exceeding ALB 1992–2001	Percent of streams exceeding ALB 2002–11
Agriculture	69	61
Mixed	45	46
Urban	53	90

replaced by the resolved isomer *S*-metolachlor, which reduces the amount of pesticide required for the same agronomic effect (Hartzler, 2000). Although metolachlor was detected in streams for nearly the same amount of time for both decades (fig. 3), the decreased use (in terms of mass applied) because of the introduction of *S*-metolachlor likely contributed to the decrease in the percent of streams that exceeded a chronic ALB during 2002–11 when compared to 1992–2001.

For streams in the urban land-use classification group, the organophosphate insecticides chlorpyrifos, diazinon, and malathion, and the carbamate insecticide carbaryl all had decreases (greater than 10 percent) in the percent of streams exceeding a chronic ALB from the first decade to the second decade (fig. 4). This is consistent with the decreasing stream concentration trends found by Ryberg and others (2010) for chlorpyrifos and diazinon in individual urban land-use streams. These pesticides also were detected less frequently in streams during 1992–2001 compared to 2002–11 (fig. 3). In contrast, the percent of streams, across all land-use classifications, exceeding a chronic ALB for fipronil during the second decade was greater than all other insecticides during both decades. As discussed previously, fipronil registration and use began toward the end of the first decade and was a suggested alternative for organophosphate insecticides during the second decade.

Summary

This report provides an overview of U.S. Geological Survey National Water-Quality Assessment (NAWQA) and National Stream Quality Accounting Network (NASQAN) findings for pesticide occurrence (percent of time pesticides were detected) in U.S. streams during 2002–11 and compares them to findings during 1992–2001. In addition, pesticide stream concentrations are compared to Human Health Benchmark (HHBs) and chronic Aquatic Life Benchmark (ALBs) and differences between the decades discussed.

Direct and simple, one to one comparisons of pesticides in stream water between the two decades are not possible because of changes in stream sampling sites, sampling designs, and pesticides monitored within the programs over the last two decades. The comparisons in this report are from a site selection and land-use classification based on 2002–11 information that is applied to evaluate results for the 1992–2001 sites. In addition, the most current chronic ALBs are used in comparison to annual concentration statistics.

During 2002–11, atrazine, deethylatrazine (atrazine degradate), carbaryl, fipronil, fipronil sulfide (fipronil degradate), metolachlor, prometon, and simazine were detected more than 50 percent of the time in streams. One or more pesticides or pesticide degradates were detected more than 90 percent of the time in streams across all land uses during both decades. The overall amount of time pesticides were detected in streams was nearly the same between the first and second decades. However, there were differences between the two decades when comparing individual pesticides. The herbicides alachlor, cyanazine, EPTC, Dacthal, and tebuthiuron were detected less frequently in streams during 2002–11 than during 1992–2001. Regulatory changes and the increased use of acetochlor and glyphosate between the first decade and the second decade may be contributing to the decrease in the amount of time these pesticides were detected in streams. The organophosphate insecticides diazinon and chlorpyrifos were detected less frequently during 2002–11 than during 1992–2001. Product registration changes as well as the registration of the insecticide fipronil during the last part of the first decade may be contributing to the decrease in the amount of time these pesticides were detected in streams.

When stream concentration statistics were compared to HHBs, only one agriculture land-use stream had an annual mean pesticide concentration that exceeded an HHB (atrazine) during 2002–11. In contrast, during 1992–2001, about 17 percent of the agriculture land-use streams and one mixed land-use stream exceeded HHBs. The HHB exceedance difference between the first and second decades was the result of regulatory changes; specifically, cancellation of pesticide registration and subsequent decreased use.

During 2002–11, most agriculture and urban land-use classification streams and nearly one-half of mixed land-use classification streams had pesticide concentration statistics that exceeded a chronic ALB. The overall percent of streams that exceeded a chronic ALB was very similar between the two decades for agricultural and mixed land-use classification streams. However, for urban land-use classification streams the percent of streams exceeding a chronic ALB during 2002–11 nearly doubled that seen during 1992–2001. The inclusion of fipronil and dichlorvos monitoring during 2002–11 was the reason for this difference.

The summaries and comparisons between the two decades in this report were intended to be simple and descriptive overviews and not substitutes for more quantitative trend analysis that account for streamflow and other factors. Pesticide stream concentration trends at individual stream sites have been evaluated with more rigorous analysis methods for regions of the U.S. and selected time periods during these decades (Sullivan and others, 2009; Ryberg and others, 2010). Pesticide stream concentration trends using NAWQA and NASQAN results will continue to be evaluated in a series of studies involving quantitative site-based trend models.

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Appendix 1.

Table 1–1. Pesticide compounds used in the 1992–2001 and 2002–11 summaries.

[CASRN, Chemical Abstracts Service Registry Number®;—, not applicable]

Pesticide compound (synonym)	Type of pesticide compound (parent pesticide, if degradate)	CASRN[1]	Parameter code	1992–2001	2002–11
Acetochlor	Herbicide	34256-82-1	49260	Yes	Yes
Alachlor	Herbicide	15972-60-8	46342	Yes	Yes
2,6-Diethylaniline	Degradate (Alachlor)	579-66-8	82660	Yes	Yes
2-Chloro-2,6-diethylacetanilide	Degradate (Alachlor)	6967-29-9	61618		Yes
alpha-Endosulfan	Insecticide	959-98-8	34362		Yes
Endosulfan ether	Degradate (alpha-Endosulfan)	3369-52-6	61642		Yes
Endosulfan sulfate	Degradate (alpha-Endosulfan, beta-Endosulfan)	1031-07-8	61590		Yes
Atrazine	Herbicide	1912-24-9	39632	Yes	Yes
Deethylatrazine	Degradate (Atrazine)	6190-65-4	04040	Yes	Yes
Azinphos-methyl (Guthion)	Insecticide	86-50-0	82686	Yes	Yes
Azinphos-methyl-oxon	Degradate (Azinphos-methyl)	961-22-8	61635		Yes
Benfluralin	Herbicide	1861-40-1	82673	Yes	Yes
2-Amino-N-isopropylbenzamide	Degradate (Bentazon)	30391-89-0	61617		Yes
beta-Endosulfan	Insecticide	33213-65-9	34357		Yes
Bifenthrin	Insecticide	82657-04-3	61580		Yes
Butylate	Herbicide	2008-41-5	04028	Yes	Yes
Carbaryl	Insecticide	63-25-2	82680	Yes	Yes
1-Naphthol	Degradate (Carbaryl, Napromide)	90-15-3	49295		Yes
Carbofuran	Insecticide	1563-66-2	82674	Yes	Yes
2,5-Dichloroaniline	Degradate (Chloramben)	95-82-9	61614		Yes
Chlorpyrifos	Insecticide	2921-88-2	38933	Yes	Yes
Chlorpyrifos_oxon	Degradate (Chlorpyrifos)	5598-15-2	61636		Yes
cis-Permethrin	Insecticide	61949-76-6	82687	Yes	Yes
cis-Propiconazole	Fungicide	112721-87-6	79846		Yes
Cyanazine	Herbicide	21725-46-2	04041	Yes	Yes
Cycloate	Herbicide	1134-23-2	04031		Yes
Cyfluthrin	Insecticide	68359-37-5	61585		Yes
cis-Methyl-3-(2,2-dichlorovinyl)-2,2-dimethyl-(1-cyclopropane)-carboxylate	Degradate (Cyfluthrin)	59897-93-7	79842		Yes
trans-Methyl-3-(2,2-dichlorovinyl)-2,2-dimethyl-(1-cyclopropane)-carboxylate	Degradate (Cyfluthrin)	59897-94-8	79843		Yes
Cypermethrin	Insecticide	52315-07-8	61586		Yes
Dacthal (DCPA)	Herbicide	1861-32-1	82682	Yes	Yes
Diazinon	Insecticide	333-41-5	39572	Yes	Yes
Diazoxon	Degradate (Diazinon)	962-58-3	61638		Yes
Dichlorvos	Insecticide/Fumigant/Degradate (Naled)	62-73-7	38775		Yes
Dicrotophos	Insecticide	141-66-2	38454		Yes

Table 1–1. Pesticide compounds used in the 1992–2001 and 2002–11 summaries.—Continued

[CASRN, Chemical Abstracts Service Registry Number®;—, not applicable]

Pesticide compound (synonym)	Type of pesticide compound (parent pesticide, if degradate)	CASRN[1]	Parameter code	1992–2001	2002–11
Dieldrin	Insecticide	60-57-1	39381	Yes	Yes
Dimethoate	Insecticide	60-51-5	82662		Yes
Disulfoton	Insecticide	298-04-4	82677	Yes	Yes
Disulfoton_sulfone	Degradate (Disulfoton)	2497-06-5	61640		Yes
Disulfoton_sulfoxide	Degradate (Disulfoton)	2497-07-6	61641		Yes
E-Dimethomorph	Fungicide	—	79844		Yes
3,4-Dichloroaniline	Degradate (Diuron)	95-76-1	61625		Yes
EPTC	Herbicide	759-94-4	82668	Yes	Yes
Ethalfluralin	Herbicide	55283-68-6	82663	Yes	Yes
Ethion	Insecticide	563-12-2	82346		Yes
Ethion_monoxon	Degradate (Ethion)	17356-42-2	61644		Yes
Ethoprophos (Ethoprop)	Insecticide	13194-48-4	82672	Yes	Yes
O-Ethyl-O-methyl-S-propylphospho-rothioate	Degradate (Ethoprophos)	76960-87-7	61660		Yes
Fenamiphos	Nematocide	22224-92-6	61591		Yes
Fenamiphos_sulfone	Degradate (Fenamiphos)	31972-44-8	61645		Yes
Fenamiphos_sulfoxide	Degradate (Fenamiphos)	31972-43-7	61646		Yes
Fenthion	Insecticide	55-38-9	38801		Yes
Fenthion_sulfoxide	Degradate (Fenthion)	3761-41-9	61647		Yes
Fipronil	Insecticide	120068-37-3	62166		Yes
Desulfinylfipronil	Degradate (Fipronil)	—	62170		Yes
Desulfinylfipronil_amide	Degradate (Fipronil)	—	62169		Yes
Fipronil_sulfide	Degradate (Fipronil)	120067-83-6	62167		Yes
Fipronil_sulfone	Degradate (Fipronil)	120068-36-2	62168		Yes
Flumetralin	Plant_Growth_Regulator	62924-70-3	61592		Yes
3-(Trifluoromethyl)aniline	Degradate (Fluometuron)	98-16-8	61630		Yes
Fonofos	Insecticide	944-22-9	04095	Yes	Yes
gamma-HCH (Lindane)	Insecticide	58-89-9	39341	Yes	Yes
alpha-HCH	Degradate (gamma-HCH)	319-84-6	34253	Yes	Yes
Hexazinone	Herbicide	51235-04-2	04025		Yes
Iprodione	Fungicide	36734-19-7	61593		Yes
3,5-Dichloroaniline	Degradate (Iprodione)	626-43-7	61627		Yes
Isofenphos	Insecticide	25311-71-1	61594		Yes
lambda-Cyhalothrin	Insecticide	91465-08-6	61595		Yes
Linuron	Herbicide	330-55-2	82666	Yes	Yes
Malathion	Insecticide	121-75-5	39532	Yes	Yes
Malaoxon	Degradate (Malathion)	1634-78-2	61652		Yes
Metalaxyl	Fungicide	57837-19-1	61596		Yes
4-Chloro-2-methylphenol	Degradate (MCPA)	1570-64-5	61633		Yes
Methidathion	Insecticide	950-37-8	61598		Yes

Table 1–1. Pesticide compounds used in the 1992–2001 and 2002–11 summaries.—Continued

[CASRN, Chemical Abstracts Service Registry Number®;—, not applicable]

Pesticide compound (synonym)	Type of pesticide compound (parent pesticide, if degradate)	CASRN[1]	Parameter code	1992–2001	2002–11
Metolachlor	Herbicide	51218-45-2	39415	Yes	Yes
2-Ethyl-6-methylaniline	Degradate (Metolaclor)	24549-06-2	61620		Yes
Metribuzin	Herbicide	21087-64-9	82630	Yes	Yes
Molinate	Herbicide	2212-67-1	82671	Yes	Yes
Myclobutanil	Fungicide	88671-89-0	61599		Yes
Napropamide	Herbicide	15299-99-7	82684	Yes	Yes
1,4-Napthaquinone	Degradate (Napromide)	130-15-4	61611		Yes
Oxyfluorfen	Herbicide	42874-03-3	61600		Yes
p,p'-DDE	Degradate (DDT)	72-55-9	34653	Yes	Yes
4,4'-Dichlorobenzophenone	Degradate (DDT, Dicofol)	90-98-2	61631		Yes
Paraoxon-ethyl	Insecticide/Degradate (Parathion)	311-45-5	61663		Yes
Parathion (Ethyl parathion)	Insecticide	56-38-2	39542	Yes	Yes
Parathion-methyl (Methyl parathion)	Insecticide	298-00-0	82667	Yes	Yes
Paraoxon-methyl	Degradate (Methyl parathion)	950-35-6	61664		Yes
Pebulate	Herbicide	1114-71-2	82669	Yes	Yes
Pendimethalin	Herbicide	40487-42-1	82683	Yes	Yes
Phorate	Insecticide	298-02-2	82664	Yes	Yes
Phorate_oxon	Degradate (Phorate)	2600-69-3	61666		Yes
Phosmet	Insecticide	732-11-6	61601		Yes
Phosmet_oxon	Degradate (Phosmet)	3735-33-9	61668		Yes
Profenofos	Insecticide	41198-08-7	61603		Yes
Prometon	Herbicide	1610-18-0	04037	Yes	Yes
Prometryn	Herbicide	7287-19-6	04036		Yes
Propachlor	Herbicide	1918-16-7	04024	Yes	Yes
Propanil	Herbicide	709-98-8	82679	Yes	Yes
Propargite	Acaricide	2312-35-8	82685	Yes	Yes
2-(4-tert-butylphenoxy)-cyclohexanol	Degradate (Propargite)	1942-71-8	61637		Yes
Propetamphos	Insecticide	31218-83-4	61604		Yes
Propyzamide (Pronamide)	Herbicide	23950-58-5	82676	Yes	Yes
Simazine	Herbicide	122-34-9	04035	Yes	Yes
Sulfotepp	Insecticide	3689-24-5	61605		Yes
Sulprofos	Insecticide	35400-43-2	38716		Yes
Tebuconazole	Fungicide	107534-96-3	62852		Yes
Tebupirimfos	Insecticide	96182-53-5	61602		Yes
Tebupirimfos_oxon	Degradate (Tebupirimfos)	—	61669		Yes
Tebuthiuron	Herbicide	34014-18-1	82670	Yes	Yes
Tefluthrin	Insecticide	79538-32-2	61606		Yes
Temephos	Insecticide	3383-96-8	61607		Yes
Terbacil	Herbicide	5902-51-2	82665	Yes	Yes

Table 1–1. Pesticide compounds used in the 1992–2001 and 2002–11 summaries.—Continued

[CASRN, Chemical Abstracts Service Registry Number®;—, not applicable]

Pesticide compound (synonym)	Type of pesticide compound (parent pesticide, if degradate)	CASRN[1]	Parameter code	1992–2001	2002–11
Terbufos	Insecticide	13071-79-9	82675	Yes	Yes
Terbufos_sulfone_oxygen_analog	Degradate (Terbufos)	56070-15-6	61674		Yes
Terbuthylazine	Herbicide	5915-41-3	04022		Yes
Thiobencarb	Herbicide	28249-77-6	82681	Yes	Yes
4-Chlorobenzylmethyl_sulfone	Degradate (Thiobencarb)	98-57-7	61634		Yes
trans-Propiconazole	Fungicide	120523-07-1	79847		Yes
Triallate	Herbicide	2303-17-5	82678	Yes	Yes
Tribuphos	Defoliant	78-48-8	61610		Yes
Trifluralin	Herbicide	1582-09-8	82661	Yes	Yes
Z-Dimethomorph	Fungicide	—	79845		Yes

[1]This report contains CAS Registry Numbers®, which is a Registered Trademark of the American Chemical Society. CAS recommends the verification of the CASRNs through CAS Client Services℠.

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.

[km², square kilometer; Cr, Creek; Ri, River; Irr Dist; Irrigation District; No., number; MA, Massachusetts; CT, Connecticut; NY, New York; NJ, New Jersey; PA, Pennsylvania; MD, Maryland; VA, Virginia; WV, West Virginia; DC, District of Columbia; NC, North Carolina; SC, South Carolina; GA, Georgia; FL, Florida; AL, Alabama; OH, Ohio; IN, Indiana; TN, Tennessee; KY, Kentucky; IL, Illinois; WI, Wisconsin; MI, Michigan; MN, Minnesota; ND, North Dakota; IA, Iowa; MT, Montana; WY, Wyoming; CO, Colorado; NE, Nebraska; MO, Missouri; AR, Arkansas; MS, Mississippi; LA, Louisiana; TX, Texas; AZ, Arizona; VT, Vermont; NV, Nevada; CA, California; WA, Washington; ID, Idaho; OR, Oregon]

Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
01102500	Aberjona River at Winchester, MA	60	Urban	2	
01104615	Charles River near Watertown, MA	695	Urban		2
01184000	Connecticut River at Thompsonville, CT	25,000	Mixed	4	3
01209710	Norwalk River at Winnipauk, CT	85	Urban	5	3
01349150	Canajoharie Creek near Canajoharie, NY	155	Agriculture	5	3
01356190	Lisha Kill northwest of Niskayuna, NY	40	Urban	1	3
01357500	Mohawk River at Cohoes, NY	9,110	Mixed	8	2
01403300	Raritan River at Bound Brook, NJ	2,070	Urban	3	6
01403900	Bound Brook at Middlesex, NJ	126	Urban	2	2
01410784	Great Egg Harbor River near Sicklerville, NJ	39	Urban	2	
01454700	Lehigh River at Easton, PA	3,520	Mixed	1	
01463500	Delaware River at Trenton, NJ	17,600	Mixed	2	2
01464907	Little Neshaminy Creek near Warminster, PA	72	Urban	2	1
01470779	Tulpehocken Creek near Bernville, PA	179	Mixed	2	
01472157	French Creek near Phoenixville, PA	152	Mixed		1
01474500	Schuylkill River at Philadelphia, PA	4,900	Mixed	2	
01485000	Pocomoke River at Willards, MD	138	Mixed	1	
01493112	Chesterville Branch near Crumpton, MD	17	Agriculture	1	
01493500	Morgan Creek near Kennedyville, MD	33	Agriculture		3
01555400	East Mahantango Creek at Klingerstown, PA	116	Agriculture	2	
01571490	Cedar Run at Eberlys Mill, PA	33	Urban	3	
01573095	Bachman Run at Annville, PA	20	Mixed	1	
01576540	Mill Creek near Lyndon, PA	141	Mixed	2	
01578310	Susquehanna River at Conowingo, MD	70,100	Mixed	2	6
01621050	Muddy Creek at Mount Clinton, VA	37	Agriculture	2	3
01636500	Shenandoah River at Millville, WV	7,880	Mixed	1	
01639000	Monocacy River at Bridgeport, MD	449	Mixed	1	
01646580	Potomac River at Washington, DC	30,000	Mixed	4	7
01654000	Accotink Creek near Annandale, VA	61	Urban	2	4
02082731	Devils Cradle Creek near Alert, NC	35	Mixed	1	
02083500	Tar River at Tarboro, NC	5,750	Mixed	1	
02083833	Pete Mitchell Swamp near Penny Hill, NC	45	Agriculture	1	
02084160	Chicod Cr near Simpson, NC	109	Mixed	1	1
02084558	Albemarle Canal near Swindell, NC	191	Agriculture	1	
02087580	Swift Creek near Apex, NC	54	Urban		5
02089500	Neuse River at Kinston, NC	7,020	Mixed	4	7

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.—Continued

[km², square kilometer; Cr, Creek; Ri, River; Irr Dist; Irrigation District; No., number; MA, Massachusetts; CT, Connecticut; NY, New York; NJ, New Jersey; PA, Pennsylvania; MD, Maryland; VA, Virginia; WV, West Virginia; DC, District of Columbia; NC, North Carolina; SC, South Carolina; GA, Georgia; FL, Florida; AL, Alabama; OH, Ohio; IN, Indiana; TN, Tennessee; KY, Kentucky; IL, Illinois; WI, Wisconsin; MI, Michigan; MN, Minnesota; ND, North Dakota; IA, Iowa; MT, Montana; WY, Wyoming; CO, Colorado; NE, Nebraska; MO, Missouri; AR, Arkansas; MS, Mississippi; LA, Louisiana; TX, Texas; AZ, Arizona; VT, Vermont; NV, Nevada; CA, California; WA, Washington; ID, Idaho; OR, Oregon]

Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
02091500	Contentnea Creek at Hookerton, NC	1,910	Agriculture	3	3
02169570	Gills Creek at Columbia, SC	154	Urban	1	2
02174250	Cow Castle Creek near Bowman, SC	62	Mixed	2	2
02175000	Edisto River near Givhans, SC	7,080	Mixed	4	3
02215100	Tucsawhatchee Creek near Hawkinsville, GA	420	Mixed	1	
02226160	Altamaha River near Everett City, GA	36,100	Mixed		4
02281200	Hillsboro Canal near Shawano, FL	806	Agriculture	3	1
02289034	U.S. Sugar Outflow Canal near Clewiston, FL	73	Agriculture	1	
02306774	Rocky Creek near Citrus Park, FL	46	Urban		2
02317797	Little River near Tifton, GA	335	Mixed	1	1
02318500	Withlacoochee River near Quitman, GA	3,860	Mixed	3	3
02326838	Lafayette Creek near Tallahassee, FL	25	Urban	2	
02335870	Sope Creek near Marietta, GA	80	Urban	2	4
02336300	Peachtree Creek at Atlanta, GA	222	Urban	1	
02338000	Chattahoochee River near Whitesburg, GA	6,250	Urban	3	7
02350080	Lime Creek near Cobb, GA	162	Mixed	2	4
02356980	Aycocks Creek near Boykin, GA	271	Mixed	1	
02359170	Apalachicola River near Sumatra, FL	49,800	Mixed		1
02424000	Cahaba River at Centreville, AL	2660	Mixed	2	1
02429500	Alabama River at Claiborne, AL	56,900	Mixed	1	3
02444490	Bogue Chitto near Memphis, AL	136	Agriculture	1	
02469762	Tombigbee River near Coffeeville, AL	47,800	Mixed		1
02470500	Mobile River at Mt. Vernon, AL	111,400	Mixed		4
03049625	Allegheny River at New Kensington, PA	29,700	Mixed	1	
03049646	Deer Creek near Dorseyville, PA	70	Urban	1	
03167000	Reed Creek at Grahams Forge, VA	669	Mixed	1	
03176500	New River at Glen Lyn, VA	9,780	Mixed	1	
03201300	Kanawha River at Winfield, WV	30,600	Mixed	1	
03267900	Mad River near Eagle City, OH	802	Agriculture	3	3
03274000	Great Miami River at Hamilton, OH	9,400	Mixed	2	
03303280	Ohio River at Cannelton Dam at Cannelton, IN	251,200	Mixed	6	10
03353637	Little Buck Creek near Indianapolis, IN	45	Urban	3	2
03357330	Big Walnut Creek near Roachdale, IN	339	Agriculture		2
03360895	Kessinger Ditch near Monroe City, IN	146	Agriculture	1	
03374100	White River at Hazleton, IN	29,300	Mixed	10	7
03378500	Wabash River at New Harmony, IN	75,700	Agriculture	5	10

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.—Continued

[km², square kilometer; Cr, Creek; Ri, River; Irr Dist; Irrigation District; No., number; MA, Massachusetts; CT, Connecticut; NY, New York; NJ, New Jersey; PA, Pennsylvania; MD, Maryland; VA, Virginia; WV, West Virginia; DC, District of Columbia; NC, North Carolina; SC, South Carolina; GA, Georgia; FL, Florida; AL, Alabama; OH, Ohio; IN, Indiana; TN, Tennessee; KY, Kentucky; IL, Illinois; WI, Wisconsin; MI, Michigan; MN, Minnesota; ND, North Dakota; IA, Iowa; MT, Montana; WY, Wyoming; CO, Colorado; NE, Nebraska; MO, Missouri; AR, Arkansas; MS, Mississippi; LA, Louisiana; TX, Texas; AZ, Arizona; VT, Vermont; NV, Nevada; CA, California; WA, Washington; ID, Idaho; OR, Oregon]

Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
03455000	French Broad River near Newport, TN	4,800	Mixed	1	
03466208	Big Limestone Creek near Limestone, TN	205	Agriculture	2	1
03467609	Nolichucky River near Lowland, TN	4,370	Mixed	2	1
03526000	Copper Creek near Gate City, VA	277	Mixed	1	
03528000	Clinch River above Tazewell, TN	3,820	Mixed	1	
03575100	Flint River near Brownsboro, AL	969	Agriculture	3	2
03609750	Tennessee River at Highway 60 near Paducah, KY	104,500	Mixed	5	4
03612500	Ohio River at Dam 53 near Grand Chain, IL	526,000	Mixed	6	10
04072050	Duck Creek near Howard, WI	247	Agriculture	3	3
04087000	Milwaukee River at Milwaukee, WI	1,810	Mixed	3	2
04159492	Black River near Jeddo, MI	1,200	Agriculture	1	
04161820	Clinton River at Sterling Heights, MI	803	Urban	1	2
04175600	River Raisin near Manchester, MI	331	Mixed		1
04178000	St. Joseph River near Newville, IN	1,600	Agriculture	2	
04183000	Maumee River at New Haven, IN	5,040	Mixed	1	
04186500	Auglaize River near Fort Jennings, OH	858	Agriculture	1	2
04193500	Maumee River at Waterville, OH	16,400	Mixed	5	3
04208504	Cuyahoga River at Cleveland, OH	2,040	Urban	1	
04211820	Grand Ri at Harpersfield, OH	1,430	Mixed	1	
04213500	Cattaraugus Creek at Gowanda, NY	1,130	Mixed	1	
05062500	Wild Rice River at Twin Valley, MN	2,410	Mixed	1	
05082625	Turtle River near Arvilla, ND	658	Agriculture	1	
05085900	Snake River above Alvarado, MN	566	Agriculture	1	
05102490	Red River of the North at Pembina, ND	92,100	Agriculture	5	
05288705	Shingle Creek at Minneapolis, MN	73	Urban	1	3
05320270	Little Cobb River near Beauford, MN	336	Agriculture	1	2
05330000	Minnesota River near Jordan, MN	42,000	Agriculture	2	
05330902	Nine Mile Creek at Bloomington, MN	116	Urban	1	
05331580	Mississippi River at Hastings, MN	96,000	Agriculture	5	3
05420500	Mississippi River at Clinton, IA	221,700	Mixed	6	10
05420680	Wapsipinicon River near Tripoli, IA	897	Agriculture		1
05449500	Iowa River near Rowan, IA	1,080	Agriculture	2	
05451210	South Fork Iowa River near New Providence, IA	581	Agriculture	2	5
05455570	English River at Riverside, IA	1,620	Agriculture	1	
05464220	Wolf Creek near Dysart, IA	775	Agriculture	2	
05465500	Iowa River at Wapello, IA	32,400	Agriculture	5	3

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.—Continued

[km², square kilometer; Cr, Creek; Ri, River; Irr Dist; Irrigation District; No., number; MA, Massachusetts; CT, Connecticut; NY, New York; NJ, New Jersey; PA, Pennsylvania; MD, Maryland; VA, Virginia; WV, West Virginia; DC, District of Columbia; NC, North Carolina; SC, South Carolina; GA, Georgia; FL, Florida; AL, Alabama; OH, Ohio; IN, Indiana; TN, Tennessee; KY, Kentucky; IL, Illinois; WI, Wisconsin; MI, Michigan; MN, Minnesota; ND, North Dakota; IA, Iowa; MT, Montana; WY, Wyoming; CO, Colorado; NE, Nebraska; MO, Missouri; AR, Arkansas; MS, Mississippi; LA, Louisiana; TX, Texas; AZ, Arizona; VT, Vermont; NV, Nevada; CA, California; WA, Washington; ID, Idaho; OR, Oregon]

Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
05490500	Des Moines River at Keosauqua, IA	36,400	Agriculture		2
05525500	Sugar Creek at Milford, IL	1,160	Agriculture	2	
05531500	Salt Creek at Western Springs, IL	291	Urban	1	2
05532500	Des Plaines River at Riverside, IL	1,630	Urban	1	1
05553500	Illinois River at Ottawa, IL	28,300	Mixed	3	
05572000	Sangamon River at Monticello, IL	1,430	Agriculture	2	2
05584500	La Moine River at Colmar, IL	1,700	Agriculture	2	
05586100	Illinois River at Valley City, IL	69,200	Mixed	5	6
05587455	Mississippi River Below Grafton, IL	443,700	Agriculture	5	7
06208500	Clarks Fork Yellowstone River near Edgar, MT	5,240	Mixed	1	
06279500	Bighorn River at Kane, WY	40,800	Mixed	1	
06295000	Yellowstone River at Forsyth, MT	102,000	Mixed	3	3
06329500	Yellowstone River near Sidney, MT	177,000	Mixed	5	4
06713500	Cherry Creek at Denver, CO	1,060	Urban	2	5
06714000	South Platte River at Denver, CO	10,000	Urban	4	
06753990	Lonetree Creek near Greeley, CO	1,480	Agriculture	2	1
06754000	South Platte River near Kersey, CO	25,000	Mixed	5	3
06795500	Shell Creek near Columbus, NE	762	Agriculture		1
06800000	Maple Creek near Nickerson, NE	955	Agriculture	5	5
06800500	Elkhorn River at Waterloo, NE	18,000	Agriculture		4
06805500	Platte River at Louisville, NE	221,000	Mixed	7	8
06923150	Dousinbury Creek near Wall Street, MO	106	Mixed	1	
06934500	Missouri River at Hermann, MO	1,353,000	Mixed	6	8
07022000	Mississippi River at Thebes, IL	1,847,000	Mixed	6	8
07031692	Fletcher Creek at Memphis, TN	79	Urban	1	
07043500	Little River Ditch No 1 near Morehouse, MO	1,140	Agriculture	2	
07053250	Yocum Creek near Oak Grove, AR	134	Agriculture	1	1
07263620	Arkansas River at David D Terry Lock and Dam below Little Rock, AR	401,000	Mixed	6	9
07288650	Bogue Phalia near Leland, MS	1,300	Agriculture	3	3
07288955	Yazoo River near Long Lake, MS	34,800	Mixed	6	10
07369500	Tensas River at Tendal, LA	721	Agriculture	4	
07373420	Mississippi River near St. Francisville, LA	2,915,000	Mixed	6	10
07374000	Mississippi River at Baton Rouge, LA	2,926,000	Mixed		7
07374525	Mississippi River at Belle Chasse, LA	2,727,000	Mixed		5
07375050	Tchefuncte River near Covington, LA	366	Mixed		1
07379960	Dawson Creek at Baton Rouge, LA	39	Urban	2	1

