

## Chapter 10

# The Impact of Integrated Pest Management and Regulation on Agricultural Pesticide Use in California

Lynn Epstein<sup>\*,1</sup> and Minghua Zhang<sup>2</sup>

<sup>1</sup>Department of Plant Pathology, University of California, One Shields Ave.,  
Davis, California 95616-5270, United States

<sup>2</sup>Department of Land, Air and Water Resources, University of California,  
One Shields Ave., Davis, California 95616-5270, United States

\*E-mail: lepstein@ucdavis.edu

The California Pesticide Use Reports (PUR) were used to investigate the impact of both regulation and Integrated Pest Management (IPM) on use of hazardous pesticides. We conclude that the U.S. Food Quality Protection Act of 1996, as implemented by the U.S. EPA, was effective in reducing use of organophosphate and carbamate insecticides in California. IPM has been broadly embraced in the United States and internationally as a strategy for achieving least-use and/or least-risk pesticide use in agriculture. Here we have asked whether IPM has been successful in reducing pesticide use and risk in California, and if so, to what extent, and in what circumstances. Our results suggest that IPM in agriculture can help to reduce pesticide risk, particularly in cases where pesticide overuse results in negative agricultural/economic consequences for growers. However, IPM may not reduce pesticide use or risk in cases that have no direct benefits to growers. While the majority of chemicals of regulatory concern have been reduced in use, most of these pesticides were replaced with other chemicals rather than with non-chemical methods. We briefly feature several case studies to illustrate key issues in pesticide use and IPM in California: 1) the limited progress in meeting Montreal Protocol guidelines for methyl bromide phase-out due to critical use exemptions for strawberry

© 2018 American Chemical Society

Ang et al.; Managing and Analyzing Pesticide Use Data for Pest Management, Environmental Monitoring, Public Health, and Public Po  
ACS Symposium Series; American Chemical Society: Washington, DC, 2018.

producers (which didn't end until 2016); 2) the increase in use of neonicotinoid insecticides, which may have a role in the current bee decline and 3) a successful IPM program to decrease use of dormant-season organophosphates that are important water pollutants.

## 1. Introduction

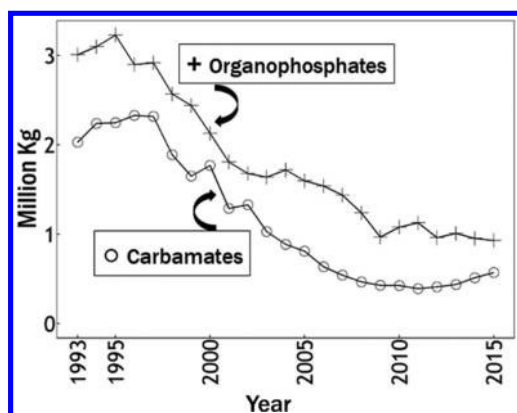
The U.S. had virtually unregulated pesticide use in the 1940's and 1950's. Chlorinated hydrocarbons, such as DDT, were used as insecticides, but their use declined after 1959 (1) as insects became resistant, and organophosphates and carbamates became more available. After Rachel Carson's *Silent Spring* in 1962, both the public and some scientists became concerned about negative externalities associated with the increasing use of broad spectrum pesticides, particularly the "pesticide treadmill," i.e., the ever-increasing need to apply increasing quantities of pesticides because of the development of pesticide resistance, the resurgence of what had been relatively minor pests, and the poisoning of birds. Also in the 1960's, agricultural scientists developed Integrated Pest Management as a method in which pesticide use could meet agricultural needs for crop protection with, purportedly, minimal health and environmental consequences. By all measures, agricultural pesticide use, particularly herbicides, continued to increase in the U.S. through the 1980's (2) as agriculture became more mechanized, more intensive, and larger-scale. In response to public concerns about adverse health and environmental effects of pesticides, pesticides have been increasingly regulated nationally, and on the state level in California. By 1993, California had a high-quality and comprehensive database of agricultural pesticide use, the Pesticide Use Report database (PUR). Here, we use the PUR (3) as a source of data on trends in pesticide use in California from 1993 to 2015, and as a way to inquire about the impact of IPM programs and regulation on agricultural pesticide use.

## 2. The Impact of Regulation on Agricultural Pesticide Use in California, 1993-2015

California agriculture is under two regulatory authorities: the state and the nation. In 1991, the California Environmental Protection Agency formed a Department of Pesticide Regulation (DPR). Part of the Mission of the DPR is "to protect human health and the environment by regulating pesticide sales and use..." (4). On the national level, the U.S. Environmental Protection Agency (U.S. EPA) registers pesticides for specific uses largely under the Federal Insecticide, Fungicide and Rodenticide Act and the Federal Food, Drug and Cosmetic Act. In 1996, the Food Quality Protection Act (FQPA), which was passed unanimously by Congress, amended the two laws. As part of the FQPA, the U.S. EPA was mandated to reassess 9,721 tolerances for pesticide residues in food by 2006 so

that a pesticide poses a “reasonable certainty of no harm” (5, 6). Pesticides of particular concern with similar modes of action were reassessed for harm as a group. The two major groups that were reassessed were organophosphates and carbamates, both of which are mostly insecticides. As a result of the FQPA, U.S. EPA revoked or modified nearly 4,000 tolerances (6). Although FQPA prohibits individual states from modifying tolerances, the state of California can, by state law, impose additional restrictions on pesticide use.

The decline in mass of all agricultural organophosphates and carbamates applied in California fields between 1993 and 2015 is shown in Figure 1. Before the FQPA, in the 1993 to 1995 period, there was an average annual use of 3.1 million kg organophosphates (OP) and 2.2 million kg carbamates in California fields. By the 2013-2015 period, use was 31% and 23% of its previous levels, respectively.



*Figure 1. Mass of active ingredient (in million kg) used in California fields between 1993 and 2015 of two groups of pesticides targeted in the 1996 U.S. Food Quality Protection Act: organophosphates and carbamates. Data are from the California Department of Pesticide Regulation's Pesticide Use Reports. Data processing in this paper are as described in (2) and (7).*

## 2.1. Insecticides

The 24 individual agricultural insecticides of regulatory concern in California that were applied in quantities of greater than 10,000 kg in either 1993 or 2015 are shown in Table 1. During the 1993-1995 period, fourteen of the compounds were, individually, used in quantities of greater than 118 thousand kg annually; 983 thousand kg of chlorpyrifos was used annually. Twenty two of the 24 compounds were either OPs or carbamates, and consequently were targeted by the FQPA. For those 22 OP and carbamate insecticides, use in the post-FQPA era declined substantially; use in the 2013-2015 period ranged from none (0%) to 73% of the use in the pre-FQPA period of 1993-1995.

