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### Authors

Woodruff, TJ  
Kyle, AD  
Bois, FY

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# Evaluating Health Risks from Occupational Exposure to Pesticides and the Regulatory Response

Tracey J. Woodruff,<sup>1</sup> Amy D. Kyle,<sup>2</sup> and Frédéric Y. Bois<sup>2</sup>

<sup>1</sup>Institute for Health Policy Studies, University of California-San Francisco, San Francisco, CA 94109 USA; <sup>2</sup>School of Public Health, University of California-Berkeley, Berkeley, CA 94720 USA

In this study, we used measurements of occupational exposures to pesticides in agriculture to evaluate health risks and analyzed how the federal regulatory program is addressing these risks. Dose estimates developed by the State of California from measured occupational exposures to 41 pesticides were compared to standard indices of acute toxicity (LD<sub>50</sub>) and chronic effects (reference dose). Lifetime cancer risks were estimated using cancer potencies. Estimated absorbed daily doses for mixers, loaders, and applicators of pesticides ranged from less than 0.0001% to 48% of the estimated human LD<sub>50</sub> values, and doses for 10 of 40 pesticides exceeded 1% of the estimated human LD<sub>50</sub> values. Estimated lifetime absorbed daily doses ranged from 0.1% to 114,000% of the reference doses developed by the U.S. Environmental Protection Agency, and doses for 13 of 25 pesticides were above them. Lifetime cancer risks ranged from 1 per million to 1700 per million, and estimates for 12 of 13 pesticides were above 1 per million. Similar results were obtained for field workers and flaggers. For the pesticides examined, exposures pose greater risks of chronic effects than acute effects. Exposure reduction measures, including use of closed mixing systems and personal protective equipment, significantly reduced exposures. Proposed regulations rely primarily on requirements for personal protective equipment and use restrictions to protect workers. Chronic health risks are not considered in setting these requirements. Reviews of pesticides by the federal pesticide regulatory program have had little effect on occupational risks. Policy strategies that offer immediate protection for workers and that are not dependent on extensive review of individual pesticides should be pursued. *Key words:* agricultural workers, agriculture-associated diseases, environmental policy, lethal dose 50, pesticides, risk, U.S. Environmental Protection Agency. *Environ Health Perspect* 102:1088–1096 (1994)

Over 140 million pounds of pesticide active ingredients were applied in agriculture in California in 1991 (1). The large volume of pesticides used in agriculture warrants evaluation of the potential for adverse effects on agricultural workers' health. Acute, chronic, and cancer effects are of concern. Occupational pesticide exposure has been linked to acute health effects including rashes, skin, eye, and respiratory illnesses, and death (2–4). Chronic effects, including neurological and repro-

ductive effects and cancer, are more difficult to ascertain, but studies have found associations between pesticide exposure and these effects (5–8).

The potential for adverse health outcomes from occupational pesticide exposures requires attention to primary prevention. By assessing occupational risks from pesticide exposures, intervention can be targeted to pesticides with the greatest potential to harm human health. Occupational health intervention strategies can be compared to determine which strategies are most effective in reducing health risks. For example, the effectiveness of technological measures, such as closed mixing systems, can be compared to the effectiveness of protective clothing. In addition, occupational pesticide regulations should be based on all health outcomes of concern, including chronic effects and cancer.

In this study, dose estimates derived from direct exposure measurements and animal dermal absorption values were compared to standard toxicological indices to assess the potential for adverse health outcomes. We used LD<sub>50</sub> values (doses lethal to 50% of a tested population), reference doses, and cancer potencies to examine a broad range of health risks. These data were compared to occupational dose estimates produced by the Worker Health and Safety Branch (WHSB) of the California Environmental Protection Agency (Cal/EPA) using direct exposure measurements for pesticides. The effects of protective clothing and technologies such as closed mixing systems on exposure levels were also evaluated. Pesticides that represent the highest risks were classified as high priority in this analysis, and the regulation of these pesticides by the U.S. Environmental Protection Agency (EPA) was assessed. Finally, the policy implications for risk reduction are discussed.