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.—Continued

[km², square kilometer; Cr, Creek; Ri, River; Irr Dist; Irrigation District; No., number; MA, Massachusetts; CT, Connecticut; NY, New York; NJ, New Jersey; PA, Pennsylvania; MD, Maryland; VA, Virginia; WV, West Virginia; DC, District of Columbia; NC, North Carolina; SC, South Carolina; GA, Georgia; FL, Florida; AL, Alabama; OH, Ohio; IN, Indiana; TN, Tennessee; KY, Kentucky; IL, Illinois; WI, Wisconsin; MI, Michigan; MN, Minnesota; ND, North Dakota; IA, Iowa; MT, Montana; WY, Wyoming; CO, Colorado; NE, Nebraska; MO, Missouri; AR, Arkansas; MS, Mississippi; LA, Louisiana; TX, Texas; AZ, Arizona; VT, Vermont; NV, Nevada; CA, California; WA, Washington; ID, Idaho; OR, Oregon]

Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
07381440	Bayou Grosse Tete at Rosedale, LA	305	Agriculture	1	
07381495	Atchafalaya River at Melville, LA	241,700	Mixed	6	10
07381590	Wax Lake Outlet at Calumet, LA	5,600	Mixed		5
07381600	Lower Atchafalaya River at Morgan City, LA	245,100	Mixed		5
08010000	Bayou Des Cannes near Eunice, LA	369	Mixed	1	
08012150	Mermentau River at Mermentau, LA	3,580	Agriculture	2	2
08012470	Bayou Lacassine near Hayes, LA	767	Agriculture	3	
08049240	Rush Creek at Arlington, TX	74	Urban	1	
08051500	Clear Creek near Sanger, TX	763	Mixed		1
08057200	White Rock Creek at Dallas, TX	173	Urban	2	5
08057410	Trinity River below Dallas, TX	16,200	Mixed	5	7
08064100	Chambers Creek near Rice, TX	2,140	Mixed	1	2
08116650	Brazos River near Rosharon, TX	117,400	Mixed		2
08178800	Salado Creek at San Antonio, TX	506	Urban	1	2
08180640	Medina River at La Coste, TX	2,100	Mixed	1	
08181800	San Antonio River near Elmendorf, TX	4,530	Urban	2	
08364000	Rio Grande at El Paso, TX	77,600	Mixed	5	9
09153290	Reed Wash near Mack, CO	36	Mixed	1	
09481740	Santa Cruz River at Tubac, AZ	3,120	Urban		1
09514000	Buckeye Canal near Avondale, AZ	117,000	Mixed	2	
09517000	Hassayampa River near Arlington, AZ	3,970	Mixed	1	1
10102200	Cub River near Richmond, UT	577	Agriculture	2	
10168000	Little Cottonwood Creek at Salt Lake City, UT	117	Urban	2	
10171000	Jordan River at Salt Lake City, UT	9,100	Mixed	3	1
10350500	Truckee River at Clark, NV	4,310	Mixed	4	2
11060400	Warm Creek near San Bernardino, CA	31	Urban	2	
11074000	Santa Ana River below Prado Dam, CA	3,730	Urban		5
11075610	Santa Ana River near Anaheim, CA	3,870	Urban	2	
11261100	Salt Slough near Stevinson, CA	1,270	Agriculture	2	
11262900	Mud Slough near Gustine, CA	1,270	Agriculture	1	
11273500	Merced River near Newman, CA	3,620	Agriculture	6	3
11274538	Orestimba Creek near Crows Landing, CA	28	Agriculture	5	3
11274560	Turlock Irr Dist Lateral No. 5 near Patterson, CA	218	Mixed	1	
11274570	San Joaquin River near Patterson, CA	9,800	Mixed	1	
11303500	San Joaquin River near Vernalis, CA	19,200	Mixed	8	7
11390890	Colusa Basin Drain near Knights Landing, CA	4,260	Agriculture	1	

Table 1–2. Stream sites used in the first decade (1992–2001) and second decade (2002–11) summaries.—Continued

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Site number	Site name	Watershed area (km²)	Land use	Number of years	
				1992–2001	2002–11
11447360	Arcade Creek near Del Paso Heights, CA	82	Urban	1	2
11447650	Sacramento River at Freeport, CA	61,700	Mixed	5	10
12113390	Duwamish River at Tukwila, WA	1,190	Urban	5	
12128000	Thornton Creek near Seattle, WA	29	Urban	2	3
12212100	Fishtrap Creek at Lynden, WA	99	Mixed	1	
12424500	Spokane River near Spokane, WA	13,000	Urban	1	
12464770	Crab Creek near Ritzville, WA	1,190	Agriculture		1
12471400	Lind Coulee Wasteway near Warden, WA	1,820	Agriculture	3	
12472380	Crab Creek Lateral near Othello, WA	146	Agriculture	1	
12473740	El 68 D Wasteway near Othello, WA	377	Agriculture	1	
12500420	Moxee Drain near Union Gap, WA	353	Mixed	1	
12505450	Granger Drain at Granger, WA	160	Agriculture	1	4
12510500	Yakima River at Kiona, WA	14,500	Mixed	1	3
13055000	Teton River near St Anthony, ID	2,290	Mixed	1	1
13092747	Rock Creek at Twin Falls, ID	623	Agriculture	5	2
13154500	Snake River at King Hill, ID	92,900	Mixed	5	6
13351000	Palouse River at Hooper, WA	6,380	Agriculture	8	2
14201300	Zollner Creek near Mt. Angel, OR	39	Agriculture		3
14202000	Pudding River at Aurora, OR	1,260	Agriculture	1	
14206950	Fanno Creek at Durham, OR	81	Urban		5
14211720	Willamette River at Portland, OR	28,900	Mixed	6	9
040863075	North Branch Milwaukee River near Random Lake, WI	130	Agriculture	1	
040869415	Lincoln Creek at Milwaukee, WI	26	Urban		5
073814675	Bayou Boeuf at Amelia, LA	3,170	Mixed	1	
094196783	Las Vegas Wash near Las Vegas, NV	2,650	Urban	5	5
0242354750	Cahaba Valley Creek at Pelham, AL	66	Urban	2	3
0357479650	Hester Creek near Plevna, AL	76	Agriculture	2	1
252414080333200	C-111 Canal near Homestead, FL	132	Mixed	1	
322023090544500	Mississippi River above Vicksburg, MS	2,929,500	Mixed		1
393944084120700	Holes Creek at Kettering, OH	52	Urban	2	2
394340085524601	Sugar Creek at New Palestine, IN	246	Agriculture	7	5

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Maine Voices: Chemical lawns a formula for trouble

pressherald.com/2014/10/05/maine-voices-chemical-lawns-a-formula-for-trouble/

By Jody Spear

HARBORSIDE — Urban streams are dangerously polluted from pesticide runoff, according to a report released Sept. 11 by the U.S. Geological Survey as part of its National Water Quality Assessment Program. Reasons for exceeding benchmarks are not specified, but the obvious source of contamination in municipal areas is lawn-care chemicals. Two of the insecticides cited by USGS as above safe levels for fish (fipronil and dichlorvos) are primarily for landscaping and household applications.

Unaccountably, the most commonly used lawn herbicides – 2,4-D (Weed ‘n Feed) and glyphosate (Roundup), highly toxic to all life forms – were not assessed. Nor did USGS scientists monitor fungicides, pyrethroids and neonicotinoid insecticides applied to kill grubs – chemicals that are decimating the bees on which we depend for pollination of food crops. It is expensive to sample for these compounds, yes, but arguably more costly not to do so.

Additional Images

The gardens and pools at Meadowmere Resort in Ogunquit, seen early last summer, are environmentally friendly. Ogunquit is considering an ordinance that would ban chemical pesticides, fertilizers and herbicides. Gabe Souza/Staff Photographer

about the author

Jody Spear is a resident of Harborside.

Bees are deprived of essential nectar sources when Roundup is sprayed on “weeds” like dandelion and clover. Glyphosate and the deadly surfactant it contains (polyoxyethylene tallow amine) are toxic to humans, too. The formulation is linked to cancer, endocrine disruption and reproductive abnormalities, and several recent studies reveal alarming evidence of intestinal damage from soil-borne pathogens it creates, especially when used on herbicide-tolerant genetically modified crops.

As Roundup Ready grass is scheduled to be marketed in 2015, the pesticide now poses an even greater threat. This will mean destruction of beneficial soil organisms and cross-contamination of non-GM plants as well as proliferation of superweeds resistant to Roundup and requiring still more toxic herbicides that will inevitably end up in water.

The problems are already manifest with Roundup Ready food crops, and will escalate when crops are genetically modified to withstand massive spraying of 2,4-D, approved by the U.S. Department of Agriculture earlier this year.

We cannot be reassured by USGS researchers' conclusions that the pollution of drinking water sources is declining. Key factors like the toxicity of many agricultural insecticides, fungicides and herbicides – both acute and chronic – have not been taken into account; and the effects of complex chemical mixtures remains to be assessed.

It is essential that we be made aware when maximum contaminant levels of compounds known to cause harm – regrettably regulations are more protective of the chemical industry than of humans and the environment – are over the limit.

With federal regulation proceeding at a glacial pace, responsibility for precautionary action lies squarely in the hands of citizens and their municipal officials.

The town of Ogunquit is not waiting for more study before taking steps to protect water and the health of residents. An amended version of the ordinance approved there in June, which prohibits cosmetic use of pesticides, will be back on the ballot in November.

With passage of this law, Ogunquit will be the first town in Maine (and second in the nation, after Takoma Park, Maryland) to ban lawn-care chemicals on private as well as public land. The action these officials have taken acknowledges that cities and towns have the power to keep toxic effluents out of lakes, rivers and bays.

Their power to control contingencies like rising sea levels and superstorms is limited, however, so emergency preparedness, especially along the coast, is critical. Our two states' recreation industries are a vital economic engine – too important to allow pesticide runoff to contaminate wells and reservoirs and to compromise the safety of fishing, boating and swimming.

Because we all live downstream, lawns must be weaned off the costly, chemical-intensive life support provided by industrial landscapers. With organic pest management – building up soil with compost and aerating, aided by earthworms – turf can be 50 percent more cost-effective after three years than chemical programs.

Replacing part of a sterile lawn with ground covers such as ornamental native grasses, bushes and flowers adds varied visual interest, provides sustenance to bees and other pollinators and cuts down on the pollution and expense of mowing.

According to the Union of Concerned Scientists, a power lawnmower emits as much smog-forming pollution in one hour as a car traveling almost 200 miles.

These are the costs Ogunquit and Takoma Park have determined to avoid. The U.S. Geological Survey would do well to note their progress.

— *Special to the Telegram*

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Newsroom

News Releases from Headquarters

EPA Announces Final Decision to Register Enlist Duo, Herbicide Containing 2, 4-D and Glyphosate/Risk assessment ensures protection of human health, including infants, children

Release Date: 10/15/2014
Contact Information: Cathy Milbourn (News Media Only) Milbourn.cathy@epa.gov 202-564-7849 202-564-4355 703-308-8162 (Other Inquiries)

WASHINGTON--The EPA is registering the herbicide, Enlist Duo with first-time ever restrictions to manage the problem of resistant weeds. The pesticide is for use in controlling weeds in corn and soybeans genetically-engineered (GE) to tolerate 2,4-D and glyphosate. The agency's decision reflects a large body of science and an understanding of the risk of pesticides to human health and the environment.

The herbicides 2,4-D and glyphosate are two of the most widely used herbicides in the world for controlling weeds. Dozens of other countries including Canada, Mexico, Japan and 26 European Union Members have approved these pesticides for use on numerous crops and residential lawns. Last year, Canada approved the use of Enlist Duo for the same uses that EPA is authorizing.

EPA scientists used highly conservative and protective assumptions to evaluate human health and ecological risks for the new uses of 2,4-D in Enlist Duo. The assessments confirm that these uses meet the safety standards for pesticide registration and, as approved, will be protective of the public, agricultural workers, and non-target species, including endangered species.

The agency evaluated the risks to all age groups, from infants to the elderly, and took into account exposures through food, water, pesticide drift, and as a result of use around homes. The decision meets the rigorous Food Quality Protection Act standard of "reasonable certainty of no harm" to human health.

The approved formulation contains the choline salt of 2,4-D which is less prone to drift than the other forms of 2,4-D. The Agency has also put in place restrictions to avoid pesticide drift, including a 30-foot in-field "no spray" buffer zone around the application area, no pesticide application when the wind speed is over 15 mph, and only ground applications are permitted. This action provides an additional tool for the agricultural community to manage resistant weeds.

To ensure that weeds will not become resistant to 2,4-D and continue increased herbicide use, EPA is imposing a new, robust set of requirements on the registrant. These requirements include extensive surveying and reporting to EPA, grower education and remediation plans. The registration will expire in six years, allowing EPA to revisit the issue of resistance. In the future, the agency intends to apply this approach to weed resistance management for all existing and new herbicides used on herbicide tolerant crops.

This assessment is the third time in recent years that EPA has evaluated the safety of 2,4-D and the safety finding is consistent with past assessments that EPA has performed for 2,4-D. EPA comprehensively reviewed 2,4-D in 2005, and once more in 2012 and now again in 2014 in response to the current application.

EPA is registering the pesticide in six states: Ill., Ind., Iowa, Ohio, SD., and Wis. The agency is accepting comments until Nov. 14, 2014 (30 days) on whether to register Enlist Duo in ten more states: Ark., Kan., La., Minn., Mo., Miss., Neb., Okla., Tenn., and ND.

The EPA's final regulatory decision document is available in EPA docket **EPA-HQ-OPP-2014-0195** at www.regulations.gov

Questions and Answers about this final regulatory decision are available at: www2.epa.gov/ingredients-used-pesticide-products/registration-enlist-duo .

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The Motley Fool

Unlikely Hero: Can Monsanto Rid the World of Pesticides?

By Maxx Chatsko | More Articles | Save For Later
October 27, 2014 | Comments (4)

Source: Stephane Mignon/Flickr.

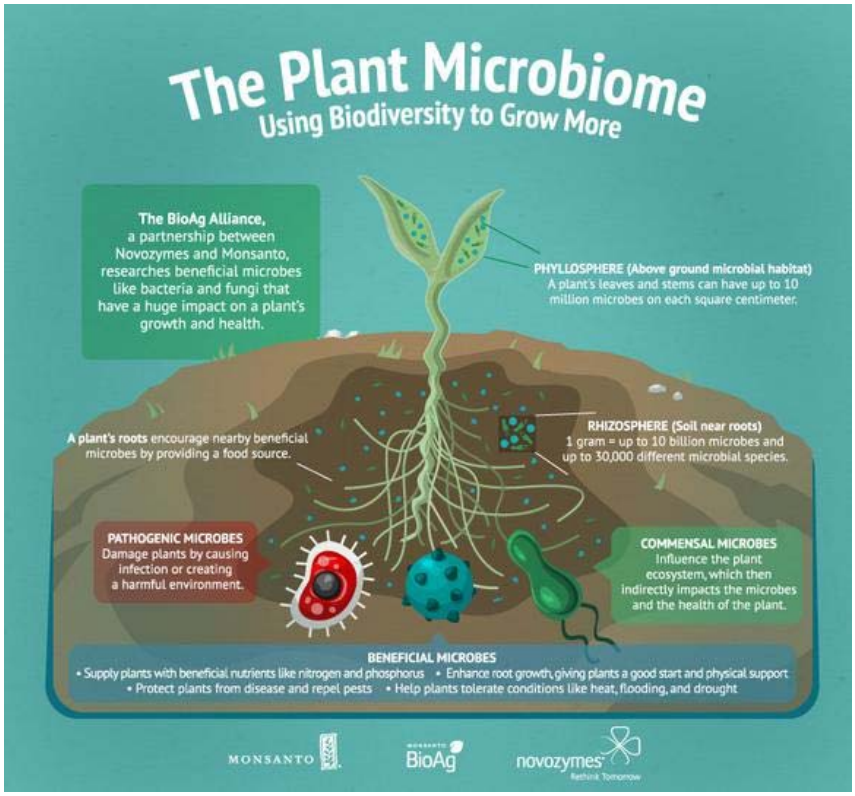
The United Nations estimates that the global population will increase from 7 billion today to 9 billion people by midcentury. When total population growth is coupled with a swelling global middle class, researchers believe the world's farmers will need to produce 70% more food to meet increased demand. As if that wasn't challenging enough, farmers will need to increase production on fewer acres of cultivated land, which will be replaced by urban sprawl.

That should hammer home this reality: The future of agriculture will be heavily dependent on novel technologies. But that doesn't necessarily mean we'll need to rely on more pesticides and synthetic fertilizers. In fact, the opportunity created by the need to produce more food with fewer inputs is directly aligned will the push to make agriculture more sustainable while protecting the environment and biodiversity. Thanks to some major help from industrial biotech powerhouse Novozymes, **Monsanto** (NYSE: MON) could prove an unlikely hero in reducing the need for pesticides and synthetic fertilizers.

Wait, what?
This was all set in motion nearly two years ago. In January 2013, Monsanto acquired certain assets of agricultural sustainability start-up Agradis, which had built a massive library of soil microbes linked to crop productivity. Monsanto also invested in and signed a five-year research and development collaboration agreement with Synthetic Genomics, one of the leading organism companies and where Agradis was born. Then, in December 2013, Novozymes and Monsanto established the BioAg Alliance to create a novel platform for developing environmentally-friendly microbial products that will help farmers around the world boost yields while reducing inputs.

What makes soil microbes so important in agriculture?

Take a field of corn as our example. We might only see or think about the stalk sticking out of the dirt, but there's an important symbiotic relationship occurring just beneath the surface. Thousands of species of soil microbes (bacteria and fungi) interact with each plant's root system -- the beneficial microbes help plants acquire nutrients from the soil, outcompete pathogenic microbes, and fend off pests. The healthier the population of microbes, the healthier the plant, and the more food a farmer can produce from each acre of land.



Source: Monsanto.

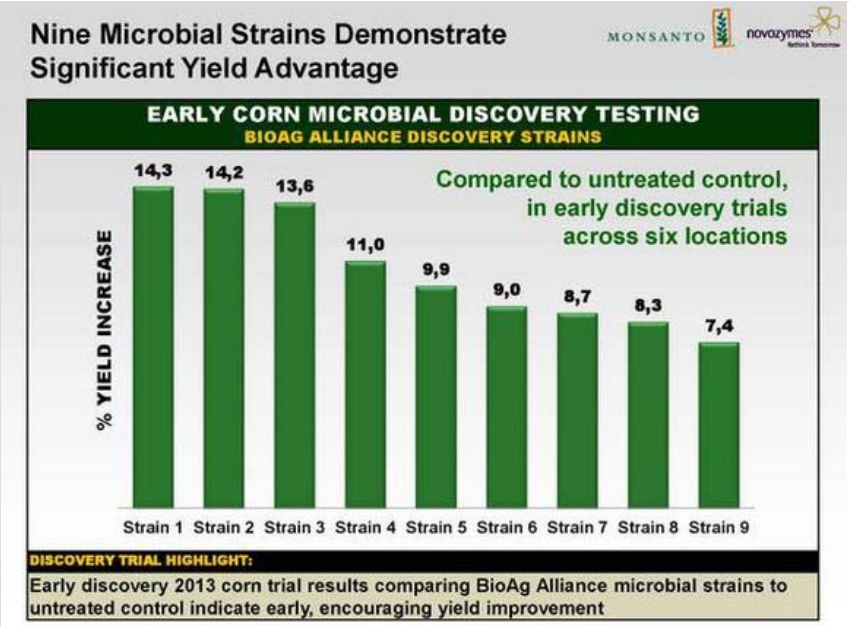
Better yet, microbial products could reduce the need for pesticides and synthetic fertilizers. And since the microbial products won't be engineered, they could even boost the dismal yields realized by organic farmers.

How will it work?
To develop soil microbes into commercial products, Monsanto and Novozymes will:

- Find and isolate soil microbes with high commercial potential.
- Determine which microbes demonstrate the ability to boost crop productivity.
- Ensure the selected soil microbes are capable of competing with microbes already present in soils from key geographies.
- Robustly screen and test microbes for human and animal health risks with medical professionals.
- Grow selected microbes in fermentation tanks, concentrate the cells, and coat them onto seeds.

Exactly how microbial products will be reported in relation to Monsanto's existing business hasn't been determined, but the concentrated cells could be sold to other seed manufacturers through the company's agricultural productivity business (selling herbicides), while coated seeds could be sold directly to farmers through Monsanto's seeds and genomics business (selling seeds and genetic traits). We might find out sooner than later.

In 2014, Monsanto and Novozymes conducted research in 170,000 field trial plots in 70 locations across the United States. The number of field trial plots is expected to more than double in 2015. After seeing initial results, it's easy to see why the companies are eager to develop the platform. Microbes with commercial potential were tested in corn plots against untreated control groups across six locations. The best strain increased corn yield by 14.3%, while the ninth-best boosted yield by 7.4%.



Source: Novozymes Twitter.

These are incredible improvements in yield for any new agricultural product, let alone in the first-ever field trials. The farmer can boost output by at least 7.4% without changing behavior (the microbial product is coated onto seeds). That's an incredible product -- and an important one for the future of agriculture.

Do good by doing good

Monsanto might be best known for its herbicide Roundup and the seeds made to tolerate its application, but its agricultural productivity business doesn't deliver nearly as much revenue or profits as its seeds and genomics business.

	2013 Revenue	2013 Gross Profit	Gross Profit Margin
Agricultural Productivity	$4,521 million	$1,570 million	34.7%
Seeds and Genomics	$10,340 million	$6,083 million	58.8%

Monsanto's 2013 fiscal year ended Aug. 31. Source: SEC filings.

Therefore, it makes good business sense to develop products (or an entire platform, in this case) that could sell in high volumes and deliver high margins. Microbial products are relatively easy to manufacture, which could enable high-margin opportunities. For instance, after determining the commercial potential of a microbe and characterizing its potential risk, Monsanto and Novozymes only have to operate standard fermentation equipment to grow cells before concentrating and coating onto seeds. Here's a video explaining the entire discovery and manufacturing process:

The microbial products being developed by Monsanto and Novozymes have the potential to create a major shift in global agricultural practices and allow farmers to create more with less. Early progress, results, and usage indicate microbial products could significantly boost crop yields. Considering the ease of use for both farmers (no change in behavior) and seed manufacturers (easily applied to seeds), Monsanto and Novozymes could realize rapid and widespread adoption throughout the agriculture industry with the BioAg Alliance. This portfolio of products could provide a significant future growth business for investors while helping to eventually reduce the need for pesticides and synthetic fertilizers applied worldwide. If that isn't a win-win scenario, then I don't know what is.

Top dividend stocks for the next decade

The smartest investors know that dividend stocks simply crush their non-dividend paying counterparts over the long term. That’s beyond dispute. They also know that a well-constructed dividend portfolio creates wealth steadily, while still allowing you to sleep like a baby. Knowing how valuable such a portfolio might be, our top analysts put together a report on a group of high-yielding stocks that should be in any income investor’s portfolio

Maxx Chatsko has no position in any stocks mentioned. Check out l

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PLOS ONE

Non-Hodgkin Lymphoma Risk and Insecticide, Fungicide and Fumigant Use in the Agricultural Health Study

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Abstract

Farming and pesticide use have previously been linked to non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). We evaluated agricultural use of specific insecticides, fungicides, and fumigants and risk of NHL and NHL-subtypes (including CLL and MM) in a U.S.-based prospective cohort of farmers and commercial pesticide applicators. A total of 523 cases occurred among 54,306 pesticide applicators from enrollment (1993–97) through December 31, 2011 in Iowa, and December 31, 2010 in North Carolina. Information on pesticide use, other agricultural exposures and other factors was obtained from questionnaires at enrollment and at follow-up approximately five years later (1999–2005). Information from questionnaires, monitoring, and the literature were used to create lifetime-days and intensity-weighted lifetime days of pesticide use, taking into account exposure-modifying factors. Poisson and polytomous models were used to calculate relative risks (RR) and 95% confidence intervals (CI) to evaluate associations between 26 pesticides and NHL and five NHL-subtypes, while adjusting for potential confounding factors. For total NHL, statistically significant positive exposure-response trends were seen with lindane and DDT. Terbufos was associated with total NHL in ever/never comparisons only. In subtype analyses, terbufos and DDT were associated with small cell lymphoma/chronic lymphocytic leukemia/marginal cell lymphoma, lindane and diazinon with follicular lymphoma, and permethrin with MM. However, tests of homogeneity did not show significant differences in exposure-response among NHL-subtypes for any pesticide. Because 26 pesticides were evaluated for their association with NHL and its subtypes, some chance finding could have occurred. Our results showed pesticides from different chemical and functional classes were associated with an excess risk of NHL and NHL subtypes, but not all members of any single class of pesticides were associated with an elevated risk of NHL or NHL subtypes. These findings are among the first to suggest links between DDT, lindane, permethrin, diazinon and terbufos with NHL subtypes.

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Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and the Supporting Information files.

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Competing Interests: The authors have the following interests. Joseph Barker and Dennis W. Buckman are employed by IMS, Inc. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials, as detailed online in the guide for authors.

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Introduction

Since the 1970s, epidemiologic studies of non-Hodgkin lymphoma (NHL) and multiple myeloma (MM) have shown increased risk among farmers and associations with the type of farming practiced [1–6]. While farmers are exposed to many agents that may be carcinogenic [7]; there has been a particular focus on pesticides. Studies from around the world have suggested increased risk of NHL or MM [8,9] and other NHL subtypes [10] in relation to the use of specific pesticides in different functional classes (i.e., insecticides, fungicides, fumigants and herbicides). A meta-analysis of 13 case-control studies published between 1993–2005 observed an overall significant meta-odds ratio (OR) between occupational exposure to pesticides and NHL (OR = 1.35; 95% CI: 1.2–1.5) [11]. This risk was greater among individuals with more than 10 years of exposure (OR = 1.65; 95% CI: 1.08–1.95) [11], but the meta-analysis lacked details about the use of specific pesticides and other risk factors [11]. Although the International Agency for Research on Cancer (IARC) has classified "Occupational exposures in spraying and application of non-arsenical insecticides" as "probably carcinogenic to humans", the human

evidence for the 17 individual pesticides evaluated in this monograph was determined to be inadequate for nine and there were no epidemiological studies for eight pesticides [12]. Since then, more studies have focused on cancer risk from specific pesticides, although the information is still relatively limited for many cancer-pesticide combinations [8,9].

To help fill the current information gap we evaluated the relationships between the use of specific insecticides, fungicides and fumigants and NHL in the Agricultural Health Study (AHS), a prospective cohort of licensed private (i.e., mostly farmer) and commercial pesticide applicators. Because the etiology of NHL and its B and T cell subtypes may differ by cell type[13], we also evaluated risk by subtype while controlling for potential confounding factors suggested from the literature [13], and the AHS data.

Novelty and Impact

These findings on occupationally exposed pesticide applicators with high quality exposure information are among the first to suggest links between DDT, lindane, permethrin, diazinon and terbufos and specific NHL subtypes in a prospective cohort study.

Materials and Methods

Study Population

The AHS is a prospective cohort study of 52,394 licensed private pesticide applicators (mostly farmers) in Iowa and North Carolina and 4,916 licensed commercial applicators in Iowa (individuals paid to apply pesticides to farms, homes, lawns, etc.), and 32,346 spouses of private applicators. Only applicators are included in this analysis. The cohort has been previously described in detail [14,15] and study questionnaires are available on the AHS website (www.aghealth.nih.gov). Briefly, individuals seeking licenses to apply restricted use pesticides were enrolled in the study from December 1993 through December 1997 (82% of the target population enrolled). At enrollment, subjects did not sign a written informed consent form. However, the cover letter of the questionnaire booklet informed subjects of the voluntary nature of participation, the ability to not answer any question, and it provided an assurance of confidentiality (including a Privacy Act Notification statement). The letter also included a written summary of the purpose of research, time involved, benefits of research, and a contact for questions about the research. The cover letter to the take-home questionnaire included all of the above and also informed the participant that they had the right to withdraw at any time. Finally, subjects were specifically informed that their contact information (including Social Security Number) would be used to search health and vital records in the future. The participants provided consent by completing and returning the questionnaire booklet. These documents and procedures were approved in 1993 by all relevant institutional review boards (i.e., National Cancer Institute Special Studies Institutional Review Board, Westat Institutional Review Board, and the University of Iowa Institutional Review Board-01).

Excluded from this analysis were study participants who had a history of any cancer at the time of enrollment (n = 1094), individuals who sought pesticide registration in Iowa or North Carolina but did not live in these states at the time of registration (n = 341) and were thus outside the catchment area of these cancer registries and individuals that were missing information on potential confounders (i.e., race or total herbicides application days [n = 1,569]). This resulted in an analysis sample of 54,306. We obtained cancer incidence information by regular linkage to the population-based cancer registry files in Iowa and North Carolina. In addition, we linked cohort members to state mortality registries of Iowa and North Carolina and the nation-wide National Death Index to determine vital status, and to the nation-wide address records of the Internal Revenue Service, state-wide motor vehicle registration files, and pesticide license registries of state agricultural departments to determine residence in Iowa or North Carolina. The current analysis included all incident primary NHL, as well as CLL and MM (which are now classified as NHL) [13] ($n = 523$) diagnosed from enrollment (1993–1997) through December 31, 2010 in North Carolina and from enrollment (1993–1997) through December 31, 2011 in Iowa, the last date of complete cancer incidence reports in each state. We ended follow-up and person-year accumulation at the date of diagnosis of any cancer, death, movement out of state, or December 31, 2010 in North Carolina and December 31, 2011 in Iowa, whichever was earlier.