**Table 1. Trends in use of insecticides of regulatory concern in agricultural fields in California between 1993 to 2015<sup>a</sup>.**

<i>Compound<sup>b</sup></i>	<i>Annual average use from 2013 to 2015, kg active ingredient</i>	<i>Ratio of use during 2013-2015 compared to 1993-1995<sup>b</sup></i>	<i>Risk groups<sup>c</sup></i>
<b>Abamectin</b>	1.72E+04	<b>6.86</b>	R
Aldicarb	3.33E+02	0.00	N
Azinphos-methyl	3.79E+02	0.00	N
Carbaryl	5.83E+04	0.18	N
Carbofuran	0	0.00	N
Chlorpyrifos	5.81E+05	0.59	N,R
Diazinon	2.56E+04	0.06	N
Dimethoate	1.34E+05	0.49	N
Disulfoton	6.52E+02	0.01	N
Endosulfan	2.44E+03	0.02	A
Ethephon	1.48E+05	0.36	N
Ethoprop	8.29E+02	0.03	C, N
Fenamiphos	6.51E+02	0.01	N
Formetanate hydrochloride	1.31E+04	0.20	N
Malathion	1.85E+05	0.67	N
Methidathion	1.54E+03	0.01	N
Methomyl	1.20E+05	0.39	N
Methyl parathion	1.98E+05	0.58	N
Naled	7.82E+04	0.41	N
Oxamyl	2.33E+04	0.73	N
Oxydemeton-methyl	3.76E+03	0.07	N
Phorate	1.18E+04	0.20	N

*Continued on next page.*

**Table 1. (Continued). Trends in use of insecticides of regulatory concern in agricultural fields in California between 1993 to 2015<sup>a</sup>.**

<i>Compound<sup>b</sup></i>	<i>Annual average use from 2013 to 2015, kg active ingredient</i>	<i>Ratio of use during 2013-2015 compared to 1993-1995<sup>b</sup></i>	<i>Risk groups<sup>c</sup></i>
Phosmet	1.81E+04	0.18	N
Propargite	1.13E+05	0.14	C, N, R

<sup>a</sup> Data are from the California Department of Pesticide Regulation's (DPR) Pesticide Use Reports. Only compounds of regulatory interest that were applied in a total quantity greater than 10,000 kg in either 1993 or 2015 are included. <sup>b</sup> The single compound in which average annual quantity is greater in the 2013 to 2015 than in the 1993 to 1995 period is highlighted in bold. <sup>c</sup> A, listed as a California DPR's toxic air contaminant; C, listed as either a U.S. EPA B2 carcinogen or in the California state Proposition 65 (CP65) as causing cancer; N, organophosphate and carbamates that are cholinesterase-inhibitors, and targeted by the U.S. Food Quality Protection Act; W, listed in the California DPR groundwater protection list, part a; and R, listed in CP65 as known to have reproductive toxicity (22).

Of the 24 insecticides of regulatory concern in California, by the 2013-2015 period, eight were only used at 5% or less of the 1993-1995 levels, primarily as a result of U.S. EPA decisions, ultimately with the manufacturers' agreement to phase out production and registration (8). We will first give context to the eight that were dramatically reduced. Endosulfan, which was first registered in the 1950s, is a highly-toxic organochlorine, and like other organochlorines such as DDT, is persistent in the environment and bioaccumulates. After the U.S. EPA was sued by a coalition of environmental and farm worker advocates in 2008, the EPA declared that endosulfan was a risk to human health and the environment, and did not meet then-current standards for registration. As a result, the manufacturer voluntarily implemented a withdrawal of all registrations (9), with a complete phase-out by July 2016. We note that, in this context, a manufacturer's voluntarily withdrawing registrations is generally a measured response to anticipated future government action under the authority of the FQPA (5). Endosulfan also is being phased out internationally as part of the Stockholm Convention on Persistent Organic Pollutants, as amended in 2011 (10). Carbofuran and aldicarb are N-methyl carbamates that inhibit cholinesterase. Aldicarb was first registered in 1970 as a systemic insecticide and nematicide; it has a lethal dose (LD<sub>50</sub>) of only 1 mg/kg. In 1980, high levels of aldicarb degradants were found in the ground water in Long Island, New York. In a separate incident in 1985, approximately 2,000 people were sickened with 17 hospitalizations and probably six deaths and two stillbirths from consuming aldicarb-contaminated watermelons. At the time, aldicarb was not registered on watermelons, and its contamination of fruit was either illegal or accidental (11). In 2010, the U.S. EPA concluded that aldicarb did not meet food safety standards and may pose unacceptable dietary risks, especially to infants and young children. Consequently, U.S. EPA and the aldicarb

manufacturer reached an agreement to phase out production by 2014 with all use ending by 2018 (12). The other five insecticides of regulatory concern that have dramatically decreased in use in California are OPs that inhibit cholinesterase. As an example, azinophos methyl was first registered for use in the U.S. in 1959. After FQPA, U.S. EPA completed their interim Reregistration Eligibility Decision (RED) of azinophos methyl in 2001. Based on concerns about the health of farmworkers and pesticide applicators and aquatic ecosystems, the RED started the process of, ultimately, a planned phase-out by 2012 (13).

Although there has been an overall decline in California use of insecticides of regulatory concern, usage of some of these insecticides is still relatively high, and consequently controversial. For example, in the 2013-2015 period, agricultural entities in California applied 581 thousand kg of chlorpyrifos annually, which is 59% of the 1993-1995 quantity. The insecticides malathion, ethephon, dimethoate, methomyl, and propargite were also used in annual quantities in excess of 100,000 kg apiece. Consequently, although regulation has been effective in reducing use of some pesticides of concern, one can argue that it has not achieved a regulatory process that permits a “reasonable certainty of no harm.” Chlorpyrifos is a cholinesterase inhibitor (14); while California’s restricted pesticide designation should help with limiting human exposure to the compound, chlorpyrifos was not designated as such until July 2015 (5). The current questions about chlorpyrifos are largely focused on to what extent low doses cause neurodevelopmental problems in fetuses and in children of either farmworkers or people who live close to agricultural fields (15). Rowe et al. concluded that prenatal proximity to organophosphate/carbamate pesticides was linked to lower childhood IQ, and was independent of the effects of neighborhood and household poverty; children in the highest quartile of proximal pesticide use *in utero* had average deficits of three to four points on multiple intelligence scales at the age of ten (16). Other studies have linked exposure *in utero* or as young children to attention deficit disorder, autism spectrum disorders, hyperactivity disorder, and childhood tremor (17–21). In 2017, California designated chlorpyrifos as a chemical that is known to cause reproductive toxicity (22). Chlorpyrifos is also toxic to bees, some birds, fish, and aquatic invertebrates; some portion of landscape use ultimately becomes water pollution (e.g. (23)). Because of its risks to humans, chlorpyrifos was banned for household use by the U.S. EPA in 2000. Over the years, the U.S. EPA also has limited use on some crops. In 2016, U.S. EPA scientists recommended banning all agricultural use of chlorpyrifos in the U.S. However, in March 2017, the Trump administration rejected the proposed ban (24).

Thus, despite legislation such as the FQPA (8), usage of certain OP insecticides such as chlorpyrifos remains relatively high in California agriculture. As a group, the compounds are efficacious and relatively inexpensive. Since 1965 when chlorpyrifos was introduced, other insecticides (e.g. pyrethroids and neonicotinoids) with less human toxicity have been registered. However, chlorpyrifos’s manufacturer Dow has aggressively lobbied for its continued registration (24, 25). We note that decreases in agricultural use of chlorpyrifos vary within California, even in areas with similar cropping patterns. Anderson et al. (23) showed that, between 2011 and 2014, there was a 86% increase in agricultural chlorpyrifos use and a 60% increase in malathion use in Imperial

County, whereas in Monterey County, there was a 68% and 39% decrease in chlorpyrifos and malathion, respectively (23). They argued that this was a result of more restrictions on organophosphate applications in Monterey County than in Imperial County. The two counties are in different regions of the California State Water Resources Control Board. Currently, Region 3, which includes Monterey County, has more rigorous monitoring of agricultural discharges than Imperial County, which has four conditional waivers for agricultural discharges. The data reflect a regulatory change in Monterey County that took effect largely through the Agricultural Commissioner's Office in 2012.