## Methods

**Exposure assessments.** The WHSB of the Department of Pesticide Regulation of Cal/EPA assessed occupational exposures to 41 agricultural pesticides as of August 1993 (9–49). Most of the pesticides had been categorized as high-priority pesticides for risk characterization by Cal/EPA. The exposure assessments rely on EPA and California registration documents, pub-

lished scientific literature, and field tests conducted by WHSB. Most involved field tests in which pesticide exposures were measured directly. WHSB evaluated the quality of each data source. Studies deemed inadequate were not used for the final assessments. Thirteen pesticides had few or no existing exposure studies, and for these WHSB used surrogate pesticide exposure estimates exclusively or in conjunction with existing studies. Surrogate pesticides selected were similar to the evaluated pesticide. Before public release, all assessments went through an internal peer review and two peer reviews in other branches within Cal/EPA. Dose estimates were derived from the exposure measurements and dermal absorption values. Dermal absorption factors were determined from animal data when available.

For each pesticide, exposures were assessed for several job categories. The categories examined in this analysis are: 1) mixers, loaders, and applicators, including workers in ground and aerial application, 2) flaggers, workers on the ground who guide aerial application, and 3) harvesters, including field workers and workers packing agricultural products.

For each pesticide, minimum and maximum dose estimates considered adequate by Cal/EPA were used in this study. Absorbed daily dose estimates (milligram/kilogram/day) and lifetime absorbed daily dose estimates (milligram/kilogram/day over a lifetime) are given. The absorbed daily dose was calculated for a single workday. The annual daily absorbed dose was used to extrapolate to lifetime absorbed daily dose assuming a 40-year work life and a 70-year lifetime. For pesticides for which only absorbed daily dose and number of days worked per year were available, we calculated the annual absorbed daily dose and the lifetime absorbed daily dose. Daily and lifetime absorbed doses given in units of milligrams/day were converted to milligrams/kilogram/day by dividing by Cal/EPA's default values for body weight: 70 kg for mixers, loaders, and applicators and 54.8 kg for flaggers or field workers.

Address correspondence to T.J. Woodruff, Environmental Protection Agency, MS 2126, 401 M Street SW, Washington DC 20460 USA.

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Exposure assessments for 40 of the pesticides reported absorbed daily doses for mixers, loaders, and applicators, 23 for harvesters, and 12 for flaggers. Twenty-eight exposure assessments reported lifetime absorbed daily doses for mixers, loaders, and applicators, 18 for harvesters, and 10 for flaggers.

**Toxicological measures.** Three standard toxicological measures were compared to the doses estimated in the exposure assessments. The LD<sub>50</sub>, expressed in milligrams/kilogram, is a measure of a chemical's ability to cause acute poisoning. For the rat, it is the single oral dose that is expected to kill 50% of exposed rats. The lower the LD<sub>50</sub>, the higher the acute toxicity.

The oral LD<sub>50</sub> values were taken from *Pesticide Fact Handbooks* (50,51). For pesticides not included in the handbooks, LD<sub>50</sub> values were obtained from *The Pesticide Manual* (52). For five pesticides (benomyl, chlorothalonil, diflubenzuron, folpet, and londax), only a lower bound was reported; this was used as the LD<sub>50</sub>. If a range of values was reported, then the midpoint of the range was used. Using these conventions, LD<sub>50</sub> values were available for all pesticides.

We used surface-area extrapolation to estimate the human oral LD<sub>50</sub> from the rat oral LD<sub>50</sub> (in milligrams/kilogram) where:  $LD_{50\text{human}} = LD_{50\text{rat}} \times (BW_{\text{rat}}/BW_{\text{human}})^{0.3}$ , and BW is body weight (53). The standard assumptions for body weight were used here.

The reference dose (RfD), expressed in milligrams/kilogram/day over a lifetime, is an estimate of lifetime daily exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of adverse chronic health effects, such as reproductive effects or neurological effects. The RfD is calculated by dividing the dose for which there is no observed adverse health effect (NOEL) in an experimental animal by an uncertainty factor and a modifying factor, typically 100. The lower the RfD, the more toxic the chemical. The RfD values were obtained from the Office of Pesticide Programs at EPA (54). RfD values were available for 39 (95%) of the pesticides.

The carcinogenic potency (q\*), calculated from data obtained from animal testing, is the upper 95% confidence limit of the estimate of a chemical's potential to cause human cancer over a lifetime, expressed in (milligrams/kilogram/day)<sup>-1</sup>. The higher the potency, the greater the chemical's potential to cause cancer. Potencies were obtained from EPA's ongoing cancer evaluation of chemicals in the Office of Pesticide Programs (55). Cancer potencies were available for 16 (39%) of the pesticides.