Tumor Characteristics

Information on tumor characteristics was obtained from state cancer registries. We followed the definition of NHL and six subtypes of NHL used by the Surveillance Epidemiology and End Results (SEER) coding scheme [16] which was based on the Pathology Working Group of the International Lymphoma Epidemiology Consortium (ICD-O-3 InterLymph modification) classification (Table S1 in File S1, [17], i.e., 1. Small B-cell lymphocytic lymphomas (SLL)/chronic B-cell lymphocytic lymphomas (CLL)/mantle-cell lymphomas (MCL); 2. Diffuse large B-cell lymphomas; 3. Follicular lymphomas; 4. 'Other B-cell lymphomas' consisting of a diverse set of B-cell lymphomas; 5. Multiple myeloma; and 6. T-cell NHL and undefined cell type). There were too few T-cell NHL cases available for analysis [n = 19] so this cell type was not included in the subtype analysis). The ICD-O-3 original definition (used in many earlier studies of pesticides and cancer) of NHL [18] was also evaluated in relation to pesticide exposure to allow a clearer comparison of our results with previous studies.

Exposure Assessment

Initial information on lifetime use of 50 specific pesticides (Table S2 in File S1), including 22 insecticides, 6 fungicides and 4 fumigants was obtained from two self-administered questionnaires [14,15] completed during cohort enrollment (Phase 1). All 57,310 applicators completed the first enrollment questionnaire, which inquired about ever/never use of 50 pesticides, as well as duration (years) and frequency (average days/year) of use for a subset of 22 pesticides including 9 insecticides, 2 fungicides and 1 fumigant. In addition, 25,291 (44%) of the applicators returned the second (take-home) questionnaire, which inquired about duration and frequency of use for the remaining 28 pesticides, including 13 insecticides, 4 fungicides and 3 fumigants.

A follow-up questionnaire, which ascertained pesticide use since enrollment, was administered approximately 5 years after enrollment (1999–2005, Phase 2) and completed by 36,342 (63%) of the original participants. The full text of the questionnaires is available at www.aghealth.nih.gov. For participants who did not complete the Phase 2 questionnaire (20,968 applicators, 37%), a data-driven multiple imputation procedure which used logistic regression and stratified sampling [19] was employed to impute use of specific pesticides in Phase 2. Information on pesticide use from Phase 1, Phase 2 and imputation for Phase 2 was used to construct three cumulative exposure metrics: (i) lifetime days of pesticide use (i.e., the product of years of use of a specific pesticide and the number of days used per year); (ii) intensity-weighted lifetime days of use (i.e., the product of lifetime days of use and a measure of exposure

intensity) and (iii) ever/never use data for each pesticide. Intensity was derived from an exposure-algorithm, which was based on exposure measurements from the literature and individual information on pesticide use and practices (e.g., whether or not they mixed pesticides, application method, whether or not they repaired equipment and use of personal protective equipment) obtained from questionnaires completed by study participants [20].

Statistical Analyses

We divided follow-up time into 2-year intervals to accumulate person-time and update time-varying factors, such as attained age and pesticide use. We fit Poisson models to estimate rate ratios (RRs) and 95% confidence intervals (95% CI) to evaluate the effects of pesticide use on rates of overall NHL and the five NHL subtypes.

We evaluated pesticides with 15 or more exposed cases of total NHL, thereby excluding aluminum phosphide, carbon tetrachloride/carbon disulfide, ethylene dibromide, trichlorfon, and ziram leaving 26 insecticides, fungicides and fumigants for analysis (permethrin for animal use and crop use were combined into one category, all insecticides, fungicides and fumigants are listed in Table S2 in File S1). For each pesticide, we evaluated ever vs. never exposure, as well as tertiles of exposure which were created based on the distribution of all NHL exposed cases and compared to those unexposed. In the NHL subtype analysis and in circumstances where multiple pesticides were included in the model we categorized exposure for each pesticide into unexposed (i.e., never users) and two exposed groups (i.e., low and high) separated at the median exposure level. The number of exposed cases included in the ever/never analysis and in the trend analysis can differ because of the lack of information necessary to construct quantitative exposure metrics for some individuals.

Several lifestyle and demographic factors associated with NHL in the AHS cohort or previously suggested as possible confounders in the NHL literature[13] were evaluated as potential confounders in this analysis. These included: age at enrollment, gender, race, state, license type, education, autoimmune diseases, family history of lymphoma in first-degree relatives, body mass index, height, cigarette smoking history, alcohol consumption per week and several occupational exposures[1–13] including number of livestock, cattle, poultry, whether they raised poultry, hogs or sheep, whether they provided veterinary services to their animals, number of acres planted, welding, diesel engine use, number of years lived on the farm, total days of any pesticide use, and total days of herbicide use. However, since most of these variables did not change the risk estimates for specific pesticides, we present results adjusted for age, race, state and total days of herbicide use, which impacted risk estimates by more than 10% for some subtypes. We also performed analyses adjusting for specific insecticides, fungicides and fumigants shown to be associated with NHL or a specific NHL subtype in the current analysis. Tests for trend used the median value of each exposure category. All tests were two-sided and conducted at $\alpha = 0.05$ level. Analysis by NHL subtype was limited to insecticides, fungicides, and fumigants with 6 or more exposed cases.

We also fit polytomous logit models, where the dependent variable was a five-level variable (i.e., five NHL subtypes) and a baseline level (i.e., no NHL) to estimate exposure-response odds ratios (ORs) and 95% confidence intervals (CIs) for each subtypes of NHL. We then used polytomous logit models to estimate exposure-response trend while adjusting for age, state, race and total days of herbicide use, as in the Poisson models, and tested homogeneity among the 5 NHL subtypes.

Poisson models were fit using the GENMOD procedure and polytomous logit models were fit using the LOGISTIC procedure of the SAS 9.2 statistical software package (SAS Institute, Cary, NC). Summary estimates of NHL and NHL subtype risks for both Poisson models and polytomous logit models incorporated imputed data and were calculated along with standard error estimates, confidence intervals, and p-values, using multiple imputation methods implemented in the MIANALYZE procedure of SAS 9.2.

We also evaluated the impact of the additional pesticide exposure information imputed for Phase 2 on risk estimates. We compared risk estimates for those who completed both the phase 1 enrollment and take-home questionnaires and the phase 2 questionnaires (n = 17,545) with risk estimates obtained from the combined completed questionnaire data plus the imputed phase 2 data (n = 54,306). We also explored the effect of lagging exposure data 5 years because recent exposures may not have had time to have an impact on cancer development. For comparison to previous studies, we also assessed the exposure-response association for NHL using the original ICD-O-3 definition of NHL [18] and the new definition [16] in Table S3 in File S1. Unless otherwise specified, reported results show un-lagged exposure information from both Phase 1 and Phase 2 including Phase 2 imputed data for lifetime exposure-days and intensity-weighted lifetime days of use and NHL defined by the InterLymph modification of ICD-O-3 [17]. Data were obtained from AHS data release versions P1REL201005.00 (for Phase 1) and P2REL201007.00 (for Phase 2).

Results

The 54,306 applicators in this analysis contributed 803,140 person-years of follow-up from enrollment through December 31, 2010 in North Carolina and December 31, 2011 in Iowa (Table 1). During this period, there were 523 incident cases of NHL, including 148 SLL/CLL/MCL, 117 diffuse large B-cell lymphomas, 67 follicular lymphomas, 53 'other B-cell lymphomas' (consisting of a diverse set of B-cell lymphomas) and 97 cases of MM. Another 41 cases consisting of T-cell lymphomas (n = 19) and non-Hodgkin lymphoma of unknown lineage (n = 22) were excluded from cell type-specific analyses because of small numbers of cases with identified cell types. Between enrollment and the end of follow-up, 6,195 individuals were diagnosed with an incident cancer other than NHL, 4,619 died without a record of cancer in the registry data, and 1,248 cohort members left the state and could not be followed-up for cancer. Person-years of follow-up accumulated for all of these study participants after enrollment until they were censored for the incident cancer, death or moving out of the state (data not shown). The risk of NHL increased significantly and monotonically with age in the AHS cohort in this analysis (p = 0.001) and age-adjusted risks were significant for state and NHL overall and race for multiple myeloma (data not shown). Total days of herbicide use had a small but significant effect on the risk of some NHL subtypes, but not on NHL overall. No other demographic or occupational factors showed evidence of confounding so they were not included in the final models.

In Table 2 we present ever/never results for 26 insecticides, fungicides and fumigants by total NHL and by NHL subtype adjusted for age, race, state and herbicide use (total life-time days). Terbufos was the only pesticide associated with an increased risk of total NHL in the ever/never use analysis (RR = 1.2 [1.0–1.5]), although the trend for increasing use and risk of total NHL was not significant (p trend = 0.43) (Table 3). In contrast, there were a few chemicals that were not associated with ever/never use, but

Table 1. Baseline characteristics of AHS study participants in the NHL incidence analysis[1,2].

Variables	All NHL cases (%)	Cohort Person-years.
Age at Enrollment		
<45	84 (16.1)	426,288
45–49	51 (9.8)	101,018
50–54	75 (14.3)	84,998
55–59	90 17.2)	74,440
60–64	78 (14.9)	56,978
65–69	79 (15.1)	35,071
≥70	66 (12.6)	24,347
Race		
White	509 (97.3)	787,799
Black	14 (2.7)	15,341
State		
IA	332 (63.5)	537,252
NC	191 (36.5)	265,888
Lifetime Total Herbicide Exposure Days		
0–146 days	170 (32.5)	251,401
147–543 days	169 (32.3)	273,107
544–2453 days	184 (35.2)	278,632

[1]During the period from enrollment (1993–1997) to December 31, 2010 in NC and December 31, 2011 in Iowa.
[2]Individuals with missing ever/never exposure information or missing confounding variable information were not included in the table.
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did show evidence of an exposure-response association. Lindane was the only pesticide that showed a statistically significant increasing trend in risk for NHL with both exposure metrics, for lifetime-days of lindane use the RR were = 1.0 (ref), 1.2 (0.7–1.9), 1.0 (0.6–1.7), 2.5 (1.4–4.4); p trend = 0.004 and intensity-weighted lifetime-days of use the: RR were: = 1.0 (ref), 1.3 (0.8–2.2), 1.1 (0.7–1.8), 1.8 (1.0–3.2); p trend = 0.04. DDT showed a significant trend for NHL risk with life-time days of use RR = 1.0 (ref), 1.3 (0.9–1.8), 1.1 (0.7–1.7), 1.7 (1.1–2.6); p trend = 0.02, while the intensity weighted lifetime days of use of DDT was of borderline significance: RR = 1.0 (ref), 1.2 (0.8–1.8), 1.1 (0.8–1.7), 1.6 (1.0–2.3); p trend = 0.06. The number of lifetime days of use of lindane and DDT was weakly correlated (coefficient of determination = 0.04), and the pattern of NHL risk showed little change when both were included in the model. The results for lindane adjusted for DDT were, RR = 1.0 (ref), 1.2 (0.7–2.0), 1.0 (0.5–1.8), 1.6 (0.9–3.3); p trend = 0.07 and the results for DDT adjusted for lindane were, RR = 1.0 (ref), 1.3 (0.9–2.0), 0.9 (0.6–1.6), 1.6 (0.9–2.6); p trend = 0.08).

We also evaluated pesticides by NHL sub-type. In the ever/never analyses (Table 2), permethrin was significantly associated with multiple myeloma, RR = 2.2 (1.4–3.5) and also demonstrated an exposure-response trend (RR = 1.0 (ref), 1.4 (0.8–2.7), 3.1 (1.5–6.2); p trend = 0.002) (Table 4). Similarly, there was an elevated risk of SLL/CLL/MCL with terbufos in ever/never analyses RR = 1.4 (0.97–2.0) and an exposure response trend (RR = 1.0 (ref), 1.3 (0.8–2.0), 1.6 (1.0–2.5); p trend = 0.05). For follicular lymphoma, lindane showed an elevated but non-significant association for ever use, RR = 1.7 (0.96–3.2) and a significant exposure-response association (RR = 1.0 (ref), 4.9 (1.9–12.6), 3.6 (1.4–9.5); p trend = 0.04). There were also two chemicals with evidence of exposure-response that were not associated with specific subtypes in the ever/never analyses: DDT (Dichlorodiphenyltrichloroethane) with SLL/CLL/MCL (RR = 1.0 (ref), 1.0 (0.5–1.8), 2.6 (1.3–4.8; p trend = 0.04); and diazinon with follicular lymphoma (RR = 1.0 (ref), 2.2 (0.9–5.4), 3.8 (1.2–11.4); p trend = 0.02) (Table 4).

The pattern of increased CLL/SLL/MCL risk with increased use of DDT and terbufos remained after both insecticides were placed in our model concurrently. CLL/SLL/MCL risk increased with DDT use (RR = 1.0 (ref), 0.9 (0.5–4.7); 2.4 (1.1–4.7); p trend = 0.04), and a pattern of increased CLL/SLL/MCL risk was also observed with terbufos use (RR = 1.0 (ref), 1.1 (0.6–2.1), 1.7 (0.9–3.3) p trend = 0.07), although the trend was not significant for terbufos. Similarly, the pattern of increased follicular lymphoma risk with lindane use and diazinon use remained after both insecticides were placed in our model concurrently. Follicular lymphoma risk increased with diazinon use (RR = 1.0 (ref), 4.1 (1.5–11.1); 2.5 (0.9–7.2); p trend = 0.09), and a similarly, pattern of increased follicular lymphoma risk was observed with lindane use (RR = 1.0 (ref), 1.6 (0.6–4.1), 2.6 (0.8–8.3) p trend = 0.09), although neither remained statistically significant (Table 4).

Three chemicals showed elevated risks in ever/never analyses for certain subtypes, with no apparent pattern in exposure-response analyses: metalaxyl and chlordane with SLL/CLL/MCL, RR = 1.6 (1.0–2.5) and RR = 1.4 (0.97–2.0) respectively, and methyl bromide with diffuse large B-cell lymphoma RR = 1.9 (1.1–3.3). Although there was evidence of association by subtype, and polytomous logit models indicated homogeneity across subtypes for lindane (p = 0.54), DDT (p = 0.44) and any other pesticide evaluated in this study (e.g., permethrin (p = 0.10), diazinon (p = 0.09), terbufos (p = 0.63), (last column in Table 4).

There was no evidence of confounding of the total NHL associations with either lindane or DDT. We also calculated RR for those who completed both the phase 1 enrollment and take-home questionnaires and the phase 2 questionnaire (n = 17,545) and found no meaningful difference in the RR that also included imputed exposures, although there was an increase in precision of

Table 2. Pesticides exposure (ever/never) and adjusted Relative Risk of total NHL and NHL Subtype[1].

Insecticide												
	Total NHL Cases[2]		SLL/CLL/MCL Cases[2]		Diffuse Large B-Cell Cases[2]		Follicular B-Cell Cases[2]		Other B-cell Cases[2]		Multiple Myeloma Cases[2]	
Pesticide (chemical-functional class)	Ever/Never Exposed	RR[3,4] (95% CI)	Ever/Never Exposed	RR[3,4] (95% CI)	Ever/Never Exposed	RR[3,4] (95% CI)	Ever/Never Exposed	RR[3,4] (95% CI)	Ever/Never Exposed	RR[3,4] (95% CI)	Ever/Never Exposed	RR[3,4] (95% CI)
Aldicarb	47/435	1	14/124	1.1	8/98	0.7	6/54	0.9	7/41	1.6	10/82	1.2
(carbamate-insecticide)		(0.7–1.4)		(0.6–1.8)		(0.4–1.5)		(0.3–2.2)		(0.7–3.5)		(0.6–2.2)
Carbofuran	147/317	1.1	48/86	1.2	26/78	0.8	18/39	1	13/31	0.8	31/56	1.3
(carbamate-insecticide)		(0.9–1.3)		(0.8–1.8)		(0.5–1.3)		(0.5–1.7)		(0.4–1.6)		(0.8–2.1)
Carbaryl	272/225	1	75/66	1	58/53	0.8	37/24	0.8	24/28	0.9	58/34	0.9
(carbamate-insecticide)		(0.8–1.2)		(0.7–1.5)		(0.5–1.3)		(0.5–1.3)		(0.5–1.6)		(0.6–1.4)
Chlorpyrifos	210/300	1	62/84	1	44/70	0.9	32/33	1.3	21/31	0.8	36/58	1
(organophosphate-insecticide)		(0.8–1.2)		(0.7–1.4)		(0.6–1.4)		(0.8–2.2)		(0.5–1.5)		(0.6–1.5)
Coumaphos	46/411	1.1	15/120	1.2	10/93	1	8/48	1.6	5/40	xxx	7/78	1
(organophos-phate-insecticide)		(0.8–1.5)		(0.7–2.1)		(0.5–2.1)		(0.8–3.5)				(0.1–2.1)
DDVP	55/407	1.1	13/124	0.8	10/93	1	8/48	1.3	6/39	1	12/73	1.7
(dimethyl phosphate-insecticide)		(0.8–1.5)		(0.5–1.5)		(0.5–1.9)		(0.6–2.7)		(0.4–2.4)		(0.9–3.2)
Diazinon	144/342	1	46/93	1.3	30/78	0.9	22/38	1.3	12/37	0.8	27/64	1
(organophosphorous-insecticide)		(0.8–1.3)		(0.9–1.9)		(0.6–1.4)		(0.7–2.3)		(0.4–1.6)		(0.6–1.6)
Fonofos	115/349	1.1	35/100	1.1	25/81	1.2	13/45	0.9	15/30	1.3	19/66	1.3
(organophosphorous-insecticide)		(0.9–1.4)		(0.7–1.6)		(0.7–1.9)		(0.5–1.7)		(0.7–2.5)		(0.8–2.3)
Malathion	332/163	0.9	99/43	1	72/37	0.9	46/14	1.3	30/21	0.6	61/32	0.9
(organophosphorous-insecticide)		(0.8–1.1)		(0.7–1.4)		(0.6–1.4)		(0.7–2.4)		(0.3–1.0)		(0.6–1.5)
Parathion (ethyl or methyl)	69/411	1.1	20/117	1	14/91	1	10/48	1.1	7/44	1.1	14/77	1
(organophosphorous insecticide		(0.8–1.4)		(0.7–1.4)		(0.6–1.4)		(0.8–1.5)		(0.7–1.5)		(0.8–1.5)
Permethrin (animal and crop applications)	112/363	1.1	32/106	1	18/81	0.7	18/81	1.1	9/14	0.8	20/72	**2.2**
(pyrethroid insecticide)		(0.8–1.3)		(0.6–1.5)		(0.4–1.2)		(0.6–2.0)		(0.4–1.6)		**(1.4–3.5)**
Phorate	160/325	1	53/87	1.1	31/76	0.9	20/40	0.9	19/31	0.9	26/64	1
(organophosphorous-insecticide)		(0.8–1.2)		(0.8–1.6)		(0.5–1.3)		(0.5–1.6)		(0.5–1.6)		(0.6–1.7)
Terbufos	201/267	**1.2**	64/72	1.4	42/63	1.1	31/26	1.2	26/19	1.8	32/59	1.2
(organophosphorous-insecticide)		**(1.0–1.5)**		(0.97–2.0)		(0.7–1.7)		(0.7–2.1)		(0.94–3.2)		(0.7–1.9)
Chlorinated Insecticides												
Aldrin	116/364	0.9	53/99	0.9	15/91	0.8	13/45	0.8	12/37	0.6	29/62	1.5
(chlorinated insecticide)		(0.7–1.1)		(0.6–1.4)		(0.4–1.6)		(0.4–1.6)		(0.3–1.3)		(0.9–2.5)
Chlordane	136/344	1	49/90	1.4	20/86	0.6	18/41	1.2	13/36	1	31/60	1.2
(chlorinated insecticide)		(0.8–1.3)		(0.99–2.1)		(0.4–1.0)		(0.7–2.1)		(0.7–2.0)		(0.8–1.9)
DDT	182/300	1	59/79	1.2	34/73	0.8	18/41	0.9	20/31	1.1	40/50	1.1

Table 2. Cont.

Insecticide												
	Total NHL Cases[2]		SLL/CLL/MCL Cases[2]		Diffuse Large B-Cell Cases[2]		Follicular B-Cell Cases[2]		Other B-cell Cases[2]		Multiple Myeloma Cases[2]	
Pesticide (chemical-functional class)	Ever/Never Exposed	RR[3,4]	Ever/Never Exposed	RR[3,4]	Ever/Never Exposed	RR[3,4]	Ever/Never Exposed	RR[3,4]	Ever/Never Exposed	RR[3,4]	Ever/Never Exposed	RR[3,4]
		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)
(chlorinated insecticide)		(0.8–1.3)		(0.8–1.8)		(0.5–1.3)		(0.5–1.6)		(0.6–2.1)		(0.7–1.8)
Dieldrin	35/442	0.9	5/130	xxx	4/101	xxx	4/54	xxx	7/42	1	10/81	0.9
(chlorinated insecticide)		(0.6–1.2)								(0.7–2.0)		(0.5–1.4)
Heptachlor	90/384	1	33/104	1.1	10/95	1.1	9/48	1.1	13/36	0.9	17/72	1.1
(chlorinated insecticide)		(0.7–1.2)		(0.7–3.0)		(0.3–3.1)		(0.5–3.2)		(0.5–2.7))		(0.6–2.0)
Lindane	85/396	1	27/113	1.2	12/95	0.6	16/41	1.7	9/40	0.7	13/73	1.1
(chlorinated insecticide)		(0.8–1.2)		(0.6–1.5)		(0.3–1.1)		(0.96–3.2)		(0.4–1.2)		(0.5–2.0)
Toxaphene	79/397	1	21/116	0.9	14/90	0.8	9/47	1	10/40	1.1	19/73	1.1
(chlorinated insecticide)		(0.7–1.2)		(0.5–1.5)		(0.4–1.4)		(0.6–2.0)		(0.6–2.0)		(0.6–1.9)
Fungicides												
Benomyl	54/428	1.1	18/123	1.2	12/95	1.1	4/51	xxx	4/51	xxx	11/80	1.1
(carbamate fungicide)		(0.8–1.5)		(0.7–2.0)		(0.6–1.9)						(0.6–2.0)
Captan	60/406	1.1	18/118	1.1	12/91	0.9	5/51	xxx	6/39	1.1	12/76	1.2
(phthalimide fungicide)		(0.8–1.4)		(0.6–1.8)		(0.5–1.8)				(0.5–2.7)		(0.6–2.2)
Chloro-thalonil	35/474	0.8	9/135	0.9	6/107	0.5	5/60	xxx	2/50	xxx	11/84	1.2
(poly-chlorinated aromatic thalonitrile fungicide)		(0.5–1.2)		(0.4–1.9)		(0.2–1.3)						(0.6–2.3)
Maneb/	44/437	0.9	13/127	1.1	12/95	1.1	4/60	xxx	5/49	xxx	10/79	0.8
Mancozeb		(0.7–1.3)		(0.6–2.1)		(0.6–2.1)						(0.4–1.7)
(dithiocarbamate fungicide)												
Metalaxyl	108/381	1	34/106	**1.6**	27/82	1.1	10/48	0.7	10/40	0.9	21/71	0.8
(acylalanine fungicide)		(0.8–1.3)		**(1.0–2.5)**		(0.6–1.8)		(0.4–1.4)		(0.4–1.7)		(0.4–1.3)
Fumigant												
Methyl bromide	85/425	1.1	18/126	0.9	28/86	**1.9**	7/58	0.6	8/44	2.2	19/76	1
(methyl halide fumigant)		(0.9–1.5)		(0.5–1.7)		**(1.1–3.3)**		(0.2–1.4)		(0.9–5.7)		(0.6–1.8)

[1]During the period from enrollment (1993–1997) to December 31, 2010 in NC and December 31, 2011 in Iowa.
[2]Numbers of cases by NHL subtype do not sum to total number of NHL cases (n = 523) due to missing data.
[3]Adjusted RR: age (<45, 45–49, 50–54, 55–59, 60–64, 65–69, ≥70), State (NC vs. IA), Race (White vs. Black), AHS herbicides (tertiles of total herbicide use-days). Statistically significant RR and 95% confidence limits are bolded.
[4]RR was not calculated if the number of exposed cases in a pesticide-NHL subtype cell was <6 and the missing RR was marked with an XXX. Statistically significant RRs and 95% confidence limits are bolded.
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Table 3. Pesticide exposure (lifetime-days & intensity weighted life-time days) and adjusted risks of total NHL incidence[1].

Insecticides						
Pesticide (chemical-functional class)	**NHL Cases[2]**	**Non-Cases[2]**	**RR[3,4] (95% CI) by Total Days of Exposure**	**NHL**	**Non-Cases**	**RR[3,4] (95% CI)**
[days of lifetime exposure for each category]				**Cases[2,**		**Intensity-weighted days of exposure**
Aldicarb (carbamate-insecticide)						
None	238	21557	1.0 (ref)	238	21557	1.0 (ref)
Low [≤8.75]	7	633	1.1 (0.5–2.3)	6	383	1.3 (0.6–3.3))
Medium [>8.75–25.5]	5	522	0.9 (0.3–2.5)	6	853	0.9 (0.4–1.9)
High [>25.5–224.75]	5	1266	0.5 (0.2–1.3)	5	1183	0.5 (0.2–1.3)
			P trend = 0.23			P trend = 0.22
Carbofuran (carbamate-insecticide)						
None	317	36296	1.0 (ref)	317	36296	1.0 (ref)
Low [≤8.75]	63	4775	1.2 (0.9–1.6)	46	3695	1.2 (0.9–1.6)
Medium [>8.75–38.75]	32	3648	0.8 (0.6–1.2)	46	4590	1.0 (0.7–1.3)
High [>38.75–767.25]	44	4370	0.97 (0.7–1.4)	45	4477	1.0 (0.7–1.4)
			P trend = 0.69			P trend = 0.74
Carbaryl (carbamate-insecticide)						
None	128	12864	1.0 (ref)	128	12864	1.0 (ref)
Low [≤8.75]	54	4128	1.1 (0.7–1.6)	46	3962	1.0 (0.7–1.5)
Medium [8.75–56]	43	5096	0.9 (0.6–1.2)	45	4433	0.9 (0.7–1.5)
High [>56–737.5]	39	3281	1.0 (0.7–1.6)	44	4029	1.0 (0.6–1.5)
			P trend = 0.87			P trend = 0.94
Chlorpyrifos (organophosphate-insecticide)						
None	300	30393	1.0 (ref)	300	30393	1.0 (ref)
Low [≤8.75]	71	6493	1.1 (0.9–1.5)	61	6383	1.1 (0.8–1.4)
Medium [>8.75–44]	65	6892	1.1 (0.8–1.4)	60	7549	0.9 (0.7–1.2)
High [>44–767.25]	67	9380	0.8 (0.6–1.1)	60	7044	1.0 (0.7–1.3)
			P trend = 0.11			P trend = 0.85
Coumaphos (organophosphate-insecticide)						
None	411	44846	1.0 (ref)	411	44846	1.0 (ref)
Low [<8.75]	16	1510	1.0 (0.6–1.7)	15	1132	1.3 (0.8–2.1)
Medium [>8.75–38.75]	14	1076	1.2 (0.7–2.1)	14	1452	1.0 (0.6–1.6)
High [>38.75–1627.5]	13	1175	1.2 (0.7–2.0)	14	1170	1.2 (0.7–2.1)
			P for trend = 0.50			P trend = 0.48
DDVP (dimethyl phosphate-insecticide)						
None	407	44551	1.0 (ref)	407	44551	1.0 (ref)
Low [≤8.75]	19	1342	1.4 (0.9–2.1)	18	1281	1.4 (0.9–2.3)
Medium [>8.75–87.5]	17	1519	1.2 (0.7–1.9)	18	1633	1.1 (0.7–1.8)
High [>87.5–2677.5]	17	1893	0.9 (0.6–1.5)	17	1824	1.0 (0.6–1.6)
			P trend = 0.78			P trend = 0.83
Diazinon (organophosphorous-insecticide)						
None	187	17943	1.0 (ref)	187	17943	1.0 (ref)
Low [≤8.75]	28	2506	1.1 (0.7–1.6)	23	2047	1.1 (0.7–1.8)
Medium [>8.75–25]	19	1515	1.0 (0.6–1.8)	24	2246	0.9 (0.5–1.5)
High [>25–457.25]	23	1990	1.2 (0.7–1.9)	22	1708	1.3 (0.8–2.1)
			P trend = 0.52			P trend = 0.33

Table 3. Cont.