## 2.2. Herbicides

Table 2 shows trends in use of 19 herbicides of regulatory concern in California between the 1993-1995 and the 2013-2015 periods. During the 1993-1995 period, of the herbicides with the greatest use during that period, there was an average of 673 thousand kg of molinate, 577 thousand kg of trifluralin, 411 thousand kg of the defoliant S,S,S-tributyl phosphorotrithioate (DEF), 317 thousand kg of EPTC, 310 thousand kg of simazine, and 248 thousand kg of cyanazine applied annually into the California environment. In contrast to the larger reductions in insecticides of regulatory concern, only three of the 19 herbicides of regulatory concern have been reduced by the 2013-2015 period to 5% or less of their 1993-1995 use in California. Of those three herbicides (molinate, DEF, and cyanazine), growers have voluntarily decreased use of DEF in the 2013-2015 period to 1% of its use in 1993-1995. DEF, which is also known as Tribufos, is an OP that was used in California as a pre-harvest cotton defoliant. During harvest of the cotton bolls, green leaves stain the fibers and clog the harvester. There are approximately five chemical alternatives to DEF that are not DPR restricted materials, whereas DEF is a restricted material (26). The other two herbicides with substantial reductions in use, molinate and cyanazine, were banned following U.S. EPA review and subsequent manufacturers' agreements. Molinate, a thiocarbamate, was primarily aerially sprayed over rice fields in the Sacramento Valley in California as a pre-emergence herbicide. It was detected in surface water in the Sacramento Valley in 1995 (27). After an EPA review that classified molinate as a suspected endocrine disrupter, reproductive toxin and neurotoxin, its registration was voluntarily phased out by the manufacturer between 2007 and 2009. Cyanazine, a triazine herbicide, was first registered in the U.S. in 1971, and became a highly-used herbicide on corn in the Midwestern U.S. As a pre-emergence herbicide, cyanazine and its degradants were detected in larger rivers at concentrations of up to 5 to 11  $\mu\text{g/L}$  and from more than 50 to 100  $\mu\text{g/L}$  in streams (28). In addition to its detection in drinking and ground water, cyanazine is a teratogen and is classified as having moderate acute toxicity. Cyanazine has also been classified as a possible carcinogen and a suspected endocrine disruptor. Following the U.S. EPA review, the manufacturers agreed to a phase-out during the 1999 to 2003 period (29).

**Table 2. Trends in use of herbicides of regulatory concern in agricultural fields in California between 1993 to 2015<sup>a</sup>.**

<i>Compound<sup>b</sup></i>	<i>Annual average applications from 2013 to 2015, kg active ingredient</i>	<i>Ratio of use during 2013-2015 compared to 1993-1995<sup>b</sup></i>	<i>Risk groups<sup>c</sup></i>
2,4-D <sup>d</sup>	1.53E+05	0.79	A
Acephate	6.23E+04	0.42	N
Atrazine	9.48E+03	0.56	W
<b>Bensulide</b>	1.42E+05	<b>6.32</b>	N
Bromacil	5.72E+03	0.16	W
Bromoxynil octanoate	2.16E+04	0.41	R
Cyanazine	2.29E+01	0.00	R
Cycloate	1.58E+04	0.70	N, R
Diuron	9.22E+04	0.37	C, W
EPTC	9.91E+04	0.31	N, R
Linuron	2.33E+04	0.63	R
Molinate	6.26E-02	0.00	N, R
Norflurazon	1.22E+04	0.18	W
<b>Oryzalin</b>	2.30E+05	<b>0.98</b>	C
Propyzamide	1.89E+04	0.38	C
Simazine	1.04E+05	0.34	W
S,s,s-tributyl phosphorotrithioate (defoliant)	5.66E+03	0.01	N
<b>Thiobencarb</b>	1.79E+05	<b>0.98</b>	N
Trifluralin	2.22E+05	0.39	A

<sup>a</sup> Data are from the California Department of Pesticide Regulation's (DPR) Pesticide Use Reports. Only compounds of regulatory interest that were applied in a total quantity greater than 10,000 kg in either 1993 or 2015 are included. <sup>b</sup> Compounds in which the average annual quantity is essentially equal or greater in the 2013 to 2015 than in the 1993 to 1995 periods are highlighted in bold. <sup>c</sup> A, listed as a California DPR's toxic air contaminant; C, listed as either a U.S. EPA B2 carcinogen or in the California state Proposition 65 (CP65) as causing cancer; N, organophosphate and carbamates that are cholinesterase-inhibitors, and targeted by the U.S. Food Quality Protection Act; R, listed in CP65 as known to have reproductive toxicity; W, listed in the California DPR groundwater protection list, part a; and R, listed in CP65 as known to have reproductive toxicity (22). <sup>d</sup> Herbicides that are likely to increase in use with the next generation of herbicide-tolerant genetically engineered crops.



The fact that there have been fewer reductions in use of herbicides of regulatory concern compared to insecticides can be attributed to several facts. First, in contrast to insecticides and fungicides for which there have been new modes of action with low human toxicity and excellent efficacy, there have been no new modes of action developed for herbicides in the last 25 years (30), even though there have been new herbicide products, which often contain combinations of herbicides. Second, conventional (i.e., non-organic) growers must use herbicides every season in order to have a profitable crop.

### 2.3. Fungicides

Table 3 shows trends in use of fungicides of regulatory concern in California between the 1993-1995 and the 2013-2015 periods; fumigants are covered in the next section. During the 1993-1995 period, of the fungicides with the greatest use during that period, there was an average of 420 thousand kg of maneb, 405 thousand kg of chlorothalonil, 275 thousand kg of captan, 218 thousand kg of iprodione and 212 thousand kg of mancozeb applied annually into the California environment. Of these fungicides, only maneb has been reduced in the 2013-2015 period to essentially no use (0.11% of its 1993-1995 levels). All the fungicides in Table 3 are relatively old materials, except for myclobutanil. PCNB was first used in agriculture as a replacement for mercurials in Germany in the 1930's. Captan was registered in the U.S. in 1949. Mancozeb and maneb were registered in 1948 and 1962, respectively. Chlorothalonil was first registered in the U.S. in 1966 and iprodione in 1979. As older fungicides, they are off-patent and relatively inexpensive. In contrast to the newer fungicides, such as myclobutanil and other demethylation inhibitors (DMI) and the strobilurins, which have specific sites of action, the older materials have broader biochemical toxicities. Consequently fungi do not develop resistance to older fungicides, which has been a problem with the newer materials. However, the broader biochemical toxicity of the older materials is often associated with mammalian toxicity, with some exceptions such as sulfur (31).

### 2.4. Fumigants Applied Pre-Plant in the Field and Used in Post-Harvest

Soil fumigants are applied to agricultural fields several days or weeks before planting a crop and form gases that have broad-spectrum pesticidal effects. Figure 2 shows changes in fumigant use between 1993 and 2015. Table 4 shows trends in use of individual fumigants of regulatory concern in California between the 1993-1995 and the 2013-2015 periods. In the 1993-1995 period, 6.7 million kg of methyl bromide and 5.2 million kg of metam sodium were used annually, with a total of 13.1 million kg of agricultural fumigants. In the 2013-2015 period, approximately the same total of 13.5 million kg of fumigants was used, but with different compounds: annual 1,3-dichloropropene use had increased to 6.2 million kg; potassium n-methyldithiocarbamate (=metam potassium), which was first registered in California in 2001, use had increased to 4.2 million kg; and chloropicrin use had increased to 3.9 million kg. Thus, while methyl bromide use has declined, it has been replaced by other fumigants of regulatory concern.