**Comparison of occupational doses of pesticides and toxicological measures.** To compare worker doses to LD<sub>50</sub> values, the absorbed daily dose estimate was divided by the estimated human LD<sub>50</sub> and multiplied by 100 to obtain a percentage of the LD<sub>50</sub>. For chronic health effects, the lifetime absorbed daily dose estimate was divided by the RfD and multiplied by 100 to obtain a percentage of the reference dose. The added lifetime risk of cancer from pesticide exposure was obtained by multiplying the lifetime absorbed daily dose estimate by the cancer potency.

Pesticides were selected for regulatory analysis if their doses represent relatively high risks according to the following criteria. A pesticide was selected if the absorbed daily dose estimate was more than 1% of the estimated human LD<sub>50</sub>, the lifetime absorbed daily dose was more than 100% of the RfD, or the cancer risk was greater than 1 per million. The selected pesticides are referred to as priority pesticides.

**Evaluation of protective measures.** For mixers and loaders and for applicators, some exposure estimates were reported for use of protective measures, including personal protective equipment (gloves and long-sleeved clothing) or technological controls on mixing or application (closed cabs, closed mixing, and pouring). To assess the impact of such measures, dose estimates obtained while protections were in use were compared with estimates without protections for the same pesticides. The estimates obtained while protections were used were further divided into those for worker-based and those for technology-based measures. Exposures measured while closed cabs were used for boom or air blast application or closed systems were used for mixing/loading were compared to exposures during use of open cabs or open mixing/loading. Exposures measured while gloves and long-sleeved shirts were used were compared to exposures without. When comparing the impact of a protective measure, other factors were held constant (e.g., for comparing closed and open mixing/loading systems, clothing type was the same). When multiple values were given for a single category of protection, the highest given dose was used to represent the dose estimate.

**Regulatory and policy analysis.** Federal regulatory requirements pertinent to occupational exposures in agriculture were identified. The status of the priority pesticides in this study under the federal regulatory program for pesticides was assessed. In particular, the status of these pesticides under the major review processes of the federal regulatory system, reregistration and special review, was assessed. Requirements for restrictions on use, personal pro-

ective equipment (PPE), and use of technological controls were identified from documents resulting from special review or registration actions and other sources (50,51). Requirements resulting from special review or registration actions were identified through review of documents about these actions. Case studies of the two pesticides in special review with the highest ratios of dose to toxicological measures were performed to determine the role of the regulatory process in protecting worker health.

## Results

In 1991, 1.6 million pounds of the 41 pesticide active ingredients studied here were applied in agriculture in California. This represents 6% of the total volume of pesticides applied.

Available data allowed comparisons of absorbed daily dose estimates to estimated human LD<sub>50</sub> values for all pesticides. Fewer data were available to allow comparisons for chronic effects. For mixers, loaders, and applicators, data were available to compare lifetime absorbed daily dose estimates to RfD values for 26 of 41 pesticides (63%). Similarly, for harvesters, 17 of 22 possible comparisons (77%) could be made. Thirteen of 41 (32%) cancer risk estimates could be determined for mixers, loaders, and applicators and 8 of 22 (36%) for harvesters.

### Comparison of Dose Estimates with Toxicological Measures

Table 1 shows comparisons of minimum and maximum absorbed daily dose estimates for mixers, loaders, and applicators to the estimated human LD<sub>50</sub> for each pesticide. The absorbed daily doses range from less than 0.0001% to 48% of the estimated human LD<sub>50</sub>. Most of the minimum doses are less than 1% of the LD<sub>50</sub>, and two are less than 0.0001%. Most of the maximum doses are also less than 1% of the LD<sub>50</sub>. Both minimum and maximum dose estimates for four pesticides are above 1% of the LD<sub>50</sub>. The maximum dose estimates for three additional pesticides are above 1% of the LD<sub>50</sub>.

For chronic effects, the percentages of the RfD represented by the lifetime absorbed daily dose estimate also span a large range of values, from 0.01% to 114,667% (Table 1). Fifteen of 26 (58%) pesticides had maximum estimated doses above the RfD.

The added lifetime cancer risks range from 0.02 per million to 2000 per million for mixers, loaders, and applicators (Table 1). Maximum estimated lifetime doses to 12 of 13 (92%) pesticides pose cancer risks greater than 1 per million.