Insecticides						
Pesticide (chemical-functional class)	**NHL Cases[2]**	**Non-Cases[2]**	**RR[3,4] (95% CI) by Total Days of Exposure**	**NHL**	**Non-Cases**	**RR[3,4] (95% CI)**
[days of lifetime exposure for each category]				**Cases[2,]**		**Intensity-weighted days of exposure**
Fonofos (organophosphorous-insecticide)						
None	349	39570	1.0 (ref)	349	39570	1.0 (ref)
Low [≤20]	47	3812	1.3 (0.96–1.8)	37	2906	1.4 (0.97–1.9)
Medium [>20–50.75]	28	2819	1.1 (0.7–1.6)	38	3487	1.1 (0.8–1.6)
High [>50.75–369.75]	37	3385	1.1 (0.7–1.5)	36	3606	1.0 (0.7–1.4)
			P trend = 0.83			P trend = 0.87
Malathion (organophosphorous-insecticide)						
None	90	8368	1.0 (ref)	90	8368	1.0 (ref)
Low [≤8.75]	75	7284	0.97 (0.7–1.3)	60	5535	1.0 (0.7–1.4)
Medium [>8.75–38.75]	47	5779	0.7 (0.5–1.1)	59	6899	0.8 (0.6–1.1)
High [>38.75–737.5]	57	5037	0.9 (0.6–1.3)	59	5588	0.9 (0.6–1.2)
			P trend = 0.63			P trend = 0.46
Parathion (ethyl or methyl) (organophosphorous insecticide)						
None	228	21457	1.0 (ref)	228	21457	1.0 (ref)
Low [≤8.75]	9	693	1.0 (0.5–2.0)	7	612	0.9 (0.4–2.0)
Medium [>8.75–24.5]	6	351	1.4 (0.6–3.2)	8	462	1.4 (0.7–2.9)
High [>.24.5–1237.5]	6	652	0.8 (0.3–1.8)	6	621	0.8 (0.4–1.9)
			P trend = 0.64			P trend = 0.74
Permethrin (animal and crop applications)						
(pyrethroid insecticide)						
None	371	37496	1.0 (ref)	371	37496	1.0 (ref)
Low [≤8.75]	38	4315	1.1 (0.8–1.5)	33	4263	0.9 (0.6–1.3)
Medium [>8.75–50.75]	31	4611	0.8 (0.5–1.2)	33	4200	1.0 (0.7–1.4)
High [>50.75–1262.25]	33	4121	1.2 (0.8–1.7)	32	4553	1.0 (0.7–1.5)
			P trend = 0.54			P trend = 0.99
Phorate (organophosphorous-insecticide)						
None	171	16834	1.0 (ref)	171	16834	1.0 (ref)
Low [≤8.75]	27	2621	0.8 (0.5–1.2)	26	2320	0.9 (0.6–1.4)
Medium [8.75–24.5]	33	1819	1.4 (0.96–2.1)	27	1951	1.1 (0.7–1.7)
High [>24.5–224.75]	18	2246	0.6 (0.4–1.1)	25	2409	0.8 (0.5–1.3)
			P trend = 0.25			P trend = 0.44
Terbufos (organophosphorous-insecticide)						
None	267	31076	1.0 (ref)	267	31076	1.0 (ref)
Low [≤24.5]	82	8410	1.2 (0.9–1.5)	64	6895	1.1 (0.9–1.5)
Medium [>24.5–56]	54	3925	1.6 (1.2–2.1)	64	4642	1.6 (1.2–2.2)
High [>56–1627.5]	57	6080	1.1 (0.8–1.5)	63	6842	1.1 (0.8–1.5)
			P trend = 0.43			P trend = 0.44
Chlorinated Insecticides						
Aldrin (chlorinated insecticide)						
None	193	19743	1.0 (ref)	193	19743	1.0 (ref)
Low [≤8.75]	27	1613	0.9 (0.6–1.4)	20	1212	0.9 (0.6–1.4)
Medium [>8.75–24.5]	16	1002	0.8 (0.5–1.3)	20	1279	0.8 (0.5–1.3)

Table 3. Cont.

Pesticide (chemical-functional class) [days of lifetime exposure for each category]	NHL Cases[2]	Non-Cases[2]	RR[3,4] (95% CI) by Total Days of Exposure	NHL Cases[2,]	Non-Cases	RR[3,4] (95% CI) Intensity-weighted days of exposure
Insecticides						
High [>24.5–457.25]	17	903	0.9 (0.5–1.5)	19	1026	0.9 (0.6–1.5)
			P trend = 0.58			P trend = 0.74
Chlordane (chlorinated insecticide)						
None	179	19115	1.0 (ref)	179	19115	1.0 (ref)
Low [≤8.75]	47	2687	1.3 (0.97–1.9)	23	1303	1.4 (0.9–2.2)
Medium[5]	0	0	xxx	24	1747	1.0 (0.6–1.5)
High [>8.75–1600]	23	1450	1.1 (0.7–1.7)	22	1085	1.4 (0.9–2.2)
			P trend = 0.43			P trend = 0.16
DDT (chlorinated insecticide)						
None	152	18543	1.0 (ref)	152	18543	1.0 (ref)
Low [≤8.75]	43	2121	1.3 (0.9–1.8)	33	1601	1.2 (0.8–1.8)
Medium [>8.75–56]	28	1598	1.1 (0.7–1.7)	32	1760	1.1 (0.8–1.7)
High [>56–1627.5]	27	953	1.7 (1.1–2.6)	32	1305	1.6 (1.0–2.3)
			P trend = 0.02			P trend = 0.06
Dieldrin (chlorinated insecticide)						
None	235	22510	1.0 (ref)	235	22510	1.0 (ref)
Low [≤8.75]	7	472	0.7 (0.3–1.5)	6	363	0.8 (0.4–1.8)
Medium [>8.75–24.5]	8	154	2.3 (1.1–4.7)	5	106	2.2 (0.9–5.3)
High [>24.5–224.75]	2	140	0.7 (0.2–2.9)	5	298	0.8 (0.3–2.0)
			P trend = 0.47			P trend = 0.84
Heptachlor (chlorinated insecticide)						
None	205	20844	1.0 (ref)	205	20844	1.0 (ref)
Low [≤8.75]	21	1261	1.0 (0.6–1.6)	15	1110	0.8 (0.5–1.4)
Medium [>8.75–24.5]	18	679	1.5 (0.9–2.4)	16	425	2.0 (1.2–3.4)
High [>24.5–457.25]	7	600	0.7 (0.3–1.4)	14	1001	0.8 (0.5–1.4)
			P trend = 0.82			P trend = 0.88
Lindane (chlorinated insecticide)						
None	205	20375	1.0 (ref)	205	20375	1.0 (ref)
Low [≤8.75]	18	1285	1.2 (0.7–1.9)	15	976	1.3 (0.8–2.2)
Medium [>8.75–56]	13	1103	1.0 (0.6–1.7)	16	1205	1.1 (0.7–1.8)
High [>56–457.25]	14	467	2.5 (1.4–4.4)	14	673	1.8 (1.0–3.2)
			P trend = 0.004			**P trend = 0.04**
Toxaphene (chlorinated insecticide)						
None	214	20911	1.0 (ref)	214	20911	1.0 (ref)
Low [≤8.75]	14	1198	0.8 (0.5–1.4)	11	630	1.3 (0.7–2.3)
Medium [>8.75–24.5]	13	564	1.5 (0.9–2.7)	12	931	0.9 (0.5–1.6)
High [>24.5–457.25]	6	686	0.6 (0.3–1.4)	10	886	0.8 (0.4–1.5)
			P trend = 0.50			P trend = 0.38
Fungicides						
Benomyl (carbamate fungicide)						
None	219	21425	1.0 (ref)	219	21425	1.0 (ref)
Low [≤12.25]	14	896	1.7 (0.9–2.9)	9	432	2.2 (1.1–4.3)
Medium [>12.25–24.5]	4	214	2.4 (0.9–6.6)	10	732	1.7 (0.9–3.2)

Table 3. Cont.

Insecticides						
Pesticide (chemical-functional class)	**NHL Cases[2]**	**Non-Cases[2]**	**RR[3,4] (95% CI) by Total Days of Exposure**	**NHL**	**Non-Cases**	**RR[3,4] (95% CI)**
[days of lifetime exposure for each category]				**Cases[2,]**		**Intensity-weighted days of exposure**
High [>24.5–457.25]	8	834	1.0 (0.5–2.1)	7	779	0.9 (0.4–2.0)
			P trend = 0.93			P trend = 0.75
Captan (phthalimide fungicide)						
None	407	43433	1.0 (ref)	407	43433	1.0 (ref)
Low [≤0.25]	15	2334	0.8 (0.5–1.4)	15	2108	0.9 (0.6–1.5)
Medium [>0.25–12.25]	16	1004	1.5 (0.8–2.6)	15	1171	1.2 (0.7–2.2)
High [>12.25–875]	14	1823	0.8 (0.5–1.5)	14	1805	0.8 (0.5–1.5)
			P trend = 0.69			P trend = 0.52
Chlorothalonil (polychlorinated aromatic thalonitrile fungicide)						
None	474	48442	1.0 (ref)	474	48442	1.0 (ref)
Low [≤12.25]	13	1509	0.9 (0.5–1.6)	10	1800	0.6 (0.3–1.2)
Medium [>12.25–64]	9	1492	0.8 (0.4–1.6)	11	1501	0.9 (0.5–1.7)
High [>64–395.25]	9	1678	0.6 (0.3–1.3)	9	1362	0.8 (0.4–1.6)
			P trend = 0.16			PP trend = 0.52
Maneb/Mancozeb (dithiocarbamate fungicide)						
None	228	21512	1.0 (ref)	228	21512	1.0 (ref)
Low [≤7]	8	400	1.9 (0.9–3.9)	8	486	1.6 (0.8–3.3)
Medium [>7–103.25]	9	990	0.9 (0.4–1.7)	9	680	1.3 (0.6–2.6)
High [>103.25–737.5]	7	454	1.4 (0.6–2.9)	7	677	0.9 (0.4–1.9)
			P trend = 0.49			P trend = 0.78
Metalaxyl (acylalanine fungicide)						
None	209	18833	1.0 (ref)	209	18833	1.0 (ref)
Low [≤6]	16	1439	1.0 (0.6–1.8)	15	1079	1.3 (0.8–2.2)
Medium [>6–28]	15	2182	0.7 (0.4–1.3)	15	2203	0.8 (0.4–1.3)
High [>28–224.75]	13	1566	1.1 (0.6–2.1)	14	1893	0.9 (0.5–1.6)
			P trend = 0.76			P trend = 0.63
Fumigant						
Methyl bromide (methyl halide fumigant)						
None	425	45265	1.0 (ref)	425	45265	1.0 (ref)
Low [≤8]	37	2060	2.0 (1.4–2.9)	26	1680	1.8 (1.2–2.7)
Medium [>8–28]	24	3011	0.9 (0.6–1.4)	25	2501	1.1 (0.7–1.8)
High [>28–387.5]	17	2768	0.6 (0.4–1.0)	25	3571	0.8 (0.5–1.2)
			P trend = 0.04			P trend = 0.10

[1]During the period from enrollment (1993–1997) to December 31, 2010 in NC and December 31, 2011 in Iowa.

[2]Numbers of cases in columns do not sum to total number of NHL cases (n = 523) due to missing data. In the enrollment questionnaire, lifetime-days & intensity weighted life-time days of pesticide use was obtained for the insecticides: carbofuran, chlorpyrifos, coumaphos, DDVP, fonofos, permethrin and terbufos; the fungicides: captan, chlothalonil and the fumigant: methyl bromide. In the take home questionnaire lifetime-days & intensity weighted life-time days of pesticide use were obtained for the insecticides: aldicarb, carbaryl, diazinon, malathion, parathion, and phorate, the chlorinated insecticides: aldrin, chlordane, DDT, dieldrin, heptachlor, lindane, and toxaphene, the fungicides: benomyl, maneb/mancozeb and metalaxyl, therefore, numbers of NHL cases can vary among pesticides listed in the table.

[3]Adjusted RR: age (<45, 45–49, 50–54, 55–59, 60–64, 65–69, ≥70), State (NC vs. IA), Race (White vs. Black), AHS herbicides (tertiles of total herbicide use-days). Statistically significant P trends are bolded.

[4]Permethrin for animal use and crop use were combined into one category.

[5]The distribution of life-time days of chlordane exposure was clumped into two exposed groups those who with, ≤8.75 life-time days of exposure and those with >8.75 life-time days of exposure.

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Table 4. Pesticide exposure (Lifetime-Days of Exposure) and adjusted risks for NHL Subtypes.

Insecticides											
	SLL, CLL, MCL		**Diffuse Large B-cell**		**Follicular B-cell**		**Other B-cell types**		**Multiple Myeloma**		
	RR[3,4] (95% CI)	**N[2]**	**RR[3,4] (95% CI)**	**N[2]**	**RR[3,4] (95% CI)**	**N[2]**	**RR[3,4] (95% CI)**	**N[2]**	**RR[3,4] (95% CI)**	**N[2]**	**NHL subtype Homo-geneity Test (p-value)**
Carbaryl											
None	1.0 (ref)	42	1.0 (ref)	29	1.0 (ref)	11	1.0 (ref)	14	1.0 (ref)	22	
Low	1.1 (0.6–2.2)	19	0.8 (0.4–1.6)	17	1.6 (0.6–3.9)	10	1.8 (0.7–4.3)	10	0.7 (0.3–1.4)	14	
High	0.6 (0.3–1.3)	15	1.3 (0.6–2.8)	15	2.8 (1.0–7.4)	10	0.4 (0.1–1.5)	3	1.1 (0.7–1.8)	13	
	p trend = 0.16		p trend = 0.33		p trend = 0.06		p trend = 0.63		p trend = 0.98		0.19
Carbofuran											
None	1.0 (ref)	87	1.0 (ref)	78	1.0 (ref)	39	1.0 (ref)	33	1.0 (ref)	56	
Low	1.1 (0.7–1.8)	28	0.9 (0.5–1.7)	13	1.3 (0.7–2.4)	15	0.8 (0.4–1.8)	8	1.9 ((1.1–3.3)	16	
High	1.5 (0.9–2.5)	19	0.8 (0.5–1.3)	13	0.4 (0.1–1.4)	3	0.7 (0.2–2.0)	4	0.9 (0.4–1.6)	12	
	p trend = 0.16		p trend = 0.37		p trend = 0.31		p trend = 0.46		p trend = 0.57		0.52
Chlorpyrifos											
None	1.0 (ref)	84	1.0 (ref)	70	1.0 (ref)	33	1.0 (ref)	31	1 (ref)	58	
Low	1.2 (0.8–1.8)	31	0.9 (0.6–1.5)	22	1.6 (0.9–2.9)	20	1.2 (0.6–2.2)	14	1.0 (0.6–1.8)	17	
High	0.9 (0.6–1.3)	30	1.1 (0.6–1.7)	22	1.0 (0.5–2.1)	11	0.5 (0.2–1.3)	7	0.7 (0.4–1.3)	14	
	p trend = 0.45		p trend = 0.80		p trend = 0.94		p trend = 0.13		p trend = 0.27		0.90
Coumaphos											
None	1.0 (ref)	120	1.0 (ref)	92	1.0 (ref)	48	1.0 (ref)	40	1.0 (ref)	78	
Low	1.1 (0.5–2.2)	8	0.7 (0.3–1.9)	4	2.1 (0.7–5.8)	4	xxx-	4	0.7 (0.2–2.2)	3	
High	1.5 (0.6–3.4)	6	1.6 (0.6–4.5)	4	1.4 (0.5–4.0)	4	xxx-	1	1.2 (0.4–4.0)	3	
	p trend = 0.35		p trend = 0.42		p trend = 0.47		p trend = xxx		p trend = 0.84		0.63
Diazinon											
None	1.0 (ref)	53	1.0 (ref)	40	1.0 (ref)	15	1.0 (ref)	20	1.0 (ref)	41	
Low	1.4 (0.7–2.7)	14	1.5 (0.7–3.2)	9	2.2 (0.9–5.4)	8	xxx	3	0.4 (0.1–1.2)	4	
High	1.9 (0.98–3.6)	12	1.1 (0.5–2.4)	8	3.8 (1.2–11.4)	7	xxx	2	0.5 (0.2–1.7)	3	
	p trend = 0.06		p trend = 0.72		**p trend = 0.02**		p trend = xxx		p trend = 0.35		0.09
DDVP											
None	1.0 (ref)	124	1.0 (ref)	93	1.0 (ref)	48	1.0 (ref)	39	1.0 (ref)	73	
Low	0.8 (0.4–1.9)	6	1.1 (0.4–2.7)	5	1.5 (0.6–3.9)	5	1.1 (0.4–3.7)	3	2.7 (1.2–5.8)	7	
High	0.7 (0.3–1.7)	6	0.9 (0.4–2.3)	5	1.0 (0.3–3.4)	3	0.9 (0.3–3.1)	3	1.0 (0.3–2.7)	4	
	p trend = 0.49		p trend = 0.87		p trend = 0.90		p trend = 0.91		p trend = 0.81		0.96
Fonofos											
None	1.0 (ref)	100	1.0 (ref)	81	1.0 (ref)	45	1.0 (ref)	30	1.0 (ref)	66	
Low	1.2 (0.7–2.0)	20	1.2 (0.7–2.2)	13	1.5 (0.8–3.0)	11	1.4 (0.6–3.1)	8	1.2 (0.6–2.5)	9	
High	1.0 (0.6–1.8)	15	1.2 (0.6–2.3)	11	0.3 (0.1–1.2)	2	1.1 (0.4–2.7)	6	1.4 (0.7–3.0)	9	
	p trend = 0.96		p trend = 0.65		p trend = 0.19		p trend = 0.84		p trend = 0.33		0.35
Malathion											
None	1.0 (ref)	27	1.0 (ref)	20	1.0 (ref)	6	1.0 (ref)	11	1.0 (ref)	17	
Low	0.7 (0.4–1.3)	29	0.96 (0.5–1.8)	23	1.0 (0.4–2.9)	12	1.0 (0.5–2.4)	11	1.0 (0.5–2.1)	18	
High	1.0 (0.6–1.8)	22	1.0 (0.5–2.0)	20	1.6 (0.6–4.4)	11	0.3 (0.1–0.8)	6	1.0 (0.5–2.0)	17	
Ever/Never	1.0 (0.7–1.4)		0.9 (0.6–1.4)		1.3 (0.7–2.4)		0.6 (0.3–1.0)		0.9 (0.6–1.5)		
	p trend = 0.65		p trend = 0.88		p trend = 0.25		p trend = 0.17		p trend = 0.86		0.33
Permethrin											

Table 4. Cont.

	SLL, CLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types		Multiple Myeloma		
	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	NHL subtype Homo-geneity Test (p-value)
Insecticides											
None	1.0 (ref)	108	1.0 (ref)	89	1.0 (ref)	41	1.0 (ref)	38	1.0 (ref)	64	
Low	1.1 (0.6–2.0)	15	0.6 (0.3–1.2)	8	1.3 (0.6–2.7)	8	0.9 (0.3–2.7)	5	1.4 (0.8–2.7)	13	
High	0.8 (0.5–1.5)	15	1.0 (0.5–2.1)	8	1.0 (0.5–2.4)	8	0.5 (0.2–1.7)	4	3.1 (1.5–6.2)	12	
	p trend = 0.53		p trend = 0.99		p trend = 0.88		p trend = 0.28		**p trend = 0.002**		0.10
Phorate											
None	1.0 (ref)	48	1.0 (ref)	37	1.0 (ref)	20	1.0 (ref)	16	1.0 (ref)	36	
Low	1.0 (0.6–1.9)	14	1.4 (0.7–2.7)	15	1.1 (0.4–3.0)	5	0.9 (0.3–2.2)	6	0.7 (0.3–1.8)	6	
High	0.8 (0.4–1.6)	11	0.7 (0.3–2.1)	4	0.8 (0.3–2.2)	5	1.1 (0.4–3.5)	4	0.8 (0.3–2.4)	4	
	p trend = 0.51		p trend = 0.80		p trend = 0.67		p trend = 0.91		p trend = 0.73		0.77
Terbufos											
None	1.0 (ref)	72	1.0 (ref)	63	1.0 (ref)	31	1.0 (ref)	19	1.0 (ref)	59	
Low	1.3 (0.8–2.0)	32	1.2 (0.8–1.9)	29	1.6 (0.9–3.1)	15	1.8 (0.9–3.6)	17	1.1 (0.6–1.9)	12	
High	1.6 (1.0–2.5)	31	1.0 (0.5–2.0)	12	0.8 (0.4–1.7)	10	1.6 (0.7–3.9)	8	1.3 (0.7–2.7)	5	
	p trend = 0.05		p trend = 0.90		p trend = 0.48		p trend = 0.29		p trend = 0.42		0.63
Chlorinated Insecticides											
Aldrin											
None	1.0 (ref)	53	1.0 (ref)	46	1.0 (ref)	22	1.0 (ref)	20	1.0 (ref)	34	
Low	1.0 (0.5–2.0)	11	xxx	2	1.2 (0.4–3.8)	4	0.4 (0.1–1.5)	3	2.1 (0.9–4.7)	8	
High	1.0 (0.5–2.0)	10	xxx	3	0.8 (0.3–2.5)	4	1.1 (0.3–3.9)	3	1.2 (0.5–3.2)	6	
	p trend = 0.70		p trend = xxx		p trend = 0.21		p trend = 0.67		p trend = 0.40		0.98
Chlordane											
None	1.0 (ref)	48	1.0 (ref)	42	1.0 (ref)	20	1.0 (ref)	21	1.0 (ref)	32	
Low	1.8 (1.0–3.1)	16	1.0 (0.5–2.2)	8	1.7 (0.7–4.3)	6	xxx	2	1.7 (0.9–3.3)	13	
High	1.5 (0.7–3.3)	8	1.4 (0.6–3.3)	7	1.3 (0.4–4.6)	3	xxx	2	0.7 (0.2–2.2)	3	
	p trend = 0.34		p trend = 0.69		p trend = 0.70		p trend = xxx		p trend = 0.57		0.85
DDT											
None	1.0 (ref)	42	1.0 (ref)	34	1.0 (ref)	17	1.0 (ref)	16	1.0 (ref)	28	
Low	1.0 (0.5–1.8)	16	1.6 (0.4–3.1)	2	3.3 (1.4–8.1)	9	0.4 (0.3–2.5))	5	1.2 (0.6–2.6)	10	
High	2.6 (1.3–4.8)	15	1.4 (0.6–3.5)	3	1.1 (0.3–3.6)	4	2.1 (0.7–6.5)	5	0.8 (0.4–1.8)	9	
	p trend = 0.04		P trend = 0.17		p trend = 0.80		p trend = 0.64		p trend = 0.37		0.44
Heptachlor											
None	1.0 (ref)	58	1.0 (ref)	47	1.0 (ref)	24	1.0 (ref)	21	1.0 (ref)	40	
Low	1.1 (0.5–2.3)	9	xxx	3	xxx	2	xxx	3	1.3 (0.4–3.8)	4	
High	1.4 (0.7–3.0)	9	xxx	1	xxx	1	xxx	2	1.2 (0.4–3.6)	4	
	p trend = 0.16		p trend = xxx		p trend = xxx		p trend = xxx		p trend = 0.91		0.68
Lindane											
None	1.0 (ref)	57	1.0 (ref)	49	1.0 (ref)	16	1.0 (ref)	21	1.0 (ref)	43	
Low	1.2 (0.6–2.5)	10	0.6 (0.2–1.7)	4	4.9 (1.9–12.6)	6	xxx	2	xxx	3	
High	2.6 (1.2–5.6)	9	2.0 (0.6–6.5)	3	3.6 (1.4–9.5)	6	xxx	1	xxx	2	
	p trend = 0.13		p trend = 0.96		**p trend = 0.04**		p trend = xxx		p trend = xxx		0.54
Toxaphene											
None	1.0 (ref)	68	1.0 (ref)	47	1 (ref)	23	1.0 (ref)	22	1.0 (ref)	40	

Table 4. Cont.

Insecticides											
	SLL, CLL, MCL		Diffuse Large B-cell		Follicular B-cell		Other B-cell types		Multiple Myeloma		
	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	RR[3,4] (95% CI)	N[2]	NHL subtype
											Homo-geneity
											Test
											(p-value)
Low	0.9 (0.4–2.3)	5	1.3 (0.5–3.3)	5	xxx	2	xxx	3	0.7 (0.2–2.0)	4	
High	0.4 (0.1–1.6)	2	0.9 (0.3–3.0)	3	xxx	2	xxx	2	0.7 (0.2–2.9)	2	
	p trend = 0.08		p trend = 0.77		p trend = xxx		p trend = xxx		p trend = 0.64		0.34
Fungicides											
Captan											
None	1.0 (ref)	118	1.0 (ref)	91	1.0 (ref)	52	1.0 (ref)	39	1.0 (ref)	76	
Low	0.9 (0.4–1.9)	7	1.1 (0.5–2.4)	7	xxx	2	xxx	3	1.4 (0.5–3.4)	5	
High	1.1 (0.5–2.6)	7	0.7 (0.1–3.1)	4	xxx	1	xxx	2	1.2 (0.5–2.9)	5	
	p trend = 0.78		p trend = 0.58		p trend = xxx		p trend = xxx		p trend = 0.75		0.92
Chlorothalonil											
None	1.0 (ref)	135	1.0 (ref)	107	1.0 (ref)	60	1.0 (ref)	50	1.0 (ref)	84	
Low	0.9 (0.4–2.3)	5	1.1 (0.4–3.1)	4	xxx	3	−xxx	1	1.1 (0.4–2.8)	5	
High	1.1 (0.4–3.3)	4	0.3 (0.1–1.2)	2	xxx	2	−xxx	1	0.7 (0.6–2.3)	3	
	p trend = 0.83		p trend = 0.09		p trend = xxx		p trend = xxx		p trend = 0.56		0.76
Metalaxyl											
None	1.0 (ref)	60	1.0 (ref)	45	1.0 (ref)	25	1.0 (ref)	23	1.0 (ref)	39	
Low	2.8 (1.4–5.8)	9	1.1 (0.4–2.6)	7	xxx	3	−xxx	2	0.4 (0.1–1.1)	4	
High	1.1 (0.4–2.8)	6	1.0 (0.4–2.7)	5	xxx	2	−xxx	1	1.1 (0.4–3.2)	4	
	p trend = 0.99		p trend = 0.97		p trend = xxx		p trend = xxx		p trend = 0.87		0.92
Maneb/ Mancozeb											
None	1.0 (ref)	69	1.0 (ref)	49	1.0 (ref)	25	1.0 (ref)	26	1.0 (ref)	41	
Low	2.1 (0.7–6.0)	4	4.0 (1.4–11.6)	4	xxx	2	−xxx	0	1.0 (0.4–2.5)	5	
High	1.2 (0.3–4.0)	3	0.9 (0.3–3.1)	3	−xxx	1	−xxx	0	2.2 (0.5–9.5)	2	
	p trend = 0.84		p trend = 0.74		p trend = xxx		p trend = xxx		p trend = 0.28		0.82
Fumigant											
Methyl Bromide											
None	1.0 (ref)	126	1.0 (ref)	86	1.0 (ref)	58	1.0 (ref)	44	1.0 (ref)	76	
Low	1.1 (0.5–2.2)	9	4.0 (2.2–7.4)	15	1.4 (0.5–4.2)	4	3.6 (1.3–9.8)	5	1.0 (0.5–2.1)	8	
High	0.8 (0.4–1.8)	8	1.0 (0.5–2.1)	11	0.3 (0.1–1.1)	3	1.3 (0.3–5.0)	3	0.8 (0.4–1.8)	8	
	p trend = 0.58		p trend = 0.67		p trend = 0.08		p trend = 0.56		p trend = 0.63		0.59

[1]During the period from enrollment (1993–1997) to December 31, 2010 in NC and December 31, 2011 in Iowa.
[2]Numbers of cases in columns do not sum to total number of NHL cases (n = 523) due to missing data. Ever/never use of all 26 pesticides (table 3) do not always match with exposure-response data in table 4 because of missing data to calculate lifetime-days of use.
[3]Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, 65–69, ≥70), State (NC vs. IA), Race (White vs. Black), AHS herbicides (in tertiles of total herbicide use-days). Significant RR and 95% confidence limits are bolded.
[4]RR was not calculated if the number of exposed cases for any NHL subtype was <6 and these cells are marked XXX. Four pesticides included in Table 2 (i.e., aldicarb, benomyl, dieldrin and parathion) were not included in Table 4 because no NHL subtype included≥6 cases of a specific cell types with lifetime-days of exposure.
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risk estimates (i.e., narrower confidence intervals) when we included phase 2 imputed data (n = 54,306) (data not shown). Lagging exposures by five years did not meaningfully change the association between lindane or DDT and total NHL (data not shown). The significant exposure-response trends linking use of a particular pesticide to NHL and certain NHL subtypes did not always correspond to a significant excess risk among those who ever used the same pesticide. For chemicals for which the detailed information was only asked about in the take-home questionnaire, we evaluated potential differences between the ever/never analyses based on the enrolment questionnaire and data from the same sub-set of participants who completed the exposure-

response in the take-home questionnaire and found no meaningful differences in the results. We also evaluated the impact of using an updated definition of NHL; when using the original ICD-O-3 definition of NHL[19], lifetime-days of lindane use remained significantly associated with NHL risk (RR = 1.0 (ref), 1.3 (0.7–2.6), 1.2 (0.6–2.8), 2.7 (1.3–5.4), p trend = 0.006). The trend between total NHL and lifetime-days of DDT, however, was less clear and not statistically significant (RR = 1.0 (ref) 1.3 (0.9–1.8), 1.1 (0.5–2.1), 1.4 (0.8–2.6), p trend = 0.32) [Table S3 in File S1]. Carbaryl and diazinon showed non-significant trends with the older definition of NHL, but not with the newer definition used here.

Discussion

A significant exposure–response trend for total NHL was observed with increasing lifetime-days of use for two organochlorine insecticides, lindane and DDT, although RRs from ever/never comparisons were not elevated. On the other hand, terbufos use showed a significant excess risk with total NHL in ever vs. never exposed analysis, but displayed no clear exposure-response trend. Several pesticides showed significant exposure-response trends with specific NHL subtypes however, when polytomous models were used to test the difference in parametric estimates of trend among the five NHL subtypes, there was no evidence of heterogeneity in the sub-types for specific chemicals. The subtype relationships that looked particularly interesting were DDT and terbufos with the SLL/CLL/MCL subtype, lindane and diazinon with the follicular subtype, and permethrin with MM. These pesticide-NHL links should be evaluated in future studies.

Lindane (gamma-hexachlorocyclohexane) is a chlorinated hydrocarbon insecticide. Production of lindane was terminated in the United States in 1976, but imported lindane was used to treat scabies and lice infestation and for agricultural seed treatment [21] until its registration was cancelled in 2009 [22], the same year production was banned worldwide [23]. In our study, 3,410 people reporting ever using lindane (6%) prior to enrollment, 433 reported use at the phase 2 questionnaire (1%), indicating that use had dropped substantially. Oral administration of lindane has increased the incidence of liver tumors in mice and less clearly, thyroid tumors in rats [24]. Lindane produces free radicals and oxidative stress (reactive oxygen species [ROS]) [25] and has been linked with chromosomal aberrations in human peripheral lymphocytes in vitro [26].

Lindane has been linked with NHL in previous epidemiologic studies. A significant association between lindane use and NHL was observed in a pooled analysis of three population-based case-control studies conducted in the Midwestern US, with stronger relative risks observed for greater duration and intensity of use [27]. NHL was also associated with lindane use in a Canadian case-control study [28]. Lindane was significantly associated with NHL risk in an earlier report from the AHS [29]. We are not aware of any previous study that assessed the association between a NHL subtype and lindane use. The exposure-response pattern with total NHL and the follicular lymphoma subtype indicates a need for further evaluation of lindane and NHL.