**Table 3. Trends in use of fungicides of regulatory concern in agricultural fields in California between 1993 to 2015<sup>a</sup>.**

<i>Compound<sup>b</sup></i>	<i>Annual average applications from 2013 to 2015, kg active ingredient</i>	<i>Ratio of use during 2013-2015 compared to 1993-1995<sup>b</sup></i>	<i>Risk groups<sup>c</sup></i>
Captan	1.80E+05	0.65	A, C, R
<b>Chlorothalonil</b>	4.57E+05	<b>1.13</b>	C
Iprodione	1.02E+05	0.47	C
<b>Mancozeb</b>	5.34E+05	<b>2.52</b>	A, C
Maneb	4.75E+02	0.00	A, C, R
Myclobutanil	2.71E+04	0.63	R
PCNB	3.35E+03	0.12	A
<b>Thiophanate methyl</b>	3.94E+04	<b>1.05</b>	R

<sup>a</sup> Data are from the California Department of Pesticide Regulation's (DPR) Pesticide Use Reports. Only compounds of regulatory interest that were applied in a total quantity greater than 10,000 kg in either 1993 or 2015 are included. <sup>b</sup> Compounds in which the average annual quantity is essentially equal or greater in the 2013 to 2015 than in the 1993 to 1995 periods are highlighted in bold. <sup>c</sup> A, listed as a California DPR's toxic air contaminant; C, listed as either a U.S. EPA B2 carcinogen or in the California state Proposition 65 (CP65) as causing cancer; N, organophosphate and carbamates that are cholinesterase-inhibitors, and targeted by the U.S. Food Quality Protection Act; W, listed in the California DPR groundwater protection list, part a; and R, listed in CP65 as known to have reproductive toxicity (22).

The use of methyl bromide, generally in combination with chloropicrin, was started in California as a method to assure maximum strawberry fruit production in the 1960's (7, 32, 33). Rates of application were often 256 kg/ha of methyl bromide with 193 kg/ha chloropicrin. In 2004, approximately 45% of the 2.9 million kg of methyl bromide used in California were applied pre-plant to fields for a single season of strawberry fruit production. Because methyl bromide depletes ozone in the upper atmosphere, thereby reducing protection from the sun's harmful UV irradiation, the Montreal Protocol and its Subsequent Agreements mandated an international phase-out of methyl bromide (34, 35). The agreement was that methyl bromide would be phased out in the U.S. and other developed nations between 1995 and 2005. However, in an amendment that was promoted by the U.S., after 2005, nations could request exemptions for cases involving quarantine, preshipment, or "critical use." A critical use exemption (CUE) could be granted if there were "no technically and economically feasible alternatives or substitutes available to the user that are acceptable ... to the crops and circumstances of the nomination" and "the specific use is critical because the lack of availability of methyl bromide for that use would result in a significant market disruption" (36). The U.S., acting on behalf of the California Strawberry Commission and other agricultural groups, was repeatedly granted exemptions, based on predicted yield

reductions without methyl bromide. However, retrospective economic analyses indicated that the CUE were based on overestimates of the value of methyl bromide for strawberry production (37, 38).

We use the data on methyl bromide in California from 1995 to 2015 to ponder the extent to which growers will voluntarily switch from one pesticide, which is highly efficacious but has health risks to others, including an increased incidence of skin cancer, to a less efficacious one. The data show that methyl bromide use in California declined at a rapid average rate of over 0.85 million kg/year from 1997 to 2001. In 2006, in recognition of the reductions in methyl bromide use, the California Strawberry Commission received a U.S. EPA Stratospheric Ozone Protection Award (39). However, from 2001 through 2015, methyl bromide use in California declined at an average rate of only 0.12 million kg/year; in 2015, California used 1.1 million kg methyl bromide. We note that current yields for strawberry fruit production in California are the highest in the world with a statewide average in 2016 of over 48 thousand kg fresh fruit/ha (40). In our view, the continued use of the critical use exemptions through 2015, particularly by strawberry fruit producers, is an indication that voluntary decreases are not a particularly useful mechanism to achieve an environmental and health goal that has no direct benefits for the growers. To further summarize, largely because of the FQPA, California has been somewhat successful in reducing many, but not all, of the OPs and carbamates. Fumigant use remains relatively high in high value crops, such as strawberry fruit production, in which growers can afford to use them.

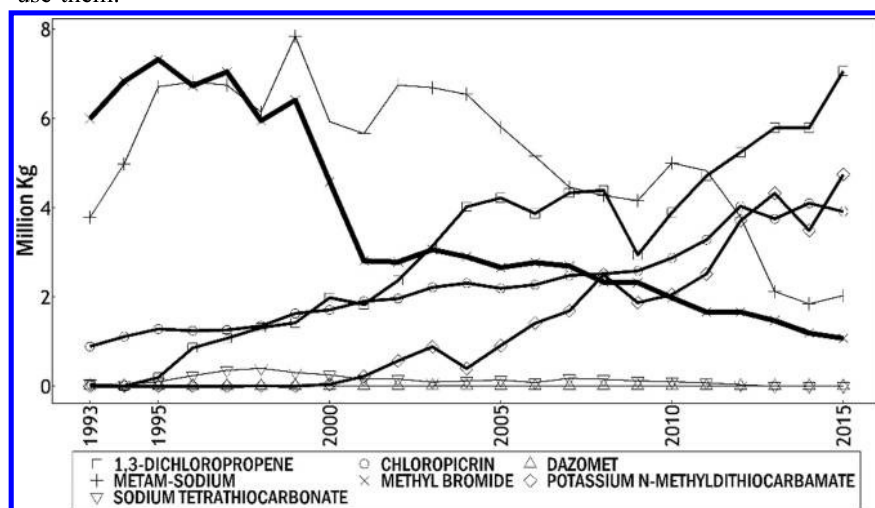


Figure 2. Mass in millions of kg of agricultural fumigants used in California between 1993 and 2015. Data include both field and post-harvest applications. The data show the partial replacement of methyl bromide (X, thickest line) with 1,3-dichloropropene ( $\square$ ), chloropicrin ( $\circ$ ), and metam potassium (potassium n-methyldithiocarbamate) ( $\diamond$ ); the three are shown as medium weight lines. Data are from the California Department of Pesticide Regulation's Pesticide Use Reports.