DDT is an organochlorine insecticide that was used with great success to control malaria and typhus during and after World War II [29] and was widely used for crop and livestock pest control in the United States from the mid-1940s to the 1960s [30]. Its registration for crop use was cancelled in the US in 1972 [30] and banned worldwide for agricultural use in 2009, but continues to be used for disease vector control in some parts of the world [23]. In our study, 12,471 participants (23%) reported ever using DDT prior to enrollment; 12%, 8.7% and 2.3% responding to the take-home questionnaire reported their first use occurred prior to the 1960s, during the 1960s, and during the 1970s, respectively. The National Toxicology Program classifies DDT as "reasonably anticipated to be a human carcinogen" [31] and IARC classifies DDT as a "possible human carcinogen (2B)" [12], both classifications were based on experimental studies in which excess liver tumors were observed in two rodent species. Epidemiology data on the carcinogenic risk of DDT is inconsistent. NHL was not associated with use of DDT in a pooled analysis of three case-control studies in the U.S. where information on exposure was obtained from farmers by questionnaire [32]. There also was no association between the use of DDT and NHL in our study when we used an earlier definition of NHL [18], suggesting some of the inconsistency may be due to disease definition. In the large Epilymph study, no meaningful links between DDT and the risk of NHL, or diffuse large B cell lymphoma were observed, and only limited support was found for a link to CLL [33], although a case-control study of farmers in Italy suggested increased risk of NHL and CLL with DDT exposure [34]. NHL was not associated with serum levels of DDT in a prospective cohort study from the U.S. [35], but NHL was associated with the DDT-metabolite p, p'-DDE, as well as chlordane and heptachlor-related compounds (oxychlordane, heptachlor epoxide) and dieldrin, in a study with exposure measured in human adipose tissue samples [36]. In a Danish cohort, a higher risk of NHL was associated with higher prediagnostic adipose levels of DDT, cis-nonachlor, and oxychlordane [37]. In a Canadian study, analytes from six insecticides/insecticide metabolites (beta-hexachlorocyclohexane, p, p'-dichloro-DDE, hexachlorobenzene (HCB), mirex, oxychlordane and transnonachlor) were linked with a significant increased risk with NHL [38]. However, in an analysis of plasma samples from a case-control study in France, Germany and Spain, the risk of NHL did not increase with plasma levels of hexachlorobenzene, beta-hexachlorobenzene or DDE [39]. In this analysis, NHL was significantly associated with reported use of DDT, but not with the other organochlorine insecticides studied (i.e., aldrin, chlordane, dieldrin, heptachlor, toxaphene). Our findings add further support for an association between DDT and total NHL and our results on SLL/CLL/MCL are novel and should be further explored.

Permethrin is a broad-spectrum synthetic pyrethroid pesticide widely used in agriculture and in home and garden use as an insecticide and acaricide, as an insect repellant, and as a treatment to eradicate parasites such as head lice or mites responsible for scabies [40]. This synthetic pyrethroid was first registered for use in the United States in 1979 [40]. The U.S. Environmental Protection Agency classified permethrin as "likely to be carcinogenic to humans" largely based on the observed increase incidence of benign lung tumors in female mice, liver tumors in rats and liver tumors in male and female mice [41]. Permethrin was not associated with NHL overall in our study, nor in pooled case-control studies of NHL from the U.S (the NHL definition in use at the time of the study did not include MM) [42]. In our analysis, however, the risk of MM increased significantly with lifetime-days of exposure to permethrin, as had been noted in an earlier analysis of AHS data [43]. We are unaware of other studies that have found this association.

Terbufos is an organophosphate insecticide and nematicide first registered in 1974 [44]. The EPA classifies terbufos as Group E, i.e., "Evidence of Non-Carcinogenicity for Humans" [44]. We found some evidence for an association between terbufos use and NHL, particularly for the SLL/CLL/MCL subtype. NHL was not associated with terbufos in the pooled case-control studies from the

U.S. [42] but there was a non-significant association between terbufos and small cell lymphocytic lymphoma [10].

Diazinon is an organophosphate insecticide registered for a variety of uses on plants and animals in agriculture [45]. It was commonly used in household insecticide products until the EPA phased out all residential product registrations for diazinon in December 2004 [45.46]. In an earlier evaluation of diazinon in the AHS, a significant exposure-response association was observed for leukemia risk with lifetime exposure-days [47]. While there was no link between diazinon and NHL overall in this analysis, there was a statistically significant exposure-response association between diazinon and the follicular lymphoma subtype and an association with the SLL/CLL/MCL subtype that was not statistically significant. Diazinon was previously associated with NHL in pooled case-control studies from the U.S. and particularly with SLL [10].

Several other insecticides, fungicides and fumigants cited in recent reviews of the pesticide-cancer literature suggested etiological associations with total NHL [8,9], these include: oxychlordane, trans-nonachlor, and cis-nonachlor which are metabolites of chlordane; and dieldrin and toxaphene among NHL cases with t(14,18) translocations. We did not find a significant association between chlordane and total NHL nor with any NHL subtype, but we did not have information about chlordane metabolites to make a more direct comparison. Similarly we did not observe a significant association between dieldrin nor toxaphene and total NHL nor with any NHL subtypes. Mirex (1,3-cyclopentadiene), an insecticide, and hexachlorobenzene, a fungicide, were also associated with NHL risk [8,9] but we did not examine these compounds in the AHS.

This study has a number of strengths. It is a large population of farmers and commercial pesticide applicators who can provide reliable information regarding their pesticide use history [48]. Information on pesticide use and application practices was obtained prior to onset of cancer. An algorithm that incorporated several exposure determinants which predicted urinary pesticide levels was used to develop an intensity-weighted exposure metric in our study [20]. Exposure was ascertained prior to diagnosis of disease, which should eliminate the possibility of case-response bias [14]. Because of the detailed information available on pesticide use, we were able to assess the impact for the use of multiple pesticides. For example, we evaluated total pesticide use-days, and specific pesticides found to be associated with NHL or its subtypes in the AHS. We found no meaningful change in the associations with DDT, lindane, permethrin, diazinon and terbufos from such adjustments. Information on many potential NHL risk factors was available and could be controlled in the analysis.

Most epidemiological investigations of NHL prior to 2007 [17] did not include CLL and MM as part of the definition. These two subtypes made up 37% (193/523) of the NHL cases in this analysis. This is a strength of our study in that the definition of NHL used here is based on the most recent classification system [16,17] and will be relevant for comparisons with future studies. On the other hand, the inclusion of MM and CLL in the recent definition of NHL makes comparisons of our findings with earlier literature challenging, because the NHL subtypes may have different etiologies. For example, DDT was not significantly associated with NHL using the older definition, but was significantly associated with the NHL using the most recent definition of NHL because of its association with the SLL/CLL/MCL subtype (Table S1 in File S1). On the other hand, carbaryl and diazinon were associated with the old definition of NHL (although non-significantly) but not with the new definition. Lindane, however, was associated with both definitions of NHL. Lindane was significantly associated with the follicular lymphoma subtype and this subtype was included in the older and newer definition of NHL. No other pesticides were significantly associated with NHL under the old definition (Table S3 in File S1).

Although this is a large prospective study, limitations should be acknowledged. A small number of cases exposed to some specific pesticides could lead to false positive or negative findings. We also had reduced statistical power to evaluate some pesticides for total days of use and intensity-weighted days of use because some participants did not complete the phase one take-home questionnaire and the tests of homogeneity between specific pesticides and specific NHL subtypes were underpowered. Some chance associations could occur because of multiple testing, i.e., a number of pesticides, several NHL subtypes, and more than one exposure metric. Despite the generally high quality of the information on pesticide use provided by AHS participants [48,50], misclassification of pesticide exposures can occur and can have a sizeable impact on estimates of relative risk, which in a prospective cohort design would tend to produce false negative results [49].

Conclusion

Our results showed pesticides from different chemical and functional classes were associated with an excess risk of NHL and NHL subtypes, but not all members of any single class of pesticides were associated with an elevated risk of NHL or NHL subtypes, nor were all chemicals of a class included on our questionnaire. Significant pesticide associations were between total NHL and reported use of lindane and DDT. Links between DDT and terbufos and SLL/CLL/MCL, lindane and diazinon and follicular lymphoma, and permethrin and MM, although based on relatively small numbers of exposed cases, deserve further evaluation. The epidemiologic literature on NHL and these pesticides is inconsistent and although the findings from this large, prospective cohort add important information, additional studies that focus on NHL and its subtypes and specific pesticides are needed. The findings from this large, prospective cohort add important new information regarding the involvement of pesticides in the development of NHL. It provides additional information regarding specific pesticides and NHL overall and some new leads regarding possible links with NHL subtypes that deserve evaluation in future studies.

Supporting Information

File S1 This file contains Table S1, Table S2, and Table S3. Table S1, Frequency of NHL in Agricultural Health Study applicators using New (Interlymph hierarchical classification of lymphoid neoplasms) and Older Definitions (ICD-O-3). Table S2, Pesticides included in the Agricultural Health Study questionnaires by Chemical/Functional Class. Table S3, Pesticide exposure (lifetime-days) and adjusted risks of total NHL incidence (Older definition [ICD-O-3]).
(DOC)

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Author Contributions

Conceived and designed the experiments: MCA DPS AB. Performed the experiments: MCA CFL KT CJH. Analyzed the data: MCA JNH CFL CJH KHB JB DWB KT DPS JAH SK GA JHL AB LEB. Contributed reagents/materials/analysis tools: MCA JB DWB CFL. Wrote the paper: MCA LEBF JNH CFL CJH KT AB DWB JHL. Designed the software: JB DWB.

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StarTribune

State considers banning class of pesticide to help bees

A bee with resin on her leg photographed on August 8, 2014, in St. Paul, Minn.

Renee Jones Schneider, Dml - Star Tribune

Article by: Tony Kennedy
Star Tribune
October 29, 2014 - 12:41 PM

Minnesota regulators, for the first time, are considering banning or restricting a controversial class of insecticides that has been linked to honeybee deaths.

The possibility, disclosed this week by the state Department of Agriculture in a revised outline for a study of the chemicals, followed an outpouring of public concern over the dramatic decline in honeybee populations in recent years.

“Obviously people are very interested in this,” said Gregg Regimbal, an official with the department’s Pesticide & Fertilizer Management Division. “It’s a very complex issue and it’s highly charged.”

More than 400 citizens wrote the agency earlier this year with comments on the proposed review of a class of insecticides called neonicotinoids, which have been linked to bee deaths around the world.

Regimbal said the public response was heavy, with many commenters wanting to know why the study, as originally outlined by the agency, didn’t include the possibility of banning the chemicals.

A revised outline published this week states that the range of state action could include “restrictions on or cancellation of products.”

“We wanted to make sure it was clear that it’s in our authority … and that that would be an option,” Regimbal said.

Lex Horan, a Minneapolis-based organizer for Pesticide Action Network of North America, said a suspension, restriction or ban in Minnesota is plausible if the state conducts a careful study of neonicotinoids and their effects on pollinators and other insects.

He said people who wrote to the agency are heartened by the revised outline, including other aspects of the upcoming review.

“The state needs to take this seriously,” Horan said. “They put out a strong scoping document because of the feedback they received.”

The in-depth review will take more than six months.

The outcry included a letter submitted in May by 17 DFL legislators, who insisted that the department broaden the scope of its review. The 2013 Legislature called for the Agriculture Department to review the chemicals, and the group of 17 was irked that the agency’s initial outline didn’t mention the possibility of a ban or other restrictions.

“The Legislature did not intend that the Department would simply rubber stamp U.S. EPA’s decisions,” they wrote, a reference to a review underway at the federal Environmental Protection Agency. Signers included Rep. Jean Wagenius, DFL-Minneapolis, who is chair of the House Environment, Natural Resources and Agriculture Finance committee.

Insecticide use in Minnesota is governed by both state and federal law. The EPA is also reviewing the effects of neonicotinoids on bees and other pollinators, while New York, Oregon, Canada and Europe all have placed bans or restrictions on them.

The chemicals are now the most widely used class of insecticides in the world, according to the state Agriculture Department, and studies have found that they can damage the navigation and reproduction abilities of honeybees and bumblebees, even at

low concentrations. Honeybees alone pollinate more than $15 billion worth of crops in the United States.

Horan said the backlash against neonicotinoids was heightened by a recent EPA finding that neonicotinoid seed treatments in soybeans provide little or no overall benefits to soybean production for most farmers.

The pesticides, which work as neurotoxins on many agricultural pests, are used to protect a broad range of crop seedlings including corn, sugar beets, potatoes and cereals.

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PLOS ONE

A Meta-Analysis of the Impacts of Genetically Modified Crops

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Abstract

Background: Despite the rapid adoption of genetically modified (GM) crops by farmers in many countries, controversies about this technology continue. Uncertainty about GM crop impacts is one reason for widespread public suspicion.

Objective: We carry out a meta-analysis of the agronomic and economic impacts of GM crops to consolidate the evidence.

Data Sources: Original studies for inclusion were identified through keyword searches in ISI Web of Knowledge, Google Scholar, EconLit, and AgEcon Search.

Study Eligibility Criteria: Studies were included when they build on primary data from farm surveys or field trials anywhere in the world, and when they report impacts of GM soybean, maize, or cotton on crop yields, pesticide use, and/or farmer profits. In total, 147 original studies were included.

Synthesis Methods: Analysis of mean impacts and meta-regressions to examine factors that influence outcomes.

Results: On average, GM technology adoption has reduced chemical pesticide use by 37%, increased crop yields by 22%, and increased farmer profits by 68%. Yield gains and pesticide reductions are larger for insect-resistant crops than for herbicide-tolerant crops. Yield and profit gains are higher in developing countries than in developed countries.

Limitations: Several of the original studies did not report sample sizes and measures of variance.

Conclusion: The meta-analysis reveals robust evidence of GM crop benefits for farmers in developed and developing countries. Such evidence may help to gradually increase public trust in this technology.

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Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper and its Supporting Information files.

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Introduction

Despite the rapid adoption of genetically modified (GM) crops by farmers in many countries, public controversies about the risks and benefits continue [1–4]. Numerous independent science academies and regulatory bodies have reviewed the evidence about risks, concluding that commercialized GM crops are safe for human consumption and the environment [5–7]. There are also plenty of studies showing that GM crops cause benefits in terms of higher yields and cost savings in agricultural production [8–12], and welfare gains among adopting farm households [13–15]. However, some argue that the evidence about impacts is mixed and that studies showing large benefits may have problems with the data and methods used [16–18]. Uncertainty about GM crop impacts is one reason for the widespread public suspicion towards this technology. We have carried out a meta-analysis that may help to consolidate the evidence.

While earlier reviews of GM crop impacts exist [19–22], our approach adds to the knowledge in two important ways. First, we include more recent studies into the meta-analysis. In the emerging literature on GM crop impacts, new studies are published continuously, broadening the geographical area covered, the methods used, and the type of outcome variables considered. For instance, in addition to other impacts we analyze effects of GM crop adoption on pesticide quantity, which previous meta-analyses could not because of the limited number of observations for this particular outcome variable. Second, we go beyond average impacts and use meta-regressions to explain impact heterogeneity and test for possible biases.

Our meta-analysis concentrates on the most important GM crops, including herbicide-tolerant (HT) soybean, maize, and cotton, as well as insect-resistant (IR) maize and cotton. For these crops, a sufficiently large number of original impact studies have

been published to estimate meaningful average effect sizes. We estimate mean impacts of GM crop adoption on crop yield, pesticide quantity, pesticide cost, total production cost, and farmer profit. Furthermore, we analyze several factors that may influence outcomes, such as geographic location, modified crop trait, and type of data and methods used in the original studies.

Materials and Methods

Literature search

Original studies for inclusion in this meta-analysis were identified through keyword searches in relevant literature databanks. Studies were searched in the ISI Web of Knowledge, Google Scholar, EconLit, and AgEcon Search. We searched for studies in the English language that were published after 1995. We did not extend the review to earlier years, because the commercial adoption of GM crops started only in the mid-1990s [23]. The search was performed for combinations of keywords related to GM technology and related to the outcome of interest. Concrete keywords used related to GM technology were (an asterisk is a replacement for any ending of the respective term; quotation marks indicate that the term was used as a whole, not each word alone): GM*, "genetically engineered", "genetically modified", transgenic, "agricultural biotechnology", HT, "herbicide tolerant", Roundup, Bt, "insect resistant". Concrete keywords used related to outcome variables were: impact*, effect*, benefit*, yield*, economic*, income*, cost*, soci*, pesticide*, herbicide*, insecticide*, productivity*, margin*, profit*. The search was completed in March 2014.

Most of the publications in the ISI Web of Knowledge are articles in academic journals, while Google Scholar, EconLit, and AgEcon Search also comprise book chapters and grey literature such as conference papers, working papers, and reports in institutional series. Articles published in academic journals have usually passed a rigorous peer-review process. Most papers presented at academic conferences have also passed a peer-review process, which is often less strict than that of good journals though. Some of the other publications are peer reviewed, while many are not. Some of the working papers and reports are published by research institutes or government organizations, while others are NGO publications. Unlike previous reviews of GM crop impacts, we did not limit the sample to peer-reviewed studies but included all publications for two reasons. First, a clear-cut distinction between studies with and without peer review is not always possible, especially when dealing with papers that were not published in a journal or presented at an academic conference [24]. Second, studies without peer review also influence the public and policy debate on GM crops; ignoring them completely would be short-sighted.

Of the studies identified through the keyword searches, not all reported original impact results. We classified studies by screening titles, abstracts, and full texts. Studies had to fulfill the following criteria to be included:

- The study is an empirical investigation of the agronomic and/or economic impacts of GM soybean, GM maize, or GM cotton using micro-level data from individual plots and/or farms. Other GM crops such as GM rapeseed, GM sugarbeet, and GM papaya were commercialized in selected countries [23], but the number of impact studies available for these other crops is very small.
- The study reports GM crop impacts in terms of one or more of the following outcome variables: yield, pesticide quantity (especially insecticides and herbicides), pesticide costs, total variable costs, gross margins, farmer profits. If only the number of pesticide sprays was reported, this was used as a proxy for pesticide quantity.
- The study analyzes the performance of GM crops by either reporting mean outcomes for GM and non-GM, absolute or percentage differences, or estimated coefficients of regression models that can be used to calculate percentage differences between GM and non-GM crops.
- The study contains original results and is not only a review of previous studies.

In some cases, the same results were reported in different publications; in these cases, only one of the publications was included to avoid double counting. On the other hand, several publications involve more than one impact observation, even for a single outcome variable, for instance when reporting results for different geographical regions or derived with different methods (e.g., comparison of mean outcomes of GM and non-GM crops plus regression model estimates). In those cases, all observations were included. Moreover, the same primary dataset was sometimes used for different publications without reporting identical results (e.g., analysis of different outcome variables, different waves of panel data, use of different methods). Hence, the number of impact observations in our sample is larger than the number of publications and primary datasets (Data S1). The number of studies selected at various stages is shown in the flow diagram in Figure 1. The number of publications finally included in the meta-analysis is 147 (Table S1).

Effect sizes and influencing factors

Effect sizes are measures of outcome variables. We chose the percentage difference between GM and non-GM crops for five different outcome variables, namely yield, pesticide quantity, pesticide cost, total production cost, and farmer profits per unit area. Most studies that analyze production costs focus on variable costs, which are the costs primarily affected through GM technology adoption. Accordingly, profits are calculated as revenues minus variable production costs (profits calculated in this way are also referred to as gross margins). These production costs also take into account the higher prices charged by private companies for GM seeds. Hence, the percentage differences in profits considered here are net economic benefits for farmers using GM technology. Percentage differences, when not reported in the original studies, were calculated from mean value comparisons between GM and non-GM or from estimated regression coefficients.

Since we look at different types of GM technologies (different modified traits) that are used in different countries and regions, we do not expect that effect sizes are homogenous across studies. Hence, our approach of combining effect sizes corresponds to a random-effects model in meta-analysis [25]. To explain impact heterogeneity and test for possible biases, we also compiled data on a number of study descriptors that may influence the reported effect sizes. These influencing factors include information on the type of GM technology (modified trait), the region studied, the type of data and method used, the source of funding, and the type of publication. All influencing factors are defined as dummy variables. The exact definition of these dummy variables is given in Table 1. Variable distributions of the study descriptors are shown in Table S2.

Statistical analysis

In a first step, we estimate average effect sizes for each outcome variable. To test whether these mean impacts are significantly

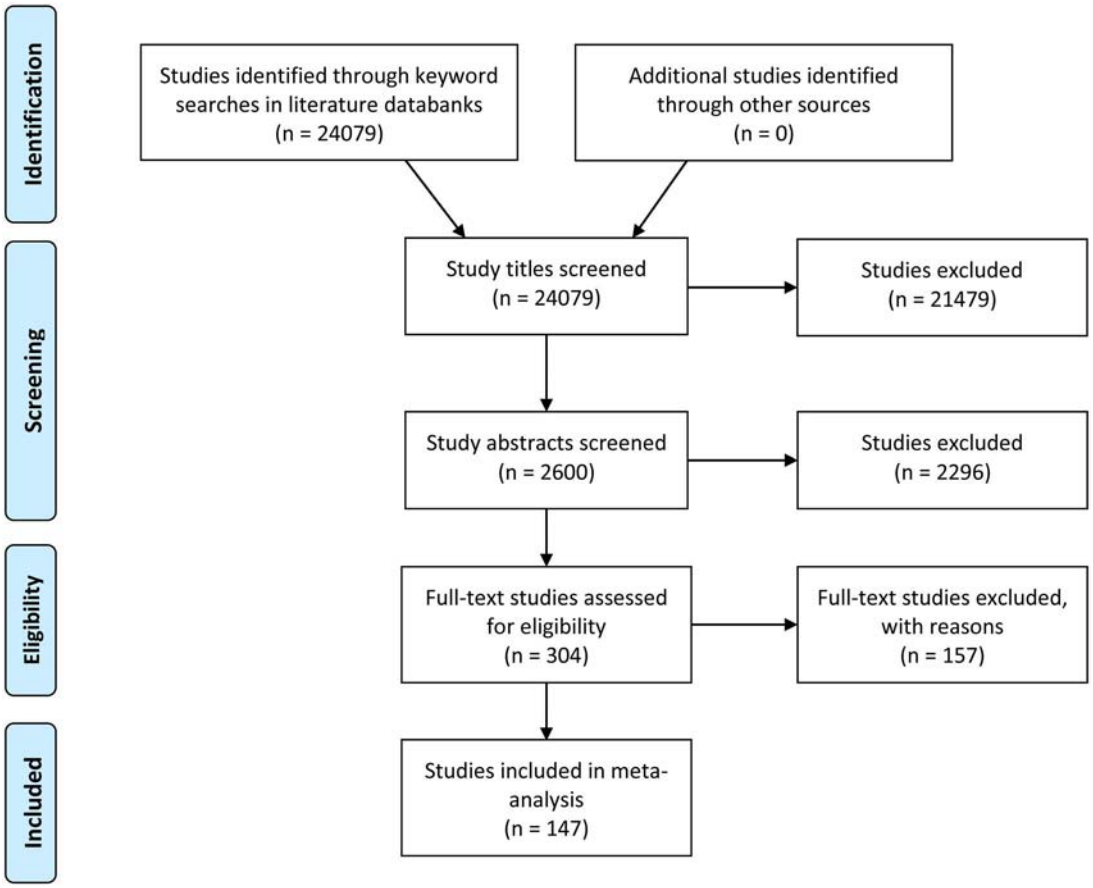

Figure 1. Selection of studies for inclusion in the meta-analysis.
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different from zero, we regress each outcome variable on a constant with cluster correction of standard errors by primary dataset. Thus, the test for significance is valid also when observations from the same dataset are correlated. We estimate average effect sizes for all GM crops combined. However, we expect that the results may differ by modified trait, so that we also analyze mean effects for HT crops and IR crops separately.

Meta-analyses often weight impact estimates by their variances; estimates with low variance are considered more reliable and receive a higher weight [26]. In our case, several of the original studies do not report measures of variance, so that weighting by variance is not possible. Alternatively, weighting by sample size is common, but sample sizes are also not reported in all studies considered, especially not in some of the grey literature publications. To test the robustness of the results, we employ a

Table 1. Variables used to analyze influencing factors of GM crop impacts.

Variable name	Variable definition
Insect resistance (IR)	Dummy that takes a value of one for all observations referring to insect-resistant GM crops with genes from *Bacillus thuringiensis* (Bt), and zero for all herbicide-tolerant (HT) GM crops.
Developing country	Dummy that takes a value of one for all GM crop applications in a developing country according to the World Bank classification of countries, and zero for all applications in a developed country.
Field-trial data	Dummy that takes a value of one for all observations building on field-trial data (on-station and on-farm experiments), and zero for all observations building on farm survey data.
Industry-funded study	Dummy that takes a value of one for all studies that mention industry (private sector companies) as source of funding, and zero otherwise.
Regression model result	Dummy that takes a value of one for all impact observations that are derived from regression model estimates, and zero for observations derived from mean value comparisons between GM and non-GM.
Journal publication	Dummy that takes a value of one for all studies published in a peer-reviewed journal, and zero otherwise.
Journal/academic conference	Dummy that takes a value of one for all studies published in a peer-reviewed journal or presented at an academic conference, and zero otherwise.

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different weighting procedure, using the inverse of the number of impact observations per dataset as weights. This procedure avoids that individual datasets that were used in several publications dominate the calculation of average effect sizes.

In a second step, we use meta-regressions to explain impact heterogeneity and test for possible biases. Linear regression models are estimated separately for all of the five outcome variables:

$$\%\Delta Y_{hij} = \alpha_h + \mathbf{X}_{hij}\boldsymbol{\beta}_h + \varepsilon_{hij}$$

$\%\Delta Y_{hij}$ is the effect size (percentage difference between GM and non-GM) of each outcome variable h for observation i in publication j, and $\mathbf{X}_{hij}$ is a vector of influencing factors. α_h is a coefficient and $\boldsymbol{\beta}_h$ a vector of coefficients to be estimated; ε_{hij} is a random error term. Influencing factors used in the regressions are defined in Table 1.

Results and Discussion

Average effect sizes

Distributions of all five outcome variables are shown in Figure S1. Table 2 presents unweighted mean impacts. As a robustness check, we weighted by the inverse of the number of impact observations per dataset. Comparing unweighted results (Table 2) with weighted results (Table S3) we find only very small differences. This comparison suggests that the unweighted results are robust.

On average, GM technology has increased crop yields by 21% (Figure 2). These yield increases are not due to higher genetic yield potential, but to more effective pest control and thus lower crop damage [27]. At the same time, GM crops have reduced pesticide quantity by 37% and pesticide cost by 39%. The effect on the cost of production is not significant. GM seeds are more expensive than non-GM seeds, but the additional seed costs are compensated through savings in chemical and mechanical pest control. Average profit gains for GM-adopting farmers are 69%.

Results of Cochran's test [25], which are reported in Figure S1, confirm that there is significant heterogeneity across study observations for all five outcome variables. Hence it is useful to further disaggregate the results. Table 2 shows a breakdown by modified crop trait. While significant reductions in pesticide costs are observed for both HT and IR crops, only IR crops cause a consistent reduction in pesticide quantity. Such disparities are expected, because the two technologies are quite different. IR crops protect themselves against certain insect pests, so that spraying can be reduced. HT crops, on the other hand, are not protected against pests but against a broad-spectrum chemical herbicide (mostly glyphosate), use of which facilitates weed control. While HT crops have reduced herbicide quantity in some situations, they have contributed to increases in the use of broad-spectrum herbicides elsewhere [2,11,19]. The savings in pesticide costs for HT crops in spite of higher quantities can be explained by the fact that broad-spectrum herbicides are often much cheaper than the selective herbicides that were used before. The average farmer profit effect for HT crops is large and positive, but not statistically significant because of considerable variation and a relatively small number of observations for this outcome variable.

Impact heterogeneity and possible biases

Table 3 shows the estimation results from the meta-regressions that explain how different factors influence impact heterogeneity. Controlling for other factors, yield gains of IR crops are almost 7 percentage points higher than those of HT crops (column 1). Furthermore, yield gains of GM crops are 14 percentage points higher in developing countries than in developed countries. Especially smallholder farmers in the tropics and subtropics suffer from considerable pest damage that can be reduced through GM crop adoption [27].

Most original studies in this meta-analysis build on farm surveys, although some are based on field-trial data. Field-trial results are often criticized to overestimate impacts, because farmers may not be able to replicate experimental conditions. However, results in Table 3 (column 1) show that field-trial data do not overestimate the yield effects of GM crops. Reported yield gains from field trials are even lower than those from farm surveys. This is plausible, because pest damage in non-GM crops is often more severe in farmers' fields than on well-managed experimental plots.

Table 2. Impacts of GM crop adoption by modified trait.

Outcome variable	All GM crops	Insect resistance	Herbicide tolerance
Yield	21.57*** (15.65; 27.48)	24.85*** (18.49; 31.22)	9.29** (1.78; 16.80)
n/m	451/100	353/83	94/25
Pesticide quantity	–36.93*** (–48.01; −25.86)	–41.67*** (–51.99; −31.36)	2.43 (–20.26; 25.12)
n/m	121/37	108/31	13/7
Pesticide cost	–39.15*** (–46.96; −31.33)	–43.43*** (–51.64; −35.22)	–25.29*** (–33.84; −16.74)
n/m	193/57	145/45	48/15
Total production cost	3.25 (–1.76; 8.25)	5.24** (0.25; 10.73)	–6.83 (–16.43; 2.77)
n/m	115/46	96/38	19/10
Farmer profit	68.21*** (46.31; 90.12)	68.78*** (46.45; 91.11)	64.29 (–24.73; 153.31)
n/m	136/42	119/36	17/9

Average percentage differences between GM and non-GM crops are shown with 95% confidence intervals in parentheses. *, **, *** indicate statistical significance at the 10%, 5%, and 1% level, respectively. *n* is the number of observations, *m* the number of different primary datasets from which these observations are derived.
doi:10.1371/journal.pone.0111629.t002

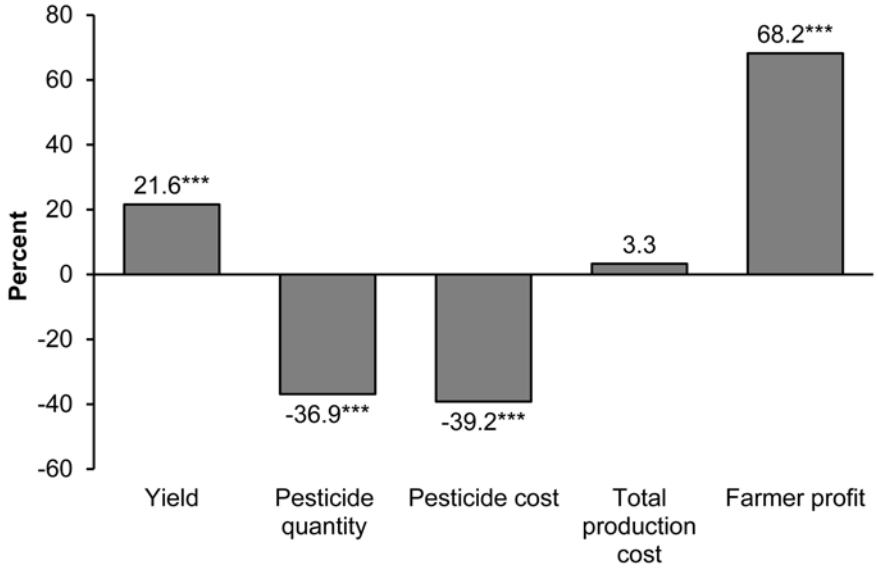

Figure 2. Impacts of GM crop adoption. Average percentage differences between GM and non-GM crops are shown. Results refer to all GM crops, including herbicide-tolerant and insect-resistant traits. The number of observations varies by outcome variable; yield: 451; pesticide quantity: 121; pesticide cost: 193; total production cost: 115; farmer profit: 136. *** indicates statistical significance at the 1% level.
doi:10.1371/journal.pone.0111629.g002

Another concern often voiced in the public debate is that studies funded by industry money might report inflated benefits. Our results show that the source of funding does not significantly influence the impact estimates. We also analyzed whether the statistical method plays a role. Many of the earlier studies just compared yields of GM and non-GM crops without considering possible differences in other inputs and conditions that may also affect the outcome. Net impacts of GM technology can be estimated with regression-based production function models that control for other factors. Interestingly, results derived from regression analysis report higher average yield effects.

Finally, we examined whether the type of publication matters. Controlling for other factors, the regression coefficient for journal publications in column (1) of Table 3 implies that studies published in peer-reviewed journals show 12 percentage points higher yield gains than studies published elsewhere. Indeed, when only including observations from studies that were published in journals, the mean effect size is larger than if all observations are included (Figure S2). On first sight, one might suspect publication bias, meaning that only studies that report substantial effects are accepted for publication in a journal. A common way to assess possible publication bias in meta-analysis is through funnel plots [25], which we show in Figure S3. However, in our case these funnel plots should not be over-interpreted. First, only studies that report variance measures can be included in the funnel plots, which holds true only for a subset of the original studies used here. Second, even if there were publication bias, our mean results would be estimated correctly, because we do include studies that were not published in peer-reviewed journals.

Further analysis suggests that the journal review process does not systematically filter out studies with small effect sizes. The journal articles in the sample report a wide range of yield effects, even including negative estimates in some cases. Moreover, when combining journal articles with papers presented at academic conferences, average yield gains are even higher (Table 3, column 2). Studies that were neither published in a journal nor presented at an academic conference encompass a diverse set of papers, including reports by NGOs and outspoken biotechnology critics. These reports show lower GM yield effects on average, but not all meet common scientific standards. Hence, rather than indicating publication bias, the positive and significant journal coefficient may be the result of a negative NGO bias in some of the grey literature.

Concerning other outcome variables, IR crops have much stronger reducing effects on pesticide quantity than HT crops (Table 3, column 3), as already discussed above. In terms of pesticide costs, the difference between IR and HT is less pronounced and not statistically significant (column 4). The profit gains of GM crops are 60 percentage points higher in developing countries than in developed countries (column 6). This large difference is due to higher GM yield gains and stronger pesticide cost savings in developing countries. Moreover, most GM crops are not patented in developing countries, so that GM seed prices are lower [19]. Like for yields, studies published in peer-reviewed journals report higher profit gains than studies published elsewhere, but again we do not find evidence of publication bias (column 7).

Conclusion

This meta-analysis confirms that – in spite of impact heterogeneity – the average agronomic and economic benefits of GM crops are large and significant. Impacts vary especially by modified crop trait and geographic region. Yield gains and pesticide reductions are larger for IR crops than for HT crops. Yield and farmer profit gains are higher in developing countries than in developed countries. Recent impact studies used better data and methods than earlier studies, but these improvements in study design did not reduce the estimates of GM crop advantages. Rather, NGO reports and other publications without scientific peer review seem to bias the impact estimates downward. But even with such biased estimates included, mean effects remain sizeable.

One limitation is that not all of the original studies included in this meta-analysis reported sample sizes and measures of variance. This is not untypical for analyses in the social sciences, especially when studies from the grey literature are also included. Future

Table 3. Factors influencing results on GM crop impacts (%).

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Variables	**Yield**	**Yield**	**Pesticide quantity**	**Pesticide cost**	**Total cost**	**Farmer profit**	**Farmer profit**
Insect resistance (IR)	6.58** (2.85)	5.25* (2.82)	−37.38*** (11.81)	−7.28 (5.44)	5.63 (5.60)	−22.33 (21.62)	−33.41 (21.94)
Developing country	14.17*** (2.72)	13.32*** (2.65)	−10.23 (8.99)	−19.16*** (5.35)	3.43 (4.78)	59.52*** (18.02)	60.58*** (17.67)
Field-trial data	−7.14** (3.19)	−7.81** (3.08)	–#	−17.56 (11.45)	−10.69* (5.79)	–#	–#
Industry-funded study	1.68 (5.30)	1.05 (5.21)	37.04 (23.08)	−7.77 (10.22)	–#	–#	–#
Regression model result	7.38* (3.90)	7.29* (3.83)	9.67 (10.40)	–#	–#	−11.44 (24.33)	−9.85 (24.03)
Journal publication	12.00*** (2.52)	–	9.95 (6.79)	−3.71 (4.09)	−3.08 (3.30)	48.27*** (15.48)	–
Journal/academic conference	–	16.48*** (2.64)	–	–	–	–	65.29*** (17.75)
Constant	−0.22 (2.84)	−2.64 (2.86)	−4.44 (10.33)	−16.13 (4.88)	−1.02 (4.86)	8.57 (24.33)	−1.19 (24.53)
Observations	451	451	121	193	115	136	136
R^2	0.23	0.25	0.20	0.14	0.12	0.12	0.14

Coefficient estimates from linear regression models are shown with standard errors in parentheses. Dependent variables are GM crop impacts measured as percentage differences between GM and non-GM. All explanatory variables are 0/1 dummies (for variable definitions see Table 1). The yield models in columns (1) and (2) and the farmer profit models in columns (6) and (7) have the same dependent variables, but they differ in terms of the explanatory variables, as shown. *, **, *** indicate statistical significance at the 10%, 5%, and 1% level, respectively. # indicates that the variable was dropped because the number of observations with a value of one was smaller than 5.

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impact studies with primary data should follow more standardized reporting procedures. Nevertheless, our findings reveal that there is robust evidence of GM crop benefits. Such evidence may help to gradually increase public trust in this promising technology.

Supporting Information

Figure S1 Histograms of effect sizes for the five outcome variables.
(PDF)

Figure S2 Impacts of GM crop adoption including only studies published in journals.
(PDF)

Figure S3 Funnel plots for the five outcome variables.
(PDF)

Table S1 List of publications included in the meta-analysis.
(PDF)

Table S2 Distribution of study descriptor dummy variables for different outcomes.
(PDF)

Table S3 Weighted mean impacts of GM crop adoption.
(PDF)

Data S1 Data used for the meta-analysis.
(PDF)

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Author Contributions

Conceived and designed the research: WK MQ. Analyzed the data: WK MQ. Contributed to the writing of the manuscript: WK MQ. Compiled the data: WK.

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Ogunquit

pressherald.com/2014/11/04/ogunquit/

Ogunquit residents voted Tuesday to ban the use of synthetic pesticides, herbicides and fertilizers on private property, the second time they have taken up the issue this year.

Residents approved the ordinance last June, but that vote was voided because town officials forgot to check with the Maine Board of Pesticides Control prior to the vote, as required.

On Tuesday, residents voted 444 to 297 in favor of the ordinance.

The Maine Board of Pesticides Control says, 24 municipalities in Maine have adopted some type of ordinance that regulates the use of pesticides, but Ogunquit is the only town to extend a ban to private property.

In 2009, Ogunquit voters approved an ordinance that prohibited the use of synthetic pesticides on public land. The new ordinance prohibits the use of synthetic pesticides, herbicides and fertilizers, except in emergency situations.

The New York Times | http://nyti.ms/1snszmI

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U.S.D.A. Approves Modified Potato. Next Up: French Fry Fans.

By ANDREW POLLACK NOV. 7, 2014

A potato genetically engineered to reduce the amounts of a potentially harmful ingredient in French fries and potato chips has been approved for commercial planting, the Department of Agriculture announced on Friday.

The potato's DNA has been altered so that less of a chemical called acrylamide, which is suspected of causing cancer in people, is produced when the potato is fried.

The new potato also resists bruising, a characteristic long sought by potato growers and processors for financial reasons. Potatoes bruised during harvesting, shipping or storage can lose value or become unusable.

The biotech tubers were developed by the J. R. Simplot Company, a privately held company based in Boise, Idaho, which was the initial supplier of frozen French fries to McDonald's in the 1960s and is still a major supplier. The company's founder, Mr. Simplot, who died in 2008, became a billionaire.

The potato is one of a new wave of genetically modified crops that aim to provide benefits to consumers, not just to farmers as the widely grown biotech crops like herbicide-tolerant soybeans and corn do. The nonbruising aspect of the potato is similar to that of genetically engineered nonbrowning apples, developed by Okanagan Specialty Fruits, which are awaiting regulatory approval.

But the approval comes as some consumers are questioning the safety of genetically engineered crops and demanding that the foods made from them be labeled. Ballot initiatives calling for labeling were rejected by voters in Oregon and Colorado this week, after food and seed companies poured millions of dollars into campaigns to defeat the measures.

The question now is whether the potatoes — which come in the Russet Burbank, Ranger Russet and Atlantic varieties — will be adopted by food companies and restaurant chains. At least one group opposed to such crops has already pressed McDonald's to reject them.

Genetically modified potatoes failed once before. In the late 1990s, Monsanto began selling potatoes genetically engineered to resist the Colorado potato beetle. But the market collapsed after big potato users, fearing consumer resistance, told farmers not to grow them. Simplot itself, after hearing from its fast-food chain customers, instructed its farmers to stop growing the Monsanto potatoes.

This time around could be different, however, because the potato promises at least potential health benefits to consumers. And unlike Monsanto, Simplot is a long-established power in the potato business and presumably has been clearing the way for acceptance of the product from its customers.

Simplot hopes the way the potato was engineered will also help assuage consumer fears. The company calls its product the Innate potato because it does not contain genes from other species like bacteria, as do many biotech crops.

Rather, it contains fragments of potato DNA that act to silence four of the potatoes' own genes involved in the production of certain enzymes. Future crops — the company has already applied for approval of a potato resistant to late blight, the cause of the Irish potato famine — will also have genes from wild potatoes.

"We are trying to use genes from the potato plant back in the potato plant," said Haven Baker, who is in charge of the potato development at Simplot. "We believe there's some more comfort in that."

That is not likely to persuade groups opposed to such crops, who say altering levels of plant enzymes might have unexpected effects.

Doug Gurian-Sherman, a plant pathologist and senior scientist at the Center for Food Safety, an advocacy group, said that the technique used to silence the genes, called RNA interference, was still not well understood.

"We think this is a really premature approval of a technology that is not being adequately regulated," he said, adding that his group might try to get a court to reverse the approval of the potato.

He said one of the substances being suppressed in the Innate potatoes appeared to be important for proper use of nitrogen by the plant and also for protection from pests.

The Agriculture Department, in its assessment, said the levels of various nutrients in the potatoes were in the normal range, except for the substances targeted by the genetic engineering. Simplot has submitted the potato for a voluntary food safety review by the Food and Drug Administration.

The company says that when the Innate potatoes are fried, the levels of acrylamide are 50 to 75 percent lower than for comparable nonengineered potatoes. It is unclear how much of a benefit that is.

The chemical causes cancer in rodents and is a suspected human carcinogen, though the National Cancer Institute says that scientists do not know with certainty if the levels of the chemical typically found in food are harmful to human health.

Still, Gregory Jaffe, biotechnology project director at the Center for Science in the Public Interest, a consumer group that deals with nutrition issues, welcomed the approval. “We support clearly trying to reduce consumers’ exposure to acrylamide and if this product helps do that, I think it’s a benefit,” he said.

Last year, the F.D.A. issued draft guidance advising the food industry how to reduce levels of acrylamide, which is also found in some baked goods, coffee and other foods. The agency listed numerous steps that could be taken in the growing, handling and cooking of potatoes. Many food companies no doubt have already taken steps to reduce acrylamide levels and might not need the genetically engineered potatoes.

Whether McDonald’s, which did not respond to requests for comment, adopts the potatoes is somewhat academic for at least another couple of years. Simplot anticipates that only a few thousand out of the nation’s more than one million acres of potatoes will be planted with Innate potatoes next year, far too little to serve fast-food chains.

Instead, the company will focus on sales of fresh potatoes and fresh-cut potatoes to supermarkets and food service companies and to potato chip manufacturers, said Doug Cole, a spokesman for Simplot.

The National Potato Council, which represents potato farmers, welcomed the approval, albeit with reservations.

John Keeling, chief executive of the trade group, said growers wanted new technology. But in comments to the Agriculture Department, the group has expressed concern that exports could be disrupted if genetically engineered

varieties inadvertently end up in shipments bound for countries that have not approved the potatoes.

China, for instance, recently turned away shipments of corn containing small amounts of a genetically engineered variety developed by Syngenta that it had not approved for import. Some corn farmers and exporters have sued Syngenta for their losses.

Mr. Cole of Simplot said growers would have to keep the genetically engineered potatoes separate from others and out of exports at least for now. The company plans to apply for approval of the potatoes in the major markets, starting with Canada, Mexico, Japan and then other parts of Asia.

A version of this article appears in print on November 8, 2014, on page B1 of the New York edition with the headline: New Potato, Hot Potato.

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Pesticide Exposure and Depression among Male Private Pesticide Applicators in the Agricultural Health Study

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Background: Pesticide exposure may be positively associated with depression. Few previous studies have considered the episodic nature of depression or examined individual pesticides.

Objective: We evaluated associations between pesticide exposure and depression among male private pesticide applicators in the Agricultural Health Study.

Methods: We analyzed data for 10 pesticide classes and 50 specific pesticides used by 21,208 applicators enrolled in 1993–1997 who completed a follow-up telephone interview in 2005–2010. We divided applicators who reported a physician diagnosis of depression (n = 1,702; 8%) into those who reported a previous diagnosis of depression at enrollment but not follow-up (n = 474; 28%), at both enrollment and follow-up (n = 540; 32%), and at follow-up but not enrollment (n = 688; 40%) and used polytomous logistic regression to estimate odds ratios (ORs) and 95% CIs. We used inverse probability weighting to adjust for potential confounders and to account for the exclusion of 3,315 applicators with missing covariate data and 24,619 who did not complete the follow-up interview.

Results: After weighting for potential confounders, missing covariate data, and dropout, ever-use of two pesticide classes, fumigants and organochlorine insecticides, and seven individual pesticides—the fumigants aluminum phosphide and ethylene dibromide; the phenoxy herbicide (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T); the organochlorine insecticide dieldrin; and the organophosphate insecticides diazinon, malathion, and parathion—were all positively associated with depression in each case group, with ORs between 1.1 and 1.9.

Conclusions: Our study supports a positive association between pesticide exposure and depression, including associations with several specific pesticides.

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Introduction

Exposure to pesticides, particularly organophosphate insecticides (OPs), may be positively associated with depression (Bazylewicz-Walczak et al. 1999; Beseler and Stallones 2008; Beseler et al. 2006, 2008; Mackenzie Ross et al. 2010; Onwuameze et al. 2013; Rehner et al. 2000; Salvi et al. 2003; Weisskopf et al. 2013; Wesseling et al. 2010). However, only a few of these studies were longitudinal (Bazylewicz-Walczak et al. 1999; Beseler and Stallones 2008; Onwuameze et al. 2013; Salvi et al. 2003)—an important consideration because many people with depression will recover and some may relapse (Colman and Ataullahjan 2010). The largest longitudinal study previously conducted (651 Colorado farmers and their spouses) assessed depression annually for three years using the Center for Epidemiological Studies-Depression Scale (CES-D) and found that individuals who reported past pesticide poisoning at baseline were twice as likely to be depressed during follow-up as those who did not (Beseler and Stallones 2008). That study, however, did not evaluate associations with chronic exposure in the absence of poisoning or to specific pesticides.

The Agricultural Health Study (AHS) is a prospective cohort study, including 52,394 licensed private pesticide applicators (mostly farmers), designed to assess associations between agricultural exposures and health end points (Alavanja et al. 1996). We previously found a higher prevalence of depression among male applicators who reported past pesticide poisoning or use of pesticides from several different classes (Beseler et al. 2008). That study, however, used a cross-sectional design and did not examine specific pesticides. The aim of the current study is to assess associations between pesticide use and depression among male pesticide applicators in the AHS.

Methods

Study population and case definition. From 1993 through 1997, pesticide applicators applying for or renewing their pesticide-use licenses at agricultural extension offices in Iowa and North Carolina were invited to enroll in the AHS (Alavanja et al. 1996). A total of 52,394 private applicators (84% of those eligible) enrolled by returning the enrollment questionnaire. An additional baseline questionnaire, the farmer questionnaire, was sent home with all enrolled applicators but returned by only 22,916 (44%). Applicators who returned the farmer questionnaire were older than those who did not, but generally similar otherwise (Tarone et al. 1997). A follow-up telephone interview in 2005–2010, an average of 12.1 years after enrollment, included questions on depression.

We excluded 6,567 applicators because they were female (1,358; 3%), were missing data on depression at enrollment and follow-up (1,894; 4%), or were missing covariate data (3,315; 6%); 45,827 (87%) applicators remained (Figure 1). In addition, 3,979 (8%) died before the follow-up interview and 20,640 (39%) did not complete it for other reasons. In total, we included 21,208 (40%) applicators in this analysis: 1,702 (8%) who reported ever receiving a physician's diagnosis

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of depression (cases) and 19,506 (92%) who did not (noncases) (Figure 1).

Information on physician-diagnosed depression came from the enrollment and farmer questionnaires and the follow-up interview (AHS 2013). The enrollment questionnaire asked "Has a *doctor* ever told you that you had…[d]epression[?]" and the farmer questionnaire asked "Has a *DOCTOR* ever told you that you had (been diagnosed with)…[d]epression requiring medication or shock therapy?" We considered an applicator who responded affirmatively to either question to have a history of depression at enrollment. At follow-up, we asked "Have you ever been diagnosed with depression?" and "How old were you when you were first diagnosed with depression?" We considered any applicator who reported an age at diagnosis less than his age at enrollment to have a history of depression at enrollment regardless of his response to the enrollment depression questions.

We divided cases into three groups based on when the physician diagnosis of depression occurred (before or after enrollment) and on when it was reported via the AHS contacts (at enrollment, at follow-up, or both). The "pre-enrollment enrollment only" (PRE-E) group included 474 (28%) applicators who reported a previous diagnosis of depression at enrollment, but who did not confirm their pre-enrollment diagnosis at follow-up. The "pre-enrollment both" (PRE-B) group included 540 (32%) applicators who reported a previous diagnosis of depression at both enrollment and follow-up (n = 395), or who reported a previous diagnosis at follow-up only but with an age at diagnosis less than their age at enrollment (n = 145). The "post-enrollment" (POST) group included 688 (40%) applicators who reported a previous diagnosis of depression at follow-up but not at enrollment, and whose reported age at diagnosis equaled or exceeded their age at enrollment. Although both the PRE-E and PRE-B groups reported a diagnosis before enrollment, we treated them as separate outcomes in our analysis because we thought that the PRE-B group might be more likely to include men who had chronic depression, thus making them more likely to report a previous diagnosis at both time points, whereas the PRE-E group might not have reported a pre-enrollment diagnosis at follow-up because they did not experience depression during the follow-up period (12.1 years, on average). In addition, associations with pesticide use differed between the two groups. We cannot, however, confirm that the prevalence of depression over time differed between the two groups. It is also possible that PRE-E cases may have been less inclined to confirm their previous diagnosis of depression at follow-up because the interview was conducted via telephone, whereas depression information was collected at enrollment via self-administered paper questionnaires.

Some information on pesticide exposure was available only from the farmer questionnaire. Of the 21,208 applicators included in the analyses, 11,982 completed the farmer questionnaire. Of these, we classified 10,990 as noncases and 306 as PRE-E, 315 as PRE-B, and 371 as POST depression cases.

The AHS was approved by the institutional review boards (IRBs) of the National Institutes of Health and its contractors. The current analysis using coded data was exempted from review by the IRB of the University of North Carolina at Chapel Hill. All participants implied informed consent by returning the enrollment questionnaires and participating in the telephone interview.

Exposure assessment. At enrollment, applicators provided information on demographics, medical conditions, lifestyle, and pesticide use up until the time of enrollment by completing self-administered questionnaires (AHS 2013; Alavanja et al. 1996). We used three types of pesticide exposure variables: *a*) general exposure, *b*) use (personally mixed or applied) of pesticide classes, and *c*) use of individual pesticides. General exposure consisted of three variables: cumulative days of use of any pesticide, physician-diagnosed pesticide poisoning, and experiencing an incident of unusually high personal pesticide exposure (high pesticide exposure event). The latter two variables were available only for applicators who completed the farmer questionnaire. We calculated cumulative days of use of any pesticide as the product of reported duration (years) and frequency (days per year) and then categorized the result into four groups based on quartiles of use among all applicators. We created variables for ever-use of pesticides from four functional classes (fumigants, fungicides, herbicides, and insecticides) and six chemical classes (phenoxy and triazine herbicides, carbamates, and organochlorine, organophosphate, and pyrethroid insecticides) based on responses for individual pesticides. Use of 50 individual pesticides included ever-use and cumulative days of use. Information on ever-use was collected via the enrollment questionnaire for all 50 pesticides, whereas information on duration and frequency, used to calculate cumulative days of use, was collected via the enrollment

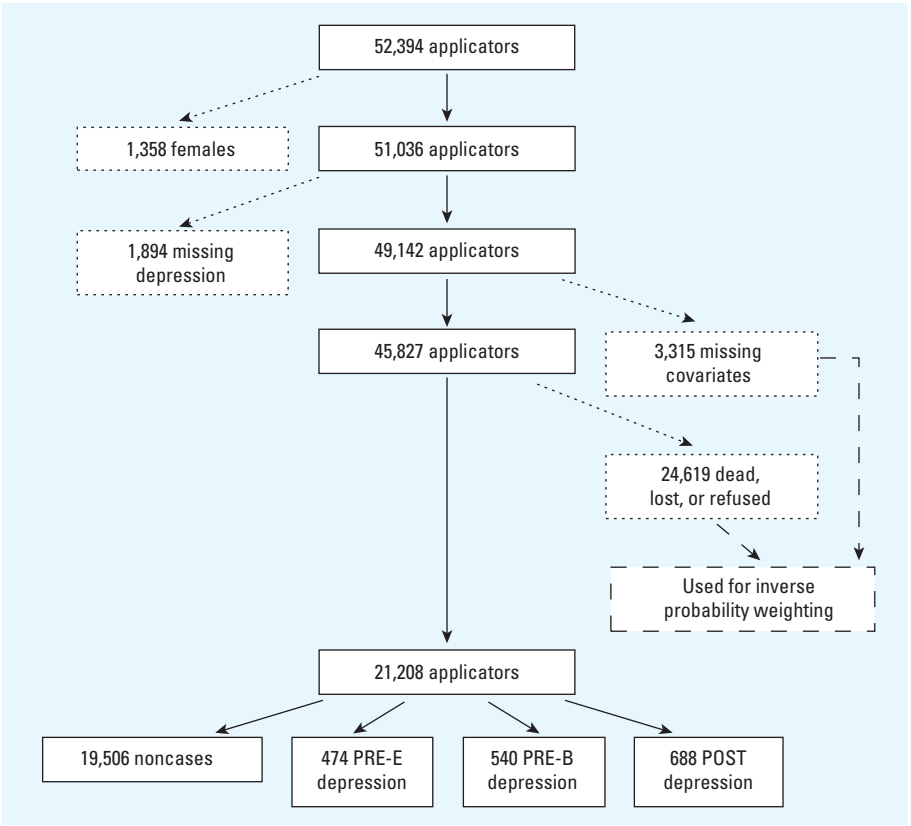

Figure 1. Flow diagram depicting the study population for an analysis of pesticide use and self-reported depression among male private pesticide applicators in the AHS. Solid boxes or lines represent individuals remaining in the study after each step; small-dashed boxes or lines represent individuals excluded after each step (see "Study population and case definition" for more details); large-dashed boxes or lines represent individuals incorporated into the analysis only indirectly via inverse probability weighting (see "Statistical analyses" for more details). Depression groups shown at the bottom of the diagram were defined as described in the text (see "Study population and case definition" for more details).

questionnaire for 22 pesticides and via the farmer questionnaire for the other 28. We calculated cumulative days of use for individual pesticides as the product of duration and frequency variables and then categorized the result into four groups: nonusers plus users categorized at tertiles. For six pesticides, at least two of the 12 exposure-category by depression-group combinations had fewer than five cases, so we instead used three groups: nonusers plus users dichotomized at the median.

Statistical analyses. We had information from the enrollment questionnaire on potential confounders identified from previous literature: age, state, education, marital status, number of children in family, usual frequency of alcohol consumption per week in the past year, cigarette smoking, diabetes (an indication of chronic disease), farm size, and wearing chemical-resistant gloves when personally handling pesticides. For applicators who completed the farmer questionnaire, we also had information on number of doctor visits in the past year (an indication of general health), number of years lived or worked on a farm, working a job off a farm, and solvent (other than gasoline) exposure in the longest-held nonfarm job.

We used a directed acyclic graph (Greenland et al. 1999) to identify two minimally sufficient adjustment sets (MSASs) among potential confounders: *a*) age, alcohol consumption, diabetes, marital status, smoking, solvents, and state; and *b*) age, diabetes, education, and state (see Supplemental Material, Figure S1). This report used the second MSAS because it had less missing covariate information; the first MSAS gave similar results (data not shown).

For our main analyses, we used stabilized inverse probability weights to adjust for confounding and to account for the loss of 3,315 applicators with missing covariate data (in diabetes and education) and 24,619 applicators who did not complete the follow-up interview (Cole and Hernán 2008). For analyses involving information from the farmer questionnaire, we added a weight to account for the loss of 9,226 applicators who did not complete that questionnaire. We used polytomous logistic regression to estimate odds ratios (ORs) and 95% CIs for associations between pesticide exposure and depression within each case group, using noncases as the reference. These ORs apply to the population of 49,142 male applicators not missing data on depression at enrollment and at follow-up. We rounded all ORs and 95% CIs to the tenths place for presentation, and considered pesticide exposure to be "positively associated" with depression if the rounded lower 95% confidence limit for the OR was at least 1.0 or if the rounded OR was at least 1.3. We used Wald chi-square tests to test differences among case group–specific ORs at $\alpha = 0.1$. We assessed linear trends for cumulative-days-of-use variables using the medians of each exposure category. We modeled the median category scores as continuous variables and scaled the trend ORs to interquartile range (IQR) increases in the original cumulative-days-of-use variables.

We used linear, logistic, or ordinal logistic regression, depending on the nature of the exposure variable, to calculate stabilized weights for confounding, missing covariate data, missing farmer questionnaire (if appropriate), and dropout for each exposure separately and then multiplied the three or four weights to obtain the overall stabilized weight (Cole and Hernán 2008; see also Supplemental Material, p. 4). In all models used to calculate the weights (see Supplemental Material, p. 4), we fit age as a restricted, quadratic spline with knots at 40, 48, and 57 years of age based on percentiles of the age distribution in all cases whereas diabetes, education, and state were modeled as shown in Table 1. We applied the overall stabilized weight to polytomous logistic regression models for depression that contained the exposure of interest as the only explanatory variable in the same way that sampling weights are applied when analyzing data from complex survey sampling designs (Cole and Hernán 2008). We calculated 95% CIs using robust variance estimates because using weights induces within-subject correlation (Hernán et al. 2000). We also conducted a sensitivity analysis without weighting; we used standard regression methods to adjust for potential confounding but without adjustment for potential biases from missing covariate data, missing farmer questionnaire, or dropout.

Table 1. Selected characteristics of male private pesticide applicators in the AHS.