**Table 4. Trends in use of fumigants of regulatory concern in California agriculture between 1993 to 2015<sup>a</sup>.**

<i>Compound<sup>b</sup></i>	<i>Annual average applications from 2013 to 2015, kg active ingredient</i>	<i>Ratio of use during 2013-2015 compared to 1993-1995<sup>b</sup></i>	<i>Risk groups<sup>c</sup></i>
<b>1,3-Dichloropropene</b>	6.21E+06	<b>87.61</b>	A, C
<b>Chloropicrin</b>	3.92E+06	<b>3.58</b>	A
Metam-sodium	2.00E+06	0.39	A, C, N, R
Methyl bromide	1.25E+06	0.19	A, R
<b>Potassium N-methyldithiocarbamate (Metam potassium)</b>	4.18E+06	<b>(new)</b>	A, C, N
Sodium tetrathiocarbonate	1.89E+02	0.00	A

<sup>a</sup> Data are from the California Department of Pesticide Regulation's (DPR) Pesticide Use Reports. Only compounds of regulatory interest that were applied in a total quantity greater than 10,000 kg in either 1993 or 2015 are included. <sup>b</sup> Compounds, in which the average annual quantity is essentially equal or greater in the 2013 to 2015 than in the 1993 to 1995 period, are highlighted in bold. <sup>c</sup> A, listed as a California DPR's toxic air contaminant; C, listed as either a U.S. EPA B2 carcinogen or in the California state Proposition 65 (CP65) as causing cancer; N, organophosphate and carbamates that are cholinesterase-inhibitors, and targeted by the U.S. Food Quality Protection Act; W, listed in the California DPR groundwater protection list, part a; and R, listed in CP65 as known to have reproductive toxicity (22).

### 3. The Impact of IPM on Agricultural Pesticide Use in California

#### 3.1. Theory versus Practice: Replacement of Older Materials with Newer Ones

Integrated Pest Management is often defined as minimizing pesticide use and/or risk, and has been selected by the state of California and the federal government as the policy that will result in reduced pesticide use (41). The University of California Statewide Integrated Pest Management (IPM) Program defines IPM as, "...an ecosystem-based strategy that focuses on long-term prevention of pests or their damage through a combination of techniques such as biological control, habitat manipulation, modification of cultural practices, and use of resistant varieties. **Pesticides are used only after monitoring indicates they are needed according to established guidelines, and treatments are made with the goal of removing only the target organism. Pest control materials are selected and applied in a manner that minimizes risks to human health, beneficial and nontarget organisms, and the environment**" (emphasis added) (42).

However, a U.S. General Accounting Office (GAO) Report states that although the goal of implementing IPM on 75% of the nation's crop acreage was nearly achieved by 2000, "the implementation rate is a misleading indicator of the progress made toward the original purpose of IPM – reducing chemical pesticide use" (43). Recently, Hokkanen argued there is a "reality gap" between the theory of ideal IPM, as promoted for more than 50 years, and the current reality in mainstream pest management, which is pesticide intensive (44). In addition to the gap between theory and practice, there can be a gap between the presentation of IPM to the public as least pesticide use and to growers as best pest management. In the U.S. GAO report, "a survey of 50 state IPM coordinators indicated that, of the 45 respondents, 20 believed that the IPM initiative is primarily intended to reduce pesticide use, 23 did not, and 2 were undecided" (43).

We argue that the IPM definition stated above ignores that different "stakeholders" – the grower, the farmworkers, the community that lives near the agricultural field, and those in the public that consume the food—bear different costs and risks associated with either use or lack of use of a particular pesticide. We also note that many standard pest management practices are not in accordance with the above definition of IPM. For example, in California, fumigation of strawberry fields is often used prophylactically. Indeed, fumigants have been used to assure maximum yield (32). Moreover, whereas economic thresholds are key components in models used to recommend applications for insect control, economic thresholds are not a component of current models for plant disease. That is, fungicide use is generally not driven by the presence of disease, but by the perceived risk of disease or the consequences of disease that occurred in previous years. Although agricultural scientists prefer to explain pesticide use as a response to a pest or a pathogen, there are many social factors that can encourage pesticide use (1, 2).

Here, using the PUR data, we present two examples in which older pesticides have been replaced with newer pesticides. As indicated above, there have been reductions in use of OP and carbamate insecticides; these have often been due to a switch to either neonicotinoids (Figure 3) or pyrethroids. Neonicotinoid applications in California fields increased from none in 1993 to 646 thousand kg in 2015, with an average increase of 25 thousand kg per year (linear regression  $R^2=0.84$ ). We note that the PUR does not include information on neonicotinoids in seed treatments, which are widely used. (The lack of reporting is because seed treatments with non-restricted materials are classified as an industrial rather than an agricultural use.) We further note that prophylactic seed treatments are not part of a classically-described IPM program (unless there is monitoring and a demonstrated need); in addition, neonicotinoid seed treatments often do not improve yield (45). While the causes of the current bee decline are complex, the increased usage of neonicotinoids and perhaps other pesticides appear to be involved (46–48).

The declines in the herbicides of regulatory concern that were shown in Table 2 were often accompanied by an increase in the use of glyphosate, with an average increase in California between 1993 and 2015 of 141 thousand kg per year (linear regression  $R^2=0.91$ ).

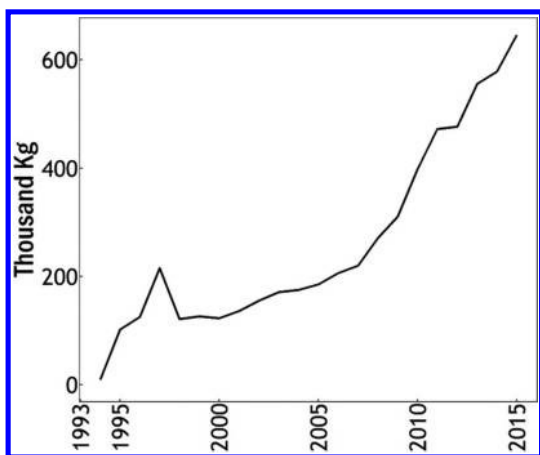


Figure 3. Mass in thousands kg active ingredient of neonicotinoids, a relatively new class of insecticides and miticides, applied in California in the field between 1993 and 2015, based on the California Department of Pesticide Regulation's Pesticide Use Reports. The mass of applied neonicotinoids does not include the mass used for seed treatments. The mass shown is the sum of the active ingredients of imidacloprid, acetamiprid, clothianidin, dinotefuran, nithiazine, thiacloprid, and thiamethoxam; imidacloprid accounts for 88-100% of the mass, depending on the year.

Newer pesticides that replace older materials often have lower application rates than the older pesticides. This is possible because the newer pesticides are toxic to the target organism at lower doses. To the extent that there is selective toxicity, i.e., the newer pesticides at lower dose are less toxic to humans and other unintended targets, a switch to a material used at a lower dose is advantageous from a human-health/environmental perspective. We note that while we have grouped pesticides with a similar mode of action and application rate (e.g. organophosphates) here, we find it unwise to group all pesticides and examine total mass applied. For example, sulfur, which has relatively low toxicity and adverse environmental consequences, is used at relatively high rates. Thus if one simply monitors mass of all pesticides, a switch from sulfur to say, myclobutanil, to control powdery mildew of grapes, would result in a reduction in mass of pesticide used, but not in a clear environmental/health advantage.

## 3.2. Selected Case Studies

### 3.2.1. Reductions in Organophosphates

In a 1994 review of IPM studies in the U.S, primarily in the 1970's and 1980's with a focus on insect control, Norton & Mullen (49) concluded, "The picture that emerges from the farm-level evaluation of IPM benefits and costs is one of generally lower pesticide use, production cost and risk, and higher net

returns to producers”. This statement is in accordance with reductions shown in Supplemental Figure 1 in (2).

There are some examples of declines in pesticide use in California that have been associated with specific IPM outreach programs, particularly for OP insecticides (50–53). The most pronounced cases involve situations in which pesticide use had negative externalities for the growers. For example, in the 1970’s, California pear growers were on a “pesticide treadmill,” with ever-increasing pest control costs, pesticide resistance and pest resurgence (53). Since then, a sustained, area-wide IPM program involving growers, the University of California (UC) and the state government has resulted in better pest control and reduced pesticide use and risk in pears.

Using PUR records in a way that allowed reconstruction of individual grower practices between 1992 and 2000, Epstein and Bassein showed that the reductions in OP use in stone fruit production were primarily due to replacement with pyrethroids (2). However, in almonds, in which there was a more sustained UC IPM education and extension program, more of the OP applications were replaced with either no treatment (presumably due to monitoring and a decision not to treat) or the use of a sustainable alternative: the biocontrol agent *Bacillus thuringiensis* at bloom time, or oil without an insecticide during the dormant season.

### 3.2.2. Environmentally-Driven Models: Powdery Mildew on Grapes

As alluded to previously, the theory of IPM often fits into a framework for insect control better than for either weed control, in which there is more constant weed pressure, or for disease control, in which there may not be a safe threshold of disease, i.e., treatments may have to be applied prophylactically. Regardless, “best management practices” particularly for plant pathogens have often included pesticide applications on a “calendar” basis. Recognizing that calendar recommendations are typically made for conditions with the greatest disease pressure, “environmentally driven models” have provided recommendations that range from the maximum calendar applications during periods of high disease pressure to a reduced number when conditions are such that there is less disease pressure (54).

Epstein and Bassein used PUR data to show that grape growers had a diversity of application programs for powdery mildew control and that on average, growers were using less fungicide than recommended in the calendar application model (2). As a result, if all growers started using the environmentally-driven model, there would have been an overall increase in fungicide use in California, not a decrease. Lybbert et al. and Sambucci and Lybbert demonstrated that in practice, growers who were trained in use of the environmentally-driven powdery mildew model actually increased, rather than decreased, their fungicide use in their vineyards (55, 56). Factors that resulted in increased use were: 1) when the estimate of disease pressure (=powdery mildew index) increased, growers increased their pesticide use to a greater extent than recommended, but when the disease pressure decreased, they maintained their usual fungicide program; and 2) growers were reluctant

to change frequency of applications, which involves rescheduling workers and equipment.

In a broader analysis, Gent et al. argued that growers do not follow predictive systems for disease control for multiple reasons, including that, unless there are regulatory requirements, growers are not motivated to reduce their pesticide use (57). Furthermore, pesticides are often used as insurance, and saving the cost of a few pesticide applications is not worth the risk of diminishing potential crop market value (58). Beckerman et al. argue that the focus on funding and developing IPM grants and programs that reduce fungicide use may have inadvertently contributed to the development of fungicide resistance, particularly in the case of apple scab (59). In contrast, Jørgensen et al. argue that pesticide label maxima rates and the number of applications are set by fungicide manufacturers and regulators to effectively control disease under the highest disease pressure (60). They contend that optimizing the doses and the number of applications will both reduce the pesticide load on the environment and slow the evolution of fungicide resistance. In conclusion, the argument that if the public supports the development of an environmentally-driven model, pesticide use will be reduced, is not clearly supported by the evidence.

### 3.2.3. Currently Available Genetically Engineered (GE) Crops

Proponents of GE have emphasized that GE can reduce pesticide use and/or risk. In theory, we agree. But in practice, the majority of GE crops that are available now and that are in the biotechnology pipeline were developed for herbicide tolerance (61). In the U.S., compared to use pre-GE or on non-GE cultivars, more herbicides (approximately 28%) were used on herbicide-tolerant soybean, the same amount on cotton, and slightly (1.2%) less on corn (62, 63). Consequently, herbicide tolerance is unlikely to decrease pesticide use *per se*. In contrast, it can affect what herbicide is used, and it gives growers greater flexibility in when those herbicides can be applied.

As expected, GE plants engineered to express *B. thuringiensis* (*Bt*) toxin have resulted in decreased insecticide use in corn and cotton (64, 65). Based on kg insecticide/ha, Perry et al. estimated that adopters of GE insect-resistant corn applied 11% less insecticide than growers who did not plant GE corn. *Bt*-corn controls the European corn borer, the corn rootworm, and the corn earworm. Interestingly, use of *Bt*-corn in the U.S. has resulted in declines in European corn borer populations (66), and in lower concentrations of fungal mycotoxins produced by *Fusarium* spp. (67). The fusaria, and some *Aspergillus* and *Penicillium* spp. that also produce toxins, are more likely to infect corn ears with injuries from insect feeding.

## 4. Concluding Comments

In summary, the California Pesticide Use Reports are an extremely valuable database for understanding agricultural pesticide use in our highly



pesticide-dependent agricultural production areas. Usage of many of the older pesticides, particularly the OPs and carbamates targeted by the U.S. FQPA, has been significantly decreased. In theory, IPM and best management practices could be used to reduce pesticide use and/or risk; and, with less pesticide applied, farmers could have lower costs. In practice, farmers have more complicated assessments of their own economic risks, and insufficient incentives to practice IPM for the social benefit of the local community. This is not an argument to decrease research into IPM. Indeed, the evidence is that more IPM research is critical for sustained food production. Nonetheless, we argue that, as currently practiced in the field, IPM is a better strategy for sustained pest control for growers than for reduced pesticide use or risk for the public and/or environment.

Could IPM programs be more effective in reducing pesticide use or risk? Of course! There are a few examples of extended educational efforts (51–53), of subsidies for area-wide mating disruption with pheromones (2), etc. We conclude that if IPM is used as the policy to reduce pesticide use or risk, then more attention needs to be given to identifying the circumstances that determine whether growers will or will not adopt practices that will result in the desired reductions.

## Acknowledgments

We thank Wan-Ru Yang and Huajin Chen for assistance with data processing and graphics.

## References

1. Epstein, L. Fifty years since Silent Spring. *Annu. Rev. Phytopathol.* **2014**, *52*, 377–402.
2. Epstein, L.; Bassein, S. Patterns of pesticide use in California and the implications for strategies for reduction of pesticides. *Annu. Rev. Phytopathol.* **2003**, *41*, 351–375.
3. Epstein, L. California's pesticide use reports and trends in pesticide use. *Outlooks Pest Manage.* **2006**, *17*, 148–154.
4. California Department of Pesticide Regulation. 2017. Mission and organization. <http://www.cdpr.ca.gov/docs/pressrls/dprguide/chapter1.pdf> (accessed Feb. 19, 2018).
5. McGarity, T. O. Politics by other means: law, science, and policy in EPA's implementation of the Food Quality Protection Act. *Admin. L. Rev.* **2001**, *53*, 103–222.
6. U.S. Environmental Protection Agency. Summary of the Food Quality Protection Act Public law 104-170 (1996). <https://www.epa.gov/laws-regulations/summary-food-quality-protection-act> (accessed Feb. 19, 2018).
7. Epstein, L.; Zhang, M. The impact of IPM programs on pesticide use in California, USA. In *Experiences with Implementation, Global Overview*; Peshin, R., Pimentel, D., Eds.; Integrated Pest Management; Springer: The Netherlands, 2014; Vol. 4, pp 173–200.