Characteristic	Noncases [*n* (%)]	PRE-E[a] Cases [*n* (%)]	PRE-E[a] Adjusted OR[b] (95% CI)	PRE-B[a] Cases [*n* (%)]	PRE-B[a] Adjusted OR[b] (95% CI)	POST[a] Cases [*n* (%)]	POST[a] Adjusted OR[b] (95% CI)	*p* for difference among ORs[c]
Total	19,506 (100)	474 (100)		540 (100)		688 (100)		
Age at enrollment (years)								
≤ 25	540 (3)	5 (1)	0.4 (0.2, 1.0)	7 (1)	0.5 (0.2, 1.0)	9 (1)	0.4 (0.2, 0.8)	
26–35	2,879 (15)	25 (5)	0.4 (0.2, 0.6)	36 (7)	0.5 (0.3, 0.7)	119 (17)	1.0 (0.8, 1.3)	
36–45	5,856 (30)	136 (29)	Reference	158 (29)	Reference	238 (35)	Reference	
46–55	4,909 (25)	143 (30)	1.3 (1.0, 1.6)	177 (33)	1.3 (1.1, 1.7)	184 (27)	0.9 (0.7, 1.1)	
56–65	3,902 (20)	120 (25)	1.3 (1.1, 1.7)	118 (22)	1.1 (0.9, 1.4)	96 (14)	0.6 (0.5, 0.8)	
> 65	1,420 (7)	45 (9)	1.4 (1.0, 2.0)	44 (8)	1.2 (0.8, 1.7)	42 (6)	0.7 (0.5, 1.0)	< 0.01
State of residence								
Iowa	13,520 (69)	329 (69)	Reference	384 (71)	Reference	460 (67)	Reference	
North Carolina	5,986 (31)	145 (31)	0.9 (0.8, 1.1)	156 (29)	0.9 (0.7, 1.1)	228 (33)	1.2 (1.0, 1.4)	0.04
Education level								
≤ Some high school or something else	1,343 (7)	48 (10)	1.4 (1.0, 1.9)	44 (8)	1.2 (0.8, 1.6)	45 (7)	1.1 (0.8, 1.5)	
High school graduate or GED	9,045 (46)	213 (45)	Reference	251 (46)	Reference	314 (46)	Reference	
1–3 years of vocational education beyond high school, some college, or college graduate	8,357 (43)	192 (41)	1.1 (0.9, 1.3)	226 (42)	1.0 (0.9, 1.2)	297 (43)	1.0 (0.8, 1.1)	
≥ 1 years of graduate or professional school	761 (4)	21 (4)	1.1 (0.7, 1.7)	19 (4)	0.9 (0.5, 1.4)	32 (5)	1.2 (0.8, 1.7)	0.79
Ever diagnosed with diabetes								
No	19,051 (98)	450 (95)	Reference	516 (96)	Reference	665 (97)	Reference	
Yes	455 (2)	24 (5)	1.9 (1.2, 2.9)	24 (4)	1.8 (1.2, 2.7)	23 (3)	1.6 (1.0, 2.5)	0.84

Abbreviations: GED, General Equivalency Diploma; POST, post-enrollment; PRE-B, pre-enrollment both; PRE-E, pre-enrollment enrollment only.
[a]Cases were divided into three groups based on when the physician diagnosis of depression occurred (before or after enrollment) and on when it was reported via the AHS contacts (at enrollment, at follow-up, or both). The PRE-E group included applicators who reported a previous diagnosis of depression at enrollment, but who did not confirm their pre-enrollment diagnosis at follow-up. The PRE-B group included applicators who reported a previous diagnosis of depression at both enrollment and follow-up, or who reported a previous diagnosis at follow-up only but with an age at diagnosis less than their age at enrollment. The POST group included applicators who reported a previous diagnosis of depression at follow-up but not enrollment, and whose reported age at diagnosis equaled or exceeded their age at enrollment. [b]Adjusted for age at enrollment (modeled with a cubic polynomial) and state of residence. [c]Differences among case group–specific ORs tested via Wald chi-square tests.

We used four criteria to evaluate the appropriateness of the weights used in our analyses: *a*) nearness of the mean weight to one, *b*) number of extreme weights (e.g., < 0.05 or > 20), *c*) positivity, and *d*) bias–variance (validity–precision) tradeoff (Cole and Hernán 2008). We did not consider the c-statistic, Hosmer–Lemeshow statistic, or any other measure of goodness-of-fit to select variables for inclusion in our models for the weights because doing so can lead to bias (from unbalanced confounders or balanced nonconfounders including instrumental variables), reduced precision, nonpositivity, and/or restricted inference (Westreich et al. 2011). To informally assess the bias–variance tradeoff (Winer 1978), we progressively truncated the overall stabilized weights by resetting weights less (or greater) than a certain percentile to the value of that percentile (Cole and Hernán 2008). Regarding the ORs derived from the untruncated weights as the "true" values, we informally evaluated bias–variance tradeoff by evaluating how features of both the weights and the corresponding ORs changed with increasing truncation. We considered nearness of the mean weight to one, reduction in number of extreme weights, and a balance between increased "bias" and reduced variance in the estimated ORs (Cole and Hernán 2008). Truncating the overall stabilized weights at the first and 99th percentiles appeared to be the best balance of validity and precision and mitigated problems identified by all of the criteria in this analysis.

We conducted several additional sensitivity analyses. We augmented models for ever-use of pesticide classes or individual pesticides by adding potentially confounding variables one at a time in models for all the different types of weights. These variables were number of children, doctor visits in the past year, farm size, use of chemical-resistant gloves, and cumulative lifetime days of use of any pesticide. We included all variables in Table 1 and in Supplemental Material, Table S1, in models for the dropout weights to evaluate whether there were selection effects beyond that captured by the covariates in the second MSAS. To account for correlations between use of different pesticides, we added the pesticide that was most strongly correlated with the pesticide of interest to models for the weights. We refit models excluding applicators who reported physician-diagnosed pesticide poisoning to evaluate whether or not results were driven by pesticide poisoning. Finally, we evaluated effect measure modification by state or by use of chemical-resistant gloves using the likelihood ratio test at $\alpha = 0.1$. We performed all analyses via SAS version 9.2 (SAS Institute Inc., Cary, NC).

Results

After adjustment for age at enrollment and state of residence, the odds of depression were higher in each case group for applicators who were past cigarette smokers compared with those who never smoked, who reported at least one visit to a medical doctor in the past year compared with no visits, and who reported a previous diagnosis of diabetes compared with none (Table 1; see also Supplemental Material, Table S1). For age, state, marital status, doctor visits in the past year, and solvent (other than gasoline) exposure in the longest-held nonfarm job, ORs for POST depression were generally different from ORs for PRE-E and PRE-B depression, whereas the latter two were generally similar (Table 1; see also Supplemental Material, Table S1).

The mean weight of all truncated overall stabilized weights was approximately one except that for the categorical version of cumulative days of carbaryl use (mean weight = 1.28). There were no extreme weights (see Supplemental Material, Tables S2–S4).

After weighting for age, diabetes diagnosis, education, state, missing covariate data, missing farmer questionnaire (where appropriate), and dropout, depression was positively associated with cumulative days of use of any pesticide, physician-diagnosed pesticide poisoning, and ever experiencing a high pesticide exposure event among PRE-E and PRE-B cases, but not among POST cases (Table 2). In each case group, depression was positively associated with ever-use of fumigants as a class and organochlorine insecticides as a class as well as the specific fumigants aluminum phosphide and ethylene dibromide; the phenoxy herbicide (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T); the organochlorine insecticide dieldrin; and the OPs diazinon, malathion, and parathion (Table 3).

Many pesticides were positively associated with depression in one or two, but not all three, case groups, but the ORs did not differ significantly (Table 3). Wald chi-square

Table 2. Pesticide use and self-reported depression among male private pesticide applicators in the AHS.

Variable	Noncases [*n* (%)]	PRE-E[a] Cases [*n* (%)]	PRE-E[a] IP-weighted OR[b] (95% CI)	PRE-B[a] Cases [*n* (%)]	PRE-B[a] IP-weighted OR[b] (95% CI)	POST[a] Cases [*n* (%)]	POST[a] IP-weighted OR[b] (95% CI)	*p* for difference among ORs[c]
Total	19,506 (100)	474 (100)		540 (100)		688 (100)		
Cumulative days personally mixed or applied pesticides[d]								
≤ 56 (median = 24.5)	4,520 (23)	79 (17)	Reference	102 (19)	Reference	164 (24)	Reference	
57–225 (median = 116.0)	6,876 (35)	164 (35)	1.2 (0.9, 1.6)	189 (35)	1.1 (0.8, 1.4)	223 (32)	0.9 (0.7, 1.1)	
226–457 (median = 369.8)	4,139 (21)	107 (23)	1.4 (1.0, 1.9)	129 (24)	1.3 (1.0, 1.8)	170 (25)	1.1 (0.9, 1.4)	
> 457 (median = 767.3)	3,968 (20)	124 (26)	1.6 (1.2, 2.2)	120 (22)	1.3 (1.1, 1.7)	131 (19)	0.9 (0.7, 1.2)	0.10
Missing	3	0		0		0		
Trend (IQR = 401.3)[e]			1.3 (1.1, 1.4)		1.1 (1.0, 1.3)		1.0 (0.9, 1.1)	0.03
Ever diagnosed with pesticide poisoning[f]								
No	10,656 (98)	274 (90)	Reference	293 (95)	Reference	362 (98)	Reference	
Yes	206 (2)	29 (10)	4.2 (2.7, 6.6)	16 (5)	2.5 (1.4, 4.4)	7 (2)	1.0 (0.4, 2.4)	0.01
Missing	128	3		6		2		
Ever experienced an incident of unusually high personal pesticide exposure[f]								
No	9,093 (85)	215 (72)	Reference	214 (71)	Reference	296 (83)	Reference	
Yes	1,642 (15)	84 (28)	2.3 (1.8, 3.1)	86 (29)	2.2 (1.6, 2.9)	60 (17)	1.1 (0.8, 1.5)	< 0.01
Missing	255	7		15		15		

Abbreviations: IP, inverse probability; POST, post-enrollment; PRE-B, pre-enrollment both; PRE-E, pre-enrollment enrollment only.
[a]See Table 1 for a description of the three case groups. [b]Weights were adjusted for age at enrollment (modeled with a restricted, quadratic spline with knots at 40, 48, and 57 years of age based on percentiles of the age distribution in cases), ever diagnosed with diabetes, education level, state of residence, not missing covariate data (conditional on age, state, the exposure, and pairwise interaction terms between each covariate and the exposure), and not dropping out of the AHS cohort (conditional on age, diabetes, education, state, the exposure, and pairwise interaction terms between each covariate and the exposure). 95% CIs were calculated with robust variance estimates. [c]Differences among case group–specific ORs were tested via Wald chi-square tests. [d]Category boundaries were set at quartiles of cumulative days of pesticide use among all male private pesticide applicators. [e]We used within-category medians and scaled the OR to an IQR-unit (days) increase in cumulative days of pesticide use among all male private pesticide applicators. [f]Data were available only for 11,982 applicators who completed the farmer questionnaire. Weights were additionally adjusted for completing the farmer questionnaire (conditional on age, diabetes, education, and state).

Table 3. Ever-use of pesticide classes and specific pesticides and self-reported depression among male private pesticide applicators in the AHS.

Ever personally mixed or applied	Noncases[a] [*n* (%)]	PRE-E[b] Cases[a] [*n* (%)]	PRE-E[b] IP-weighted OR[c,d] (95% CI)	PRE-B[b] Cases[a] [*n* (%)]	PRE-B[b] IP-weighted OR[c,d] (95% CI)	POST[b] Cases[a] [*n* (%)]	POST[b] IP-weighted OR[c,d] (95% CI)	*p* for difference among ORs[e]
Total	19,506 (100)	474 (100)		540 (100)		688 (100)		
Fumigants	4,363 (23)	131 (29)	1.4 (1.1, 1.8)	166 (32)	1.8 (1.5, 2.3)	177 (27)	1.2 (1.0, 1.5)	0.03
Aluminum phosphide	940 (5)	32 (7)	1.4 (0.9, 2.0)	38 (7)	1.3 (0.9, 1.9)	49 (8)	1.6 (1.1, 2.2)	0.75
Carbon tetrachloride/carbon disulfide (80/20 mix)	1,164 (6)	46 (10)	1.8 (1.3, 2.6)	53 (11)	1.9 (1.4, 2.7)	44 (7)	1.2 (0.8, 1.7)	0.11
Ethylene dibromide	676 (4)	24 (5)	1.7 (1.0, 2.7)	25 (5)	1.5 (1.0, 2.4)	29 (5)	1.3 (0.9, 2.1)	0.79
Methyl bromide	2,853 (15)	75 (16)	1.2 (0.7, 1.9)	90 (17)	1.6 (1.0, 2.4)	109 (16)	1.2 (0.8, 1.8)	0.57
Fungicides	6,850 (36)	184 (40)	1.2 (1.0, 1.5)	213 (41)	1.3 (1.1, 1.6)	256 (39)	1.1 (0.9, 1.3)	0.33
Benomyl[f]	1,793 (10)	50 (11)	1.5 (1.0, 2.2)	48 (9)	1.1 (0.7, 1.7)	70 (11)	1.3 (0.9, 1.8)	0.67
Captan	2,301 (12)	62 (14)	1.2 (0.9, 1.5)	86 (17)	1.4 (1.1, 1.8)	90 (14)	1.2 (0.9, 1.5)	0.52
Chlorothalonil	1,326 (7)	31 (7)	0.9 (0.5, 1.5)	43 (8)	1.3 (0.8, 2.0)	55 (8)	1.2 (0.8, 1.7)	0.58
Maneb/mancozeb	1,775 (10)	50 (11)	1.3 (0.8, 2.0)	51 (10)	1.2 (0.7, 1.8)	65 (10)	1.2 (0.8, 1.8)	0.95
Metalaxyl	4,157 (22)	120 (27)	1.5 (1.1, 1.9)	122 (24)	1.3 (1.0, 1.7)	151 (23)	1.0 (0.8, 1.3)	0.12
Ziram	276 (2)	10 (2)	1.6 (0.8, 3.1)	5 (1)	0.8 (0.3, 2.0)	12 (2)	1.4 (0.8, 2.6)	0.46
Herbicides	19,086 (98)	469 (99)	1.6 (0.7, 4.0)	533 (99)	1.8 (0.8, 3.9)	677 (99)	1.1 (0.6, 2.1)	0.62
Alachlor	10,526 (56)	287 (63)	1.3 (1.0, 1.6)	325 (62)	1.2 (1.0, 1.4)	384 (59)	1.1 (0.9, 1.3)	0.61
Butylate	6,338 (34)	162 (36)	1.1 (0.9, 1.3)	196 (39)	1.1 (0.9, 1.3)	234 (36)	1.1 (0.9, 1.3)	0.80
Chlorimuron-ethyl	7,077 (38)	160 (36)	0.9 (0.8, 1.2)	199 (39)	1.1 (0.9, 1.3)	261 (40)	1.0 (0.9, 1.2)	0.59
Dicamba	10,237 (55)	248 (54)	0.9 (0.7, 1.1)	292 (57)	1.0 (0.8, 1.2)	365 (57)	1.0 (0.8, 1.2)	0.74
EPTC	4,013 (22)	113 (25)	1.2 (0.9, 1.5)	105 (21)	0.9 (0.7, 1.2)	156 (24)	1.0 (0.8, 1.3)	0.44
Glyphosate	15,053 (78)	376 (80)	1.2 (0.9, 1.6)	426 (79)	1.1 (0.9, 1.4)	540 (79)	1.1 (0.9, 1.3)	0.80
Imazethapyr	8,480 (46)	207 (46)	1.0 (0.8, 1.3)	220 (43)	0.9 (0.7, 1.1)	304 (47)	1.1 (0.9, 1.3)	0.42
Metolachlor	9,121 (49)	229 (51)	1.1 (0.9, 1.3)	231 (45)	0.8 (0.7, 1.0)	311 (48)	1.0 (0.8, 1.1)	0.20
Paraquat	4,402 (24)	120 (26)	1.2 (1.0, 1.5)	123 (25)	1.1 (0.9, 1.4)	158 (24)	1.1 (0.9, 1.3)	0.77
Pendimethalin	8,372 (45)	218 (48)	1.2 (1.0, 1.4)	217 (42)	0.9 (0.8, 1.1)	282 (43)	0.9 (0.8, 1.1)	0.09
Petroleum oil	9,408 (51)	260 (58)	1.3 (1.1, 1.6)	285 (57)	1.2 (0.9, 1.5)	336 (52)	1.0 (0.9, 1.2)	0.11
Trifluralin	10,286 (55)	266 (59)	1.2 (1.0, 1.5)	299 (58)	1.1 (0.9, 1.3)	363 (56)	1.1 (0.9, 1.3)	0.63
Phenoxy herbicides	15,742 (82)	391 (84)	1.1 (0.9, 1.5)	456 (86)	1.3 (1.0, 1.7)	541 (80)	0.9 (0.8, 1.1)	0.11
2,4-D	15,371 (79)	378 (81)	1.1 (0.8, 1.4)	442 (82)	1.2 (0.9, 1.5)	526 (78)	1.0 (0.8, 1.2)	0.45
2,4,5-T	4,517 (24)	157 (35)	1.6 (1.3, 2.0)	178 (35)	1.6 (1.3, 1.9)	157 (24)	1.2 (1.0, 1.5)	0.10
2,4,5-TP	1,841 (10)	71 (16)	1.7 (1.3, 2.2)	73 (14)	1.7 (1.3, 2.2)	67 (11)	1.1 (0.9, 1.5)	0.07
Triazine herbicides	15,768 (82)	393 (84)	1.1 (0.8, 1.5)	445 (83)	1.0 (0.8, 1.3)	556 (82)	1.1 (0.8, 1.3)	0.91
Atrazine	14,554 (75)	372 (79)	1.2 (1.0, 1.6)	415 (77)	1.0 (0.8, 1.3)	511 (75)	1.0 (0.8, 1.2)	0.44
Cyanazine	8,399 (45)	233 (51)	1.3 (1.0, 1.6)	258 (50)	1.1 (0.9, 1.3)	304 (46)	1.1 (0.9, 1.4)	0.55
Metribuzin	9,061 (49)	236 (52)	1.1 (0.9, 1.4)	264 (52)	1.0 (0.9, 1.3)	322 (49)	1.0 (0.9, 1.2)	0.83
Insecticides	18,379 (95)	458 (97)	1.3 (0.7, 2.2)	510 (95)	1.0 (0.6, 1.5)	655 (97)	1.5 (1.0, 2.4)	0.34
Carbamates[f]	13,037 (68)	335 (71)	1.0 (0.8, 1.3)	389 (73)	1.0 (0.8, 1.3)	475 (70)	1.1 (0.9, 1.3)	0.95
Aldicarb	1,891 (10)	42 (9)	0.9 (0.6, 1.5)	52 (10)	1.4 (1.0, 2.2)	81 (13)	1.4 (1.0, 1.9)	0.28
Carbaryl	10,984 (58)	295 (64)	1.2 (0.9, 1.5)	336 (64)	1.2 (1.0, 1.5)	411 (62)	1.1 (0.9, 1.4)	0.87
Carbofuran	5,576 (30)	153 (34)	1.2 (1.0, 1.5)	181 (35)	1.2 (1.0, 1.5)	180 (28)	0.9 (0.8, 1.1)	0.14
Organochlorine insecticides	10,316 (55)	333 (72)	1.9 (1.5, 2.4)	334 (64)	1.2 (1.0, 1.4)	368 (56)	1.2 (1.0, 1.5)	0.01
Aldrin	3,991 (22)	140 (31)	1.4 (1.1, 1.9)	159 (31)	1.5 (1.2, 1.9)	137 (21)	1.2 (0.9, 1.5)	0.36
Chlordane	5,321 (28)	185 (41)	1.6 (1.3, 2.0)	179 (35)	1.3 (1.0, 1.6)	185 (29)	1.1 (0.9, 1.3)	0.03
DDT	5,152 (28)	174 (38)	1.8 (1.4, 2.3)	175 (34)	1.3 (1.0, 1.7)	143 (22)	1.0 (0.7, 1.3)	0.01
Dieldrin	1,476 (8)	56 (13)	1.6 (1.1, 2.3)	59 (12)	1.6 (1.1, 2.2)	48 (7)	1.3 (0.9, 1.8)	0.63
Heptachlor	3,354 (18)	131 (29)	1.6 (1.3, 2.1)	126 (25)	1.3 (1.0, 1.7)	100 (16)	1.0 (0.8, 1.3)	0.04
Lindane	4,053 (22)	146 (32)	1.6 (1.3, 2.0)	141 (28)	1.3 (1.0, 1.6)	152 (23)	1.2 (0.9, 1.4)	0.08
Toxaphene	2,899 (16)	97 (22)	1.5 (1.1, 1.9)	110 (22)	1.5 (1.2, 1.9)	104 (16)	1.1 (0.9, 1.4)	0.12
Organophosphate insecticides	17,563 (91)	442 (94)	1.6 (1.1, 2.3)	494 (92)	1.2 (0.8, 1.7)	629 (93)	1.3 (1.0, 1.8)	0.56
Chlorpyrifos	8,457 (44)	221 (47)	1.2 (1.0, 1.4)	272 (50)	1.3 (1.1, 1.5)	300 (44)	1.0 (0.9, 1.2)	0.10
Coumaphos	1,799 (10)	57 (13)	1.2 (0.9, 1.7)	63 (13)	1.3 (1.0, 1.7)	54 (9)	0.8 (0.6, 1.1)	0.03
Diazinon	6,211 (33)	182 (40)	1.4 (1.1, 1.7)	207 (41)	1.3 (1.1, 1.6)	235 (36)	1.2 (1.0, 1.4)	0.51
Dichlorvos	1,856 (12)	61 (14)	1.1 (0.8, 1.5)	96 (19)	1.6 (1.3, 2.1)	99 (15)	1.3 (1.0, 1.6)	0.11
Fonofos	4,396 (24)	132 (29)	1.3 (1.0, 1.7)	144 (28)	1.1 (0.9, 1.4)	146 (23)	0.9 (0.7, 1.2)	0.18
Malathion	13,941 (74)	369 (80)	1.3 (1.0, 1.7)	410 (79)	1.2 (1.0, 1.6)	503 (76)	1.1 (1.0, 1.4)	0.62
Parathion	2,903 (16)	102 (23)	1.5 (1.2, 1.9)	95 (19)	1.2 (1.0, 1.6)	116 (18)	1.3 (1.0, 1.6)	0.51
Phorate	6,523 (35)	191 (42)	1.3 (1.0, 1.6)	196 (38)	1.0 (0.8, 1.2)	228 (35)	1.0 (0.8, 1.2)	0.25
Terbufos	7,746 (42)	223 (50)	1.4 (1.1, 1.7)	240 (47)	1.2 (1.0, 1.4)	265 (41)	1.0 (0.8, 1.2)	0.07
Trichlorfon	123 (1)	5 (1)	1.5 (0.6, 3.7)	2 (1)	—[g]	1 (< 1)	—[g]	—[g]
Pyrethroid insecticides	4,805 (26)	128 (28)	1.2 (1.0, 1.5)	146 (28)	1.1 (0.9, 1.4)	164 (25)	0.9 (0.8, 1.1)	0.17
Permethrin (for animals)	2,841 (15)	78 (17)	1.2 (0.9, 1.5)	87 (17)	1.0 (0.8, 1.4)	104 (16)	1.0 (0.8, 1.3)	0.74
Permethrin (for crops)	2,539 (14)	68 (15)	1.2 (0.9, 1.6)	85 (17)	1.3 (1.0, 1.7)	82 (13)	0.9 (0.7, 1.2)	0.09

Abbreviations: 2,4-D, (2,4-dichlorophenoxy)acetic acid; 2,4,5-T, (2,4,5-trichlorophenoxy)acetic acid; 2,4,5-TP, (*RS*)-2-(2,4,5-trichlorophenoxy)propionic acid; DDT, 1,1,1-trichloro-2,2-bis(4-chlorophenyl) ethane; EPTC, *S*-ethyl dipropyl(thiocarbamate); IP, inverse probability; POST, post-enrollment; PRE-B, pre-enrollment both; PRE-E, pre-enrollment enrollment only.
[a]Information for specific pesticides was missing for < 1–6% of male private pesticide applicators. [b]See Table 1 for a description of the three case groups. [c]Male private pesticide applicators who did not use each pesticide class or specific pesticide were the reference. [d]Weights were adjusted for age at enrollment (modeled with a restricted, quadratic spline with knots at 40, 48, and 57 years of age based on percentiles of the age distribution in cases), ever diagnosed with diabetes, education level, state of residence, not missing covariate data (conditional on age, state, the exposure, and pairwise interaction terms between each covariate and the exposure), and not dropping out of the AHS cohort (conditional on age, diabetes, education, state, the exposure, and pairwise interaction terms between each covariate and the exposure). 95% CIs were calculated with robust variance estimates. [e]Differences among case group–specific ORs were tested via Wald chi-square tests. [f]Benomyl is also included in carbamates. [g]OR (95% CI) and *p* for difference not shown because fewer than five PRE-B or POST cases ever personally mixed or applied trichlorfon.

tests indicated that associations for ever-use of two pesticide classes and nine specific pesticides differed significantly at $\alpha = 0.1$ among case groups. ORs for PRE-B depression were higher than those for PRE-E and POST depression for fumigants as a class, whereas ORs for PRE-E depression were higher than those for PRE-B and POST depression for organochlorine insecticides as a class (Table 3). For the nine specific pesticides, the most consistent finding was that ORs were elevated (lower 95% confidence limit ≥ 1.0 or OR ≥ 1.3) for PRE-E and PRE-B depression, but not for POST depression; this pattern was observed for the phenoxy herbicide (*RS*)-2-(2,4,5-trichlorophenoxy)propionic acid (2,4,5-TP); the organochlorine insecticides chlordane, 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (DDT), heptachlor, and lindane; and the OP terbufos (Table 3).

We observed positive trend ORs, based on the medians of each exposure category and scaled to IQR increases in the original cumulative-days-of-use variables, for associations between depression and cumulative days of use of the fumigants ethylene dibromide and methyl bromide; the fungicide captan; and the organochlorine insecticide lindane in each case group (see Supplemental Material, Table S5). For none of these agents, however, were the categorical ORs monotonically increasing in each case group (see Supplemental Material, Table S5). We also observed positive trend ORs for several other pesticides in at least one case group and several pesticides had significantly different trend ORs at $\alpha = 0.1$ among case groups (see Supplemental Material, Table S5).

Augmenting models for ever-use of pesticide classes or individual pesticides by including additional variables (number of children, doctor visits in the past year, farm size, use of chemical-resistant gloves, cumulative lifetime days of use of any pesticide, or the pesticide that was most strongly correlated with the pesticide of interest) one at a time in models for all the different types of weights did not meaningfully change results, nor did including all variables in Table 1 and Supplemental Material, Table S1, in the models for the dropout weights (data not shown). Excluding applicators who reported physician-diagnosed pesticide poisoning did not change results (data not shown). We saw no consistent evidence of effect measure modification by state or by use of chemical-resistant gloves (data not shown). Finally, results were similar when we used standard regression methods (see Supplemental Material, Tables S6–S7).

Discussion

We found positive associations between use of some pesticides and depression among male private pesticide applicators in the AHS. Depression was positively associated in each case group with ever-use of two pesticide classes, fumigants and organochlorine insecticides, as well as with ever-use of seven individual pesticides: the fumigants aluminum phosphide and ethylene dibromide; the phenoxy herbicide 2,4,5-T; the organochlorine insecticide dieldrin; and the OPs diazinon, malathion, and parathion. Positive relationships between depression and cumulative days of use were evident, though nonmonotonic, in each case group for the fumigants ethylene dibromide and methyl bromide, the fungicide captan, and the organochlorine insecticide lindane.

Positive associations between depression and acute, high-intensity pesticide exposures, such as pesticide poisoning or high pesticide exposure events, were reported previously in a longitudinal study of 651 Colorado farmers and their spouses (Beseler and Stallones 2008) and cross-sectional studies of 208 Costa Rican banana plantation workers (Wesseling et al. 2010), and 17,585 male private pesticide applicators (Beseler et al. 2008) and 29,074 wives in the AHS (Beseler et al. 2006). In our study, depression was positively associated with physician-diagnosed pesticide poisoning and high pesticide exposure events among PRE-E and PRE-B cases, but not among POST cases.

Previous studies have observed positive associations between depression and exposure to any pesticides or to some pesticide classes, particularly OPs: a follow-up study in Brazil that compared 25 agricultural workers assessed after 3 months of OP exposure with themselves assessed again after 3 months of no OP exposure (Salvi et al. 2003); a 3-month follow-up study in Poland that compared 26 OP-exposed greenhouse workers with 25 unexposed canteen, kitchen, and administrative workers (Bazylewicz-Walczak et al. 1999); a 3-year follow-up study of 257 farm operators in Iowa that compared those exposed to pesticides with those who were not (Onwuameze et al. 2013); a cross-sectional study in England that compared 127 current and retired sheep dippers exposed to OPs with 78 unexposed current and retired police officers (Mackenzie Ross et al. 2010); and a cross-sectional study of 17,585 male private pesticide applicators in the AHS that separately compared those exposed to any pesticide or to seven pesticide classes (carbamates, fumigants, fungicides, herbicides, insecticides, organochlorine insecticides, OPs) with those who were not (Beseler et al. 2008). A study of 567 agricultural workers in France that evaluated exposure to any pesticide, three pesticide classes, or 13 herbicide families, using no exposure to the pesticide class/family in question as the reference, reported positive associations between depression and exposure to herbicides in general and dinitrophenol herbicides, but not exposure to any pesticide, fungicides, insecticides, or the other 12 herbicide families (Weisskopf et al. 2013). In contrast, a cross-sectional survey of 9,844 sheep dippers in England and Wales that used no exposure to any pesticides as the common reference found no association between depression and use of sheep dip (usually diazinon or other OPs), other insecticides, herbicides, fungicides, or wood preservatives (Solomon et al. 2007). In our study, depression was positively associated with cumulative days of use of any pesticide among PRE-E and PRE-B cases, ever-use of the pesticides classes fumigants and organochlorine insecticides in each case group, and ever-use of several other pesticide classes, including OPs, in at least one case group. Results appeared to be independent of pesticide poisoning, because we observed similar results when we excluded applicators who reported physician-diagnosed pesticide poisoning (data not shown).

Only one previous study evaluated the association between depression and a specific pesticide, finding a cross-sectional association between parathion exposure and CES-D scores indicative of clinical depression among 115 adults in Jackson County, Mississippi (Rehner et al. 2000). We found that ever-use or trend versions of cumulative lifetime days of use of several individual pesticides, including parathion, were positively associated with depression.

In general, we observed fewer positive associations between pesticide use and depression among POST cases than among PRE-E or PRE-B cases. Reverse causation—where depression increases exposure, perhaps through careless handling of pesticides—is unlikely to explain the differences in associations among case groups because use of chemical-resistant gloves was not inversely associated with depression after adjustment for age and state, and because including use of chemical-resistant gloves in models for the weights did not change results. Alternatively, differences among case group–specific associations might be attributable to exposure being evaluated closer to first reported diagnosis of depression for PRE-E and PRE-B cases than for POST cases, which could be particularly important for pesticides, such as organochlorine insecticides, with marked secular trends in use. Using information on past instead of ongoing pesticide use could have obscured associations with POST depression. Differences among case group–specific associations might be attributable to residual confounding from observed differences in personal characteristics or in cumulative days of use of any pesticide among case groups; for example, the average cumulative days of use of any pesticide reported by POST cases was 343 compared with 424 for PRE-E and 387 for PRE-B cases (Kruskal–Wallis $p = 0.02$).

Finally, although we asked about ever-diagnosis of depression at both enrollment and follow-up, some PRE-E depression cases were likely misclassified because they did not report a previous diagnosis at follow-up; in other words, they should have been classified as PRE-B cases. Possible reasons for this omission include recovering from depression before the follow-up interview (which was administered 12.1 years, on average, after enrollment) or, due to the sensitive nature of mental health conditions, being less inclined to confirm a previous diagnosis of depression because the follow-up interview was conducted via telephone, whereas depression information was collected at enrollment via self-administered paper questionnaires. We cannot, however, confirm either of these possibilities. Despite this possible misclassification, we analyzed PRE-E depression as a separate case group because the number of applicators in this group was large (n = 474) and associations with pesticide use differed from those observed with PRE-B depression.