8. Van Steenwyk, R. A.; Zalom, F. G. Food quality protection act (FQPA) launches search for pest management alternatives. *Calif. Agric.* **2005**, *59*, 7–10.
9. Cone, M. Endosulfan to be banned, pesticide poses “Unacceptable risks,” EPA says. *Scientific American*, 2010, <https://www.scientificamerican.com/article/endosulfan-banned-epa/>.
10. Lubick, N. Endosulfan’s exit: U.S. EPA pesticide review leads to a ban. *Science* **2010**, *328*, 1466.
11. Goldman, L. R.; Smith, D. F.; Neutra, R. R.; Saunders, L. D.; Pond, E. M.; Stratton, J.; Waller, K.; Jackson, R. J.; Kizer, K. W. Pesticide food poisoning from contaminated watermelons in California, 1985. *Arch. Environ. Health* **1990**, *45*, 229–236.
12. Cone, M. Toxic Pesticide Banned after Decades of Use. *Scientific American*, 2010, <https://www.scientificamerican.com/article/toxic-pesticide-banned-after-decades-of-use/>.
13. U.S. Environmental Protection Agency. Reregistration eligibility decision for Azinphos-Methyl. 2006. [https://archive.epa.gov/pesticides/reregistration/web/pdf/azm\\_red.pdf](https://archive.epa.gov/pesticides/reregistration/web/pdf/azm_red.pdf) (accessed Feb. 22, 2018).
14. Solomon, K. R.; Williams, W. M.; Mackay, D.; Purdy, J.; Giddings, J. M.; Giesy, J. P. Properties and Uses of Chlorpyrifos in the United States. In *Ecological Risk Assessment for Chlorpyrifos in Terrestrial and Aquatic Systems in the United States*; Giesy, J.; Solomon, K., Eds.; Reviews of Environmental Contamination and Toxicology; Springer International Publishing: Berlin, Germany, 2014; Vol. 231, pp 13–34.
15. Bennett, D.; Bellinger, D. C.; Birnbaum, L. S. Project tenDr: targeting environmental neuro-developmental risks the tenDr consensus statement. *Environ. Health Perspect.* **2016**, *124*, A118.
16. Rowe, C.; Gunier, R.; Bradman, A.; Harley, K. G.; Kogut, K.; Parra, K.; Eskenazi, B. Residential proximity to organophosphate and carbamate pesticide use during pregnancy, poverty during childhood, and cognitive functioning in 10-year-old children. *Environ. Res.* **2016**, *150*, 128–137.
17. Bouchard, M. F.; Bellinger, D. C.; Wright, R. O.; Weisskopf, M. G. Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. *Pediatrics* **2010**, *125*, DOI: 10.1542/peds.2009–3058.
18. Rauh, V.; Arunajadai, S.; Horton, M.; Perera, F.; Hoepner, L.; Barr, D. B.; Whyatt, R. Seven-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. *Environ Health Perspect.* **2011**, *119*, 1196–201.
19. Rauh, V. A.; Perera, F. P.; Horton, M. K.; Whyatt, R. M.; Bansal, R.; Hao, X.; Liu, J.; Barr, D. B.; Slotkin, T. A.; Peterson, B. S. 2012. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109*, 7871–7876.
20. Rauh, V. A.; Garcia, W. E.; Whyatt, R. M.; Horton, M. K.; Barr, D. B.; Louis, E. D. Prenatal exposure to the organophosphate pesticide chlorpyrifos and childhood tremor. *Neurotoxicology* **2015**, *51*, 80–86.
21. Shelton, J. F.; Geraghty, E. M.; Tancredi, D. J.; Delwiche, L. D.; Schmidt, R. J.; Ritz, B.; Hansen, R. L.; Hertz-Picciotto, I. Neurodevelopmental disorders

- and prenatal residential proximity to agricultural pesticides: the CHARGE study. *Environ. Health Perspect.* **2014**, *122*, 1103–1109.
22. California Office of Environmental Health Hazard Assessment. 2017. Chemicals Listed Effective December 15, 2017 as Known to the State of California to Cause Reproductive Toxicity: Chlorpyrifos and n-Hexane. <https://oehha.ca.gov/proposition-65/crn/chemicals-listed-effective-december-15-2017-known-state-california-cause> (accessed Feb. 19, 2018).
  23. Anderson, B. S.; Phillips, B. M.; Voorhees, J. P.; Deng, X.; Geraci, J.; Worcester, K.; Tjeerdema, R. S. Changing patterns in water toxicity associated with current use pesticides in three California agriculture regions. *Integr. Environ. Assess. Manage.* **2018**, *14*, 270–281.
  24. Associated Press. EPA chief met with Dow Chemical CEO before deciding not to ban toxic pesticide. *Los Angeles Times*, June 30, 2017, <http://times.com/business/la-fi-epa-pesticide-dow-20170627-story.html>.
  25. Lerner, S. Poison Fruit: Dow Chemical wants farmers to keep using a pesticide linked to autism and ADHD. *The Intercept*, Jan. 1, 2017, <https://theintercept.com/2017/01/14/dow-chemical-wants-farmers-to-keep-using-a-pesticide-linked-to-autism-and-adhd/> (accessed Mar. 27, 2018).
  26. Wright, S. D.; Hutmacher, R. B. Cotton: harvest aid chemicals. In *How to Manage Pests, UC IPM Management Guidelines: Cotton*; UC ANR Publication 3444; 2013. <http://ipm.ucanr.edu/PMG/r114800111.html>.
  27. Bennett, K.; Singhasemanon, N.; Miller, N.; Gallavan, R. *Rice Pesticides Monitoring in the Sacramento Valley, 1995*; California Environmental Protection Agency; Environmental Hazards Assessment Program, California Department of Pesticide Regulation: Sacramento, CA, 1998.
  28. Goolsby, D. A.; Battaglin, W. A. *Occurrence, distribution, and transport of agricultural chemicals in surface waters of the midwestern United States*. U.S. Geological Survey Open-File Report 93-418; 1993.
  29. Environmental Protection Agency. Cynazine. *Federal Register* **1996**, *61*, 39024 [OPP-30000/60B; FRL-5385-7].
  30. Duke, S. O. Why have no new herbicide modes of action appeared in recent years? *Pest Manage. Sci.* **2012**, *68*, 505–512.
  31. DeWaard, M. A.; Georgopoulos, S. G.; Hollomon, D. W.; Ishii, H.; Leroux, P.; Ragsdale, N. N.; Schwinn, F. J. Chemical control of plant diseases: problems and prospects. *Annu. Rev. Phytopathol.* **1993**, *31*, 403–421.
  32. Johnson, H., Jr.; Holland, A. H.; Paulus, A. O.; Wilhelm, S. Soil fumigation found essential for maximum strawberry yields in Southern California. *Calif. Agric.* **1962**, *16*, 5–6.
  33. Wilhelm, S.; Paulus, A. O. How soil fumigation benefits the California strawberry industry. *Plant Dis.* **1980**, *64*, 264–270.
  34. Gareau, B. J. *From Precaution to Profit: Contemporary Challenges to Environmental Protection in the Montreal Protocol*; Yale University Press: 2013.
  35. DuPuis, E. M.; Gareau, B. J. Neoliberal knowledge: The decline of technocracy and the weakening of the Montreal Protocol. *Social Sci. Q.* **2008**, *89*, 1212–1229.