We used three strategies to account for exposure to multiple pesticides. First, we grouped individual pesticides into 10 pesticide classes (4 functional, 6 chemical) because the pesticide that was most strongly correlated with the pesticide of interest was often in the same class. We also conducted sensitivity analyses in which we additionally weighted for cumulative days of use of any pesticide or for the pesticide that was most strongly correlated with the pesticide of interest. Although neither strategy meaningfully changed our results (data not shown), we cannot rule out the possibility that associations between depression and use of individual pesticides were confounded by use of other pesticides.

We used inverse probability weighting to adjust for potential confounding and for potential biases from missing covariate data, missing farmer questionnaires, or dropout. One limitation of inverse probability weighting is that residual confounding, missing data bias, and/or selection bias could still occur. In addition, c-statistics for the dropout models, while not used to select variables for inclusion in our models for the weights, ranged from 0.60 to 0.61, which suggests that dropout in the AHS is mostly random or that our models did not predict dropout well. The former seems more likely because Montgomery et al. (2010) found that applicators who reported physician-diagnosed depression at enrollment were equally likely to drop out of the AHS before the first follow-up interview in 1998–2003 as applicators who did not report depression (OR = 0.92; 95% CI: 0.82, 1.02 after adjustment for age, state, education, and smoking).

Our information on pesticide use was self-reported and could be misclassified. Using data from orchardists in Washington State reported during the year of use as the gold standard, Engel et al. (2001) found sensitivities for reporting ever-use of pesticides 25 years later were 1.00 for any pesticides, 0.87–1.00 for pesticides classes included in our study, and 0.80–0.94 for individual pesticides included in our study. A case–control study of cancer in Montreal, Canada, found the specificity of self-reported ever-exposure to pesticides or fertilizers was 0.95 when compared with expert assessment (Fritschi et al. 1996). In a reliability study of a subset of AHS applicators in Iowa who completed the enrollment questionnaire twice 1 year apart, percent exact agreement for ever-use of 10 individual pesticides ranged from 0.79 to 0.88 (Blair et al. 2002). Another study found that < 1–5% of AHS applicators overestimated duration of use of 19 individual pesticides relative to the years the pesticide active ingredients were first registered for use with the U.S. Environmental Protection Agency (Hoppin et al. 2002). The effect of depression on recall of past pesticide use is unknown. Cancer cases and controls, however, were found to report pesticide use with similar accuracy in a validation study in Kansas (Blair and Zahm 1993), and there is little evidence for differential recall in the self-reporting of occupational exposures among cases and controls of other diseases (Teschke et al. 2002).

We also relied on self-reports of ever physician-diagnosed depression. Using information from a validation study conducted in a cohort of university graduates in Spain, the calculated sensitivity and specificity of self-reported ever physician-diagnosed depression was 0.85 and 0.68, respectively, when the Structured Clinical Interview for the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, was used as the gold standard (Sanchez-Villegas et al. 2008). In addition, associations we observed with pesticide poisoning and patient characteristics were similar to those reported in other studies, increasing confidence in the accuracy of our outcome. For example, depression was more common among applicators who were past smokers (Strine et al. 2008) or who had visited a medical doctor in the past year or had poorer health (Beseler and Stallones 2008). Therefore, the validity of self-reported ever physician-diagnosed depression in our study is likely good.

Our cohort is imperfect for longitudinal analyses of pesticide exposure and depression because we collected information on depression at only two points in time on average 12.1 years apart, and we assessed ever physician-diagnosed depression rather than current depression. Thus, we were unable to use longitudinal or life-course statistical methods.

Our study has several strengths, including its large size. Its prospective nature provided the opportunity to identify POST cases of depression as well as PRE-E and PRE-B cases. We had detailed information on applicators' exposures, including general pesticide exposure, use of pesticide classes, and use of individual pesticides. We could control for many potential confounders and demonstrated the robustness of our results to additional potential confounders not included in the main models (data not shown). Finally, we used inverse probability weighting to adjust for potential biases from missing covariate data, missing farmer questionnaires, or dropout. Overall, the effect of missing data and dropouts on our results appeared to be small because results were similar when we used standard regression methods (see Supplemental Material, Tables S6–S7).

Conclusions

Our study supports a positive association between depression and occupational pesticide use among applicators. Furthermore, it suggests several specific pesticides that deserve further investigation in animal studies and other human populations.

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Maine Man Pleads Guilty to Lying About Pesticide

MPBN Nov. 20th, 2014

By THE ASSOCIATED PRESS

PORTLAND, Maine - The U.S. Attorney's Office for Maine says a Calais man pleaded guilty to making a false statement to federal agents regarding his sale of a pesticide.

U.S. and Canadian agents asked Clyde Eldridge in 2010 to identify anyone he sold cypermethrin and whether he had records of the sales. Eldridge owned C&E Feeds, a feed and pet store in Calais. Attorneys say Eldridge told investigators that he did not keep track of the sales.

Investigators later learned Eldridge recorded sales of the pesticide to a production manager for a subsidiary of Cooke Aquaculture. That company pleaded guilty in a Canadian court to illegally using pesticides that killed hundreds of lobsters in waters near Maine's border.

Eldridge faces up to five years in prison and a $250,000 fine.

The New York Times | http://nyti.ms/1BG1ncD

U.S.

Agencies Look for Cause of Fatal Gas Leak in Texas

By MANNY FERNANDEZ NOV. 16, 2014

LA PORTE, Tex. — One day after a leak of toxic gas killed four workers at a DuPont chemical plant here, federal and state agencies were assembling to investigate the accident and response.

As a steady rain fell Sunday, teams from the Environmental Protection Agency, the Texas Commission on Environmental Quality and the United States Chemical Safety Board gathered in this city of 34,000 about 25 miles east of downtown Houston.

The air was being monitored, and initial results did not show elevated levels of the chemical beyond the plant, a spokeswoman for the E.P.A. said Sunday.

About 4 a.m. on Saturday, a valve began to release methyl mercaptan gas. The leak was contained two hours later, company officials said.

Randall Clements, the plant manager, said DuPont was working with the authorities and conducting its own "top-to-bottom review" of the accident. Asked how the leak had begun and whether the problem had been a result of equipment failure or human error, a company spokesman, Gregg M. Schmidt, said answering those questions was part of the investigation.

The La Porte plant uses methyl mercaptan in the early stages of its production of methomyl, a highly toxic pesticide that kills insects, ticks and mites in vegetable and fruit crops, cotton fields and poultry houses. DuPont markets it under the name Lannate.

"Every one of these plants has got something that will kill you multiple times over," said Ed Hirs, a lecturer and energy economist at the University of Houston who has toured the plant. "We go through the day and try not to get paper cuts and slam the door on our hand. These folks are dealing with pumps and valves and boilers that if any one of them has an issue, it can turn into a fatal issue very, very

quickly.

"I've been in that La Porte plant," he added. "It is really rare for DuPont to have a failure like this."

Another chemical produced at the plant, methyl isocyanate, is the same one that was linked to the 1984 leak at a Union Carbide chemical plant in Bhopal, India, which killed thousands of people. Two months later, Texas officials, with the support of community leaders here, gave DuPont permission to produce the chemical in small amounts. Mr. Schmidt, the company spokesman, said methyl isocyanate was not involved in the leak on Saturday.

The company took hours to confirm the deaths and notify relatives. DuPont officials said no qualified medical personnel could enter the contaminated unit because they were not trained to use protective equipment. The first workers who responded with the proper equipment were not medically trained and reported the employees as nonresponsive and most likely dead.

"It was on that basis that the unit was barricaded for investigation just before 8 a.m.," a company statement said. "The incident scene was deemed safe to enter just before noon and the fatalities were confirmed by the medical examiner around 1:30 p.m., and we immediately began to inform families thereafter."

Asked if any of the four workers were alive but nonresponsive before the unit was barricaded, Mr. Schmidt said, "We can't answer that definitively until the investigation is completed."

A version of this article appears in print on November 17, 2014, on page A12 of the New York edition with the headline: Agencies Look for Cause of Fatal Gas Leak in Texas.

BANGOR DAILY NEWS

Calais man who sold pesticide that killed lobsters admits lying to agents

By Bill Trotter and Judy Harrison, BDN Staff
Posted Nov. 20, 2014, at 10:53 a.m.

BANGOR, Maine — A Calais man waived indictment and pleaded guilty Wednesday in federal court to making a false statement to federal agents in connection with the illegal use of a pesticide in Canada five years ago.

Clyde Eldridge, 65, owner of local feed and pet store C&E Feeds, was questioned by U.S. Environmental Protection Agency officials as part of an investigation into the illegal use of cypermethrin on the New Brunswick side of Passamaquoddy Bay in 2009. The pesticide application killed hundreds of lobsters off Deer Island and Grand Manan in November and December 2009.

Cypermethrin is a synthetic insecticide used to control many pests, including moth pests of cotton, fruit and vegetable crops, according to information posted online by the Extension Toxicology Network. In aquaculture operations, it is used to treat infestations of sea lice, a parasitic crustacean that can weaken fish and expose them to infection and disease.

The pesticide is banned in Canada but not in Maine, where it can be used with prior permission from state officials. The use of pesticides in or near the ocean has long been a concern to Maine lobster fishermen who fear that it could harm the state's $364 million lobster fishery.

In April 2013, Kelly Cove Salmon Ltd. pleaded guilty in New Brunswick to using the banned pesticide in Canadian waters and was fined $500,000 in Canadian currency, which at the time was equal to about $490,000 in U.S. dollars. Kelly Cove Salmon is a subsidiary of Cooke Aquaculture, which is based in Blacks Harbour, New Brunswick, and is the largest aquaculture firm in Maine.

On Sept. 23, 2010, two EPA special agents assisting Environment Canada in the case asked Eldridge to identify anyone to whom he had sold cypermethrin and whether he had kept records of the sales, according to a press release issued Thursday by the U.S. attorney's office. Eldridge told investigators he sold different amounts of cypermethrin to different people and that he did not keep track of the sales, prosecutors indicated.

The investigation revealed, however, that Eldridge sold cypermethrin on 10 or 11 occasions to a regional production manager employed by Kelly Cove Salmon, a subsidiary of Cooke Aquaculture, and that on each occasion, Eldridge made a note of the quantity picked up by the manager, the release said.

Assistant U.S. Attorney Jim Moore said Thursday that Eldridge later told investigators that he

knew at the time that the person buying the pesticide was doing so on behalf of Cooke Aquaculture.

Court documents did not detail why Eldridge lied to investigators or why Kelly Cove Salmon used the pesticide illegally.

Moore said U.S. federal prosecutors did not have information about what quantity of the pesticide Eldridge sold to Kelly Cove Salmon. According to an agreed statement of facts accepted in New Brunswick Provincial Court at the time of the Canadian firm's plea, Kelly Cove Salmon purchased 72 gallons of cypermethrin "from a specialized supplier" in 2009.

Eldridge, who is free on personal recognizance bail, faces up to 5 years in prison and a fine of up to $250,000.

The investigation was conducted by the EPA's Criminal Investigation Division and Environment Canada.

CORRECTION:

An earlier version of this story reported that The pesticide application killed hundreds of lobsters off Deer Island and Grand Manan in November and December 2010. It was 2009.

http://www.houstonchronicle.com/news/houston-texas/houston/article/Deadly-DuPont-leak-exposes-safety-response-5911929.php#/0

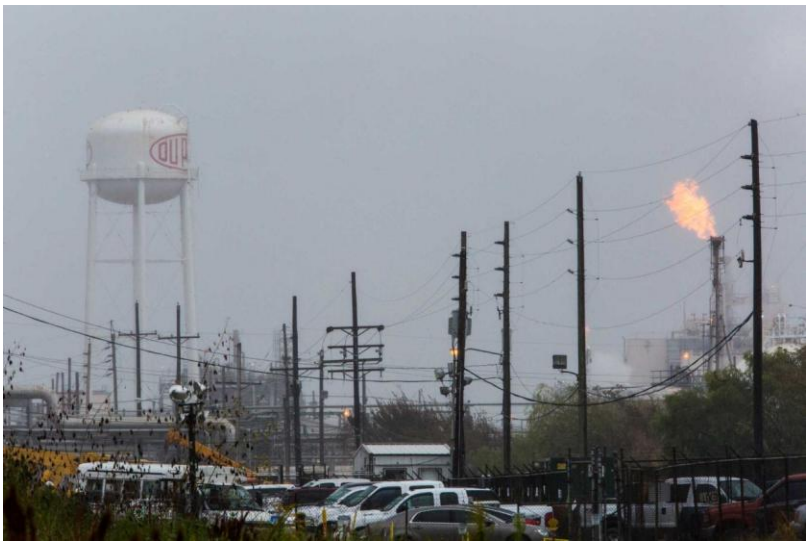
Houston

Deadly DuPont leak exposes safety, response failures

Chemical plant officials slow to react to disaster, minimized risk to fire crews, public in first 911 call

By Lise Olsen and Mark Collette

November 22, 2014 Updated: November 23, 2014 12:21pm



Marie D. De Jesus/Staff

Four workers died at DuPont's chemical plant in La Porte after being exposed to a chemical called methyl mercaptan. Federal and state officials have launched an investigation. Friday, Nov. 21, 2014, in La Porte. (Marie D. De Jesus / Houston Chronicle)

Five DuPont workers - four of them already dead or dying - had been trapped for an hour by poisonous gases inside a pesticide plant when another worker called 911 to report an emergency at 4:13 a.m.

The accident scene - a multistory building where DuPont makes a pesticide that is rated highly toxic to human life - typically housed between 50 to 250 tons of highly flammable methyl mercaptan. Nearby, there was a much smaller but unknown amount of one of the most notorious substances in industrial manufacturing: methyl isocyanate, according to public records and former DuPont employees interviewed by the Houston Chronicle.

It is so-called MIC that escaped a Bhopal, India, pesticide plant and formed a toxic cloud in 1984, initially killing more than 2,200 people in the world's worst industrial disaster.

But last Saturday, on Nov. 15, DuPont shift supervisor Jody Knowles gave no details about the chemicals involved and minimized the risk in the 911 call to the La Porte fire department.

"We have a possible casualty five (workers) my medics are telling me," he told a dispatcher.

She immediately asked: "Can you tell me is this any risk to the public? Is it gonna be a possible escaping from your premises?"

"No ma'am, it is not," Knowles responded.

At that time, public records show, no air tests had been conducted outside the plant, and it's unknown whether Knowles - or anyone else at DuPont - knew what the gas levels were beyond the fence line.

The incident is the worst loss of life in an industrial accident at the world's biggest petrochemical complex since 2005, when a refinery explosion killed 15 workers in Texas City.

Investigations are ongoing, but already it's clear that the response to the emergency was inadequate and slow, especially given the scope of the disaster, that the accident site had been plagued with recurring maintenance problems, and that workers lacked quick access to breathing equipment that would have given them a better chance at survival.

Those killed included Crystle Rae Wise, 53, the first to alert others of a leak; Wade Baker, 60, a longtime supervisor; and brothers Gilbert and Robert Tisnado, 48 and 39, respectively.

No DuPont official contacted a special emergency industrial response network called the Channel Industries Mutual Aide, a nonprofit formed to deal with potentially deadly disasters. It took hours before DuPont verified that anyone had died - and the name of the worker who survived the accident has not been provided. DuPont has refused to clarify how many pounds of toxins were released.

Local

"There are inter-related plants that use emergency vehicles from others … but in this case, the response did not work," said U.S. Rep. Gene Green, whose district includes half of the Houston Ship Channel. "That's one of the things I find most alarming: Why didn't the regional emergency response group come?"

Not enough oxygen masks

Robert Cooper, who acts as chairman of the CIMA, first formed in 1955, confirmed that his group was not summoned until after La Porte city officials arrived and assessed the situation.

"(DuPont) didn't set up an incident command center and connect with CIMA," he said.

Based on preliminary information, Cooper said CIMA might not have been able to save the workers who died. "But at least we would have had the opportunity to try."

Nor did DuPont disclose the size of its toxic inventory in a report that the company files each year with La Porte emergency management officials. Texas requires disclosure of the chemicals but not the amounts, according to Jeff Suggs, the La Porte emergency response coordinator.

Volunteer firefighters from Deer Park, who responded to the company's 911 call, had to rely on word-of-mouth to confirm quantities, Suggs said.

Nearly a week after the accident, officials have said only that the release exceeded the minimum reportable quantity of 100 pounds. The accident remains under investigation by the Occupational Safety and Health Administration, the Chemical Safety Board and by DuPont officials, who declined comment.

The unit where workers died had been shut down for five days before the accident and workers had reported persistent maintenance problems, according to Green, who belongs to a congressional committee that oversees the Chemical Safety Board. For months before that, according to Green and others, workers had complained about inadequate ventilation in the unit, which produces Lannate, DuPont's brand name for methomyl, a crop pesticide.

Despite persistent problems, DuPont apparently did not have enough emergency oxygen and masks on hand that Saturday for the workers who died trying to fix a leak or help others escape, according to Green, whose district includes other plants, though not the La Porte complex.

It was about 3:15 a.m. when Giilbert Tisnado, known as "Gibby," told his wife via cellphone that something had gone wrong at the Lannate unit. At some point, Tisnado learned that workers - including his younger brother and at least three others - were trapped inside, his father said.

Tisnado got at least one "escape pack" - possibly from another building - and ran to the rescue. He either ran out of oxygen or took off his mask to help his brother, his father said.

Firefighters later encountered three bodies but only two tanks and masks inside the plant. Each is equipped with only five minutes of air. That's intended to be enough for an emergency escape, not for a rescue mission, according to Deer Park Volunteer Fire Department Chief Greg Bridges.

The firefighters did not see the fourth victim during that first and only foray into the Lannate unit because their own tanks couldn't provide enough air to explore the entire facility. They didn't know the layout of the building - a maze filled with pipes, towers, tanks and platforms, Bridges said, so they had to move deliberately. DuPont had already labeled the mission a recovery of the dead, not a rescue, Bridges said.

Community left in the dark

In DuPont's only statement on the incident, released two days after the accident, it acknowledged that medical personnel could not reach the employees because they were not trained in the use of protective equipment. Those who did respond - before 7 a.m. - reported that the employees were "nonresponsive and likely fatalities," according to the statement.

Bridges said firefighters did not attempt to re-enter the building right away because there was still uncertainty as to the release of other chemicals, including the deadly MIC.

While the 911 call came from DuPont at 4:13 a.m., more than two hours passed before any agency conducted "fenceline" air monitoring to determine if hazardous levels of chemicals had escaped the plant.

A Harris County hazardous materials crew, dispatched at 6:17 a.m., detected nothing toxic in the air. A separate county crew later confirmed those readings.

But for the first two hours, the community depended on DuPont to know whether it was safe to go outside. Emergency managers, relying on assurances from the company, chose not to use La Porte's reverse 911 system to call until 8 a.m. Nearby Pasadena has no reverse 911 system.

The 8 a.m. call informed thousands of La Porte and Deer Park homes that lingering, pungent cabbage odors were harmless. The human nose detects methyl mercaptan at levels far less than what's considered a threat - that's why it has been used as an additive to natural gas to help detect leaks.

But no one - then or now - has revealed how much mercaptan or any other material leaked. While MIC is lethal at concentrations 50 times lower, methyl mercaptan can still kill at concentrations as low as 150 parts per million, a mere drop in 12 ounces.

The assurances from plant personnel began even before the mercaptan leak had been assessed and stabilized, according to dispatch logs and 911 recordings.

"It's probably not even likely DuPont would have had comprehensive toxics fenceline monitoring," said Adrian Shelley, director of the advocacy group Air Alliance Houston.

The refining industry, especially, has balked at calls for continuous fenceline monitoring, which provides streams of data about what gases are leaving a plant but can cost tens or hundreds of thousands of dollars, Shelley said. A U.S. Environmental Protection Agency rule that would require such systems at refineries is under review. Even if adopted, it wouldn't apply to the DuPont plant because it doesn't refine fossil fuels.

Shelley and other environmentalists say the ideal solution is a continuous feed of monitoring information directly accessible online by the public, so they aren't waiting to hear alarms or get messages on notification systems for which they may not even have registered.

It's unclear if the workers killed had advance warning of the degree of toxicity inside the unit.

"I wish they had something more accurate so you got to know the problem right away, and you're not waiting an hour or two hours after somebody got hurt," said Juan Alvarado, a truck driver who smelled the mercaptan at about 7 a.m. on his Saturday shift in the industrial corridor. He had no idea what it was; he thought it might be a truck exhaust problem.

"You are exactly right: We have to trust the company in telling us what they have," said Suggs, the coordinator for La Porte.

Mercaptan in the air

Where emergency responders usually have experts from a plant on hand to explain the intricacies of a malfunctioning unit or the safety concerns about a particular chemical, the experts this time were dead inside the building. Firefighters smelled mercaptan on their way to the plant, but experienced no symptoms. They saw no cloud, no spray, no mist.

"They see nothing out of the ordinary, and so that's why they believed what they had from DuPont at that time," Suggs said.

The plant is one of the oldest and most sprawling complexes on the Houston Ship Channel, and for years, DuPont has been selling off parts of its operations and cutting its staff. The plant itself has employees trained in basic firefighting. Robert Tisnado was one. But the internal response duties are now shared by more than one company, and it's unclear who was leading up the internal effort on Saturday or how many employees were on duty for DuPont during the overnight shift.

The Lannate unit is the largest one left on the site, said Ken Martin, who retired from DuPont in 2011 but still works as a safety consultant. Martin said when he worked at DuPont, there was a row of masks and tanks to use in emergencies just outside the control room near the accident site and full emergency gear elsewhere on plant property. Other former company workers said that DuPont normally keeps an ambulance there in case of emergencies.

Mechanical failure suspected

Over the last several decades, the unit has been redesigned several times to make it safer and to minimize the volumes and the risks, specifically of working with MIC, the chemical associated with the Bhopal disaster. Engineers even won a design award for one of those efforts, which allowed MIC to be created on site and used immediately to eliminate transportation and storage.

DuPont's La Porte plant has reported three previous accidents with major injuries, involving four people, that prompted evacuations and property damages in the last five years, according to data archived by the Right To Know Network, a project of the nonprofit Center for Effective Government. Only four other major industrial plants nationwide have reported more than three recent accidents, according to that data.

Martin said he has no inside information or answers for what caused such a leak and loss of life - he and others described one of the employees who died Saturday, Wade Baker, as one of the company's most seasoned managers.

Former engineers and chemists who worked on the Lannate process said they believe a mechanical failure must be involved, though it surprised those employees, who said DuPont was a stickler for safety on its process systems.

"There are many parallel investigations taking place," Martin said. "We have to let those people do their work and deal with facts and deal with data. … We learn lessons from every incident investigation that we do."

Chronicle reporter Karen Chen contributed to this story.

WATER: State Water Board stream pollution report shows trends in chemical contamination, toxicity

THURSDAY, 20 NOVEMBER 2014 00:34 LAKE COUNTY NEWS REPORTS

Detections and concentrations of pyrethroid pesticides are increasing in California stream sediments, according to a new report by the Stream Pollution Trends Monitoring Program of the State Water Resources Control Board.

The program is a statewide effort to measure trends in pollution levels and toxicity in major California watersheds.

The latest report, “Trends in Chemical Contamination, Toxicity and Land Use in California Watersheds,” summarizes results from the first five years of annual surveys assessing stream pollution concentrations and how they are affected by land use.

According to the report, which summarized data from 2008 to 2012, pyrethroid pesticides showed an increasing trend in all watersheds, but most significantly in urban watersheds.

Pyrethroids are the active ingredients in many currently used pesticides available to urban consumers in the United States, and are also widely used in agriculture.

Pyrethroid-based pesticides replaced organophosphate pesticides when the use of organophosphates was dramatically reduced.

They are widely used by professional residential pest control firms as well as by consumers. Many are extremely toxic to aquatic organisms, and are a known endocrine disruptor. Many may be carcinogenic, according to the U.S. EPA.

Chlorinated compounds such as DDT and PCBs declined over the five years, according to the report, as did detections and concentrations of organophosphate pesticides in sediment.

However, DDT and PCBs continue to be of concern in California because of their potential to bioaccumulate.

While concentrations in fish do not often exceed thresholds of concern, fish consumption advisories have been issued due to these contaminants for lakes, rivers, bays, and coastal areas.

Concentrations of hydrocarbons, flame retardants and selected metals remained relatively constant.

The Stream Pollution Trends Monitoring Program (SPoT) is aimed at understanding long term trends of watershed contamination and associated toxicity.

The program investigates the impacts of land use on water quality, helps prioritize water bodies in need of water quality management, and evaluates the effectiveness of management programs designed to improve stream health.

The data provides a statewide perspective on the impact of pollution on stream health and allows local and regional water quality managers to evaluate how conditions in their streams compare to those in other California watersheds.

The SPoT program measures contaminant concentrations and toxicity in sediments that accumulate in the lower reaches of large watersheds.

In 2012, samples were collected from 100 of the nearly 200 major hydrologic units in California. Sediment samples are collected once per year when streams return to base flow conditions after the high flows that carry pollutants washed from watershed surfaces during storms.

Sediments are monitored because the majority of contaminants entering streams accumulate in sediments.

Each sample is analyzed for industrial compounds, pesticides and metals, and is tested for toxicity to a resident aquatic crustacean, the amphipod Hyalella azteca.

Additional toxicity test species and contaminant classes are being addressed in future surveys as SPoT monitoring proceeds.

Results are compared across watersheds throughout the state, and pollutant concentrations are compared to land use and

other human activities.

The pesticides and some of the other pollutants identified in the report are considered non-point pollution sources, meaning that they are not generated at a single source, such as a manufacturing plant or sewer outfall.

The State Water Resources Control Board has programs in place to reduce nonpoint pollution sources.

November 25, 2014

Ontario to restrict use of pesticide linked to bee deaths

By ERIC ATKINS

In North America first, moves to cut farmers' reliance on a pesticide by 80 per cent within two years

The Ontario government plans to restrict the use of a class of agricultural pesticides linked to the widespread declines in honeybees and other pollinators.

The move is opposed by the province's chemical and agriculture industries, which say neonicotinoid pesticides are vital tools that growers of corn and soybeans use to protect their harvests from yield-destroying insects.

The pesticide, which renders plants toxic to pests, has been blamed for the deaths of honeybees and other beneficial insects that are responsible for pollinating one-third of the food we eat.

The province said on Tuesday it wants to reduce the acreage planted with neonic-treated seeds by 80 per cent within two years.

To do so, the government is proposing to restrict the sale of corn and soybean seeds treated with neonics to farmers who can show their fields are susceptible to pests, verified by a third party. Farmers must also complete pest management training and document their efforts to eliminate pests such as wire worms and grubs.

The proposals will be subject to public consultations and in place by July 1, which is when growers begin buying seed and supplies for the following growing season.

Ontario would become the first province or state in North America to regulate the pesticides, which are halfway through a two-year moratorium in Europe amid concerns over environmental impacts.

"We know, and farmers recognize, there are risks associated with the use of neonicotinoid pesticides. We also know that, in certain circumstances, they are an important tool for farmers and help to increase production and maintain a reliable food supply for our province," said Jeff Leal, Ontario's Minister of Agriculture.

The Grain Farmers of Ontario said the steep target is effectively a ban that disregards efforts its members have taken to reduce risks to honeybees. Farmers changed their planting methods in the past spring to minimize the amount of neonic-laced dust that is kicked up during seeding by fitting their machines with deflectors, at the direction of Health Canada. And neonic-treated seed now comes with a wax-based fluency agent that is intended to reduce the dust that can be immediately fatal to bees.

"A reduction at this level puts our farmers at a competitive disadvantage with the rest of the country and the rest of the North America," said Barry Senft, chief executive officer of the group that represents 28,000 farmers. "It will mean

smaller margins for grain farmers and could signal the transition away from family farms to large multinational farming operations that can sustain lower margins."

More than half of the hives in Ontario did not survive the past winter, losses that beekeepers and some scientists say are attributable to neonic poisoning on top of the other threats to bees, which include virus-carrying mites and starvation over long winters. Losses across Canada averaged 25 per cent, higher than the 15 per cent that is considered normal and sustainable, said the Canadian Association of Professional Apiarists.

Ontario said it wanted to reduce winter bee deaths to 15 per cent by 2020.

In Ontario, all corn, canola and most soybean seeds are coated with neonics. The province has said just 10 to 20 per cent of the five million corn and soybean acreage requires neonics to ward of yield-destroying insects. The pesticide is also used by growers of flowers, fruits, vegetables and sod. The Ontario plan covers only corn and soybean, which are grown for animal feed or biofuels.

Meanwhile, Health Canada is re-evaluating its approval of products containing the three most widely used neonics in partnership with the U.S. regulator.

Beekeepers in Ontario and Quebec have launched a class-action lawsuit again the chemical companies to recover the financial losses they allege they have suffered as a result of bee deaths. These costs include lost honey production and replacing dead bees.

Tibor Szabo, president of the Ontario Beekeepers Association, said a raft of studies has shown "overuse" of neonics is the core problem for honeybee health. The blanket use of the chemicals has discouraged farmers from trying other methods to control pests, Mr. Szabo said.

"There's a growing preponderance of research showing [neonics] are quite dangerous and they stay in the environment for a long time," said Glen Murray, Ontario's Minister of the Environment. "We're not doing this on an emotional basis. We're doing this on an evidence basis."

The chemical companies that make neonics and are the main sellers of pesticide-coated seeds say the pesticides are safe if used as directed, and are less harmful to people and the environment than older classes of chemicals.

A representative of the chemical and agricultural companies said the plan places a "burden" on vendors to police who can buy which kinds of seed. And the pesticide makers might simply overlook the Canadian market as a place to make investments or introduce new crop technologies, said Pierre Petelle of CropLife Canada, which represents pesticide makers Bayer, Syngenta and others.

"When they look at markets where they should invest, where they should register the newest technologies, Canada hasn't always been at the top of that list, mostly because of market size," Mr. Petelle said in an interview. "But when you add this layer of intereference, if you will, at the provincial level, it's going to make Canada an even less interesting place to invest. The real risk I see is future innovations, the new technologies."