36. United Nations Environment Programme. *Handbook for the Montreal Protocol Substances that Deplete the Ozone Layer*, 7th ed.; Nairobi, Kenya: 2006.
37. Mayfield, E. N.; Norman, C. S. Moving away from methyl bromide: Political economy of pesticide transition for California strawberries since 2004. *J. Environ. Manage.* **2012**, *106*, 93–101.
38. Wolverton, A. Retrospective evaluation of costs associated with methyl bromide critical use exemptions for open field strawberries in California. *J. Ben.-Cost Anal.* **2014**, *5*, 225–257.
39. Anonymous. EPA honors California Strawberry Commission. Progressive Grocer. <https://progressivegrocer.com/epa-honors-california-strawberry-commission> (accessed Feb. 22, 2018).
40. Crop Nutrition. World strawberry production. 2016. <http://www.yara.co.uk/crop-nutrition/crops/soft-fruit/key-facts/world-production/> (accessed Mar. 27, 2018).
41. Kenworth, T.; Schwartz, J. 3 U.S. agencies announce joint commitment to cut pesticide use. *Washington Post*, June 26, 1993, p A5.
42. University of California. What is integrated pest management (IPM)? <http://www2.ipm.ucanr.edu/WhatIsIPM/> (accessed Mar. 27, 2018).
43. U.S. Gen. Account. Off. *Agricultural pesticides management: improvements needed to further promote integrated pest management*; GAO-01-815, GAO: Washington, DC, 2001. <http://www.gao.gov/new.items/d01815.pdf> (accessed Mar. 27, 2018).
44. Hokkanen, H. M. T. Integrated pest management at the crossroads: Science, politics, or business (as usual)? *Arthr.-Plant Interact.* **2015**, *9*, 543–545.
45. Krupke, C. H.; Holland, J. D.; Long, E. Y.; Eitzer, B. D. Planting of neonicotinoid-treated maize poses risks for honey bees and other non-target organisms over a wide area without consistent crop yield benefit. *J. Appl. Ecol.* **2017**, *54*, 1449–1458.
46. Rundlöf, M.; Andersson, G. K.; Bommarco, R.; Fries, I.; Hederström, V.; Herbertsson, L.; Jonsson, O.; Klatt, B. K.; Pedersen, T. R.; Yourstone, J.; Smith, H. G. Seed coating with a neonicotinoid insecticide negatively affects wild bees. *Nature* **2015**, *521*, 77–80.
47. Sánchez-Bayo, F.; Goulson, D.; Pennacchio, F.; Nazzi, F.; Goka, K.; Desneux, N. Are bee diseases linked to pesticides?—A brief review. *Environ Int.* **2016**, *89*, 7–11.
48. Wood, T. J.; Goulson, D. The environmental risks of neonicotinoid pesticides: a review of the evidence post 2013. *Environ. Sci. Pollut. Res.* **2017**, *24*, 17285–17325.
49. Norton, G. W.; Mullen, J. *Economic Evaluation of Integrated Pest management Programs: A Literature Review*; VA Coop. Ext., Publ. 448-120; Virginia Polytech. Inst. State Univ.: Blacksburg, VA, 1994.
50. Hendricks, L. C. Almond growers reduce pesticide use in Merced County field trials. *Calif. Agric.* **1995**, *49*, 5–10.
51. Epstein, L.; Bassein, S.; Zalom, F. Almond and stone fruit growers reduce OP, increase pyrethroid use in dormant sprays. *Calif. Agric.* **2000**, *54*, 14–19.

52. Epstein, L.; Bassein, S.; Zalom, F. G.; Wilhoit, L. R. Changes in pest management practice in almond orchards during the rainy season in California, USA. *Agric., Ecosyst. Environ.* **2001**, *83*, 111–120.
53. Weddle, P. W.; Welter, S. C.; Thomson, D. History of IPM in California pears—50 years of pesticide use and the transition to biologically intensive IPM. *Pest Manage. Sci.* **2009**, *65*, 1287–1292.
54. Gubler, W. D.; Rademacher, M. R.; Vasquez, S. J.; Thomas, C. S. Control of Powdery Mildew Using the UC Davis Powdery Mildew Risk Index. *APS Net: Plant Pathol. On-Line*, 1999. <http://www.apsnet.org/publications/apsnetfeatures/pages/UCDavisRisk.aspx> (accessed Mar. 27, 2018).
55. Lybbert, T. J.; Magnan, N.; Gubler, W. D. Multidimensional responses to disease information: how do winegrape growers react to powdery mildew forecasts and to what environmental effect? *Am. J. Agric. Econ.* **2016**, *98*, 383–405.
56. Sambucci, O.; Lybbert, T. J. Behavioral responses to disease forecasts: from precision to automation in powdery mildew management. *ARE Update* **2016**, *20*, 5–8 (University of California Giannini Foundation of Agricultural Economics).
57. Gent, D. H.; Mahaffee, W. F.; McRoberts, N.; Pfender, W. F. The use and role of predictive systems in disease management. *Annu. Rev. Phytopathol.* **2013**, *51*, 267–289.
58. Shtienberg, D. Will decision-support systems be widely used for the management of plant diseases? *Annu. Rev. Phytopathol.* **2013**, *51*, 1–16.
59. Beckerman, J. L.; Sundin, G. W.; Rosenberger, D. A. Do some IPM concepts contribute to the development of fungicide resistance? Lessons learned from the apple scab pathosystem in the United States. *Pest Manage. Sci.* **2015**, *71*, 331–342.
60. Jørgensen, L. N.; van den Bosch, F.; Oliver, R. P.; Heick, T. M.; Paveley, N. Targeting Fungicide Inputs According to Need. *Annu. Rev. Phytopathol.* **2017**, *55*, 181–203.
61. CropLife. Biotechnology pipeline, 2016. [https://croplife-r9qnrxt3qxxgja4.netdna-ssl.com/wp-content/uploads/2016/09/CropLifePlantBiotechPipeline2016\\_LoRes1.pdf](https://croplife-r9qnrxt3qxxgja4.netdna-ssl.com/wp-content/uploads/2016/09/CropLifePlantBiotechPipeline2016_LoRes1.pdf) (accessed Mar. 6, 2018).
62. Coupe, R. H.; Capel, P. D. Trends in pesticide use on soybean, corn and cotton since the introduction of major genetically modified crops in the United States. *Pest Manage. Sci.* **2016**, *72*, 1013–1022.
63. Perry, E. D.; Ciliberto, F.; Hennessy, D. A.; Moschini, G. Genetically engineered crops and pesticide use in US maize and soybeans. *Sci. Adv.* **2016**, *2*, e1600850.
64. Benbrook, C. M. Impacts of genetically engineered crops on pesticide use in the US—the first sixteen years. *Environ. Sci. Eur.* **2012**, *24*, 24.
65. Klümper, W.; Qaim, M. A. Meta-analysis of the impacts of genetically modified crops. *PLoS ONE* **2014**, *9*, e111629.
66. Hutchison, W. D.; Burkness, E. C.; Mitchell, P. D.; Moon, R. D.; Leslie, T. W.; Fleischer, S. J.; Raun, E. S. Areawide suppression of European corn borer with Bt maize reaps savings to non-Bt maize growers. *Science* **2010**, *330*, 222–225.

67. Munkvold, G. P. Crop management practices to minimize the risk of mycotoxins contamination in temperate-zone maize. In *Mycotoxin Reduction in Grain Chains*; Leslie, J. F., Logrieco, A., Eds.; J. Wiley: 2014; pp 59–75.