Estimated doses to flaggers were available for 12 pesticides. For flaggers, com-

parisons of doses to toxicological measures are similar to those for mixers, loaders, and applicators (data not shown).

Table 2 shows comparisons of dose estimates to toxicological measures for harvesters. As with the mixers, loaders, and applicators, most of the absorbed daily dose estimates are less than 1% of the estimated human LD<sub>50</sub>. The dose is greater than 1% of the LD<sub>50</sub> for four pesticides; the highest is 3% of the LD<sub>50</sub>. For chronic effects, as with mixers, loaders, and applicators, lifetime absorbed daily dose estimates exceed the RfD for 8 of 17 (47%) pesticides, 7 of which are the same as for mixers, loaders, and applicators. The added lifetime cancer risks range from 0.03 per million to 200 per million. The four pesticides posing the highest cancer risks are the same as for mixers, loaders, and applicators.

Twenty-four pesticides are selected as priority pesticides. For mixers, loaders, and applicators, 7 of 40 (17%) pesticides had

an absorbed daily dose estimate over 1% of the estimated human LD<sub>50</sub>. Thirteen of 26 (50%) had lifetime absorbed daily dose estimates over 100% of the RfD, and 11 of 13 (85%) had a cancer risk higher than 1 in a million. The percentages of pesticides classified as high priority by toxicity category were similar for harvesters.

**Comparison of dose estimates for different job categories.** Estimated absorbed daily doses were compared across job categories. In general, doses for mixers, loaders, and applicators are higher than those for flaggers and harvesters. For the 20 pesticides for which doses are available, 16 (80%) of the mixer, loader, and applicator doses are 2–100 times higher than those for harvesters. Doses for mixers, loaders, and applicators are 2–4750 times higher than for flaggers for 11 out of 12 pesticides (92%) for which doses are available. Between harvesters and flaggers, doses are not higher for either category. The com-

parisons are similar for lifetime absorbed daily dose estimates.

### Effects of Protective Measures

Figure 1 shows the reduction in estimated absorbed daily dose associated with use of technology-based and worker-based protective measures for mixers, loaders, and applicators. For most of the pesticides, using protective measures results in more than an order of magnitude decrease in exposure. Similar reductions are seen for harvesters using gloves compared to those not using gloves. Eight of the 11 pesticides depicted in the graph are high-priority pesticides for either acute, chronic, or cancer effects.

### Regulation of Pesticides for Occupational Health

The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) vests EPA with authority to regulate pesticides. FIFRA establishes a registration process to evaluate risks posed by pesticides and to compel testing (56). Pesticides are to be registered if they perform without unreasonable adverse effects on the environment (57), which is defined to be “any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide.” (58). EPA is to balance the potential for “unreasonable” adverse effects against benefits from use. EPA approves or “registers” pesticides that pass this test and can put restrictions on pesticides to reduce risks to levels it deems acceptable (59).

EPA has also assumed lead responsibility for regulation of pesticide exposure in the agricultural workplace. This responsibility was shifted from the Occupational Safety and Health Administration (OSHA) to EPA during the 1970s as a result of court decisions. In 1973, OSHA asserted jurisdiction over occupational exposure to pesticides in agriculture and proposed emergency regulations (60). The regulations were vacated by the court on the grounds that use of emergency powers had not been justified (61). In 1974, EPA proposed regulations with field reentry intervals for 12 pesticides and limited protections for field laborers (62). Farmworker organizations concluded that EPA’s proposal was inadequate and filed suit to compel OSHA to issue more complete regulations (63). The EPA regulations became effective while the suit was pending (64). The Department of Labor moved to dismiss the farmworkers’ case, arguing that EPA had preempted action by OSHA through adoption of its regulations. The court ruled that EPA had jurisdiction because it had acted first and thereby preempted OSHA (63). The result is that

**Table 1.** Maximum and minimum acute and chronic doses as a percent of the relevant toxicological measures for mixers, loaders, and applicators<sup>a</sup>

Pesticide	Absorbed daily dose as % of estimated human LD <sub>50</sub>		Lifetime absorbed daily dose as % of RfD		Added lifetime cancer risk/1,000,000	
	Min	Max	Min	Max	Min	Max
Abamectin	0.001	0.04	—	—	—	—
Alachlor	—	0.008	0.2	4	2	29
Aldicarb	3	38	—	—	—	—
Amitraz	0.2	0.7	112	464	140	580
Atrazine	<0.0001	0.06	0.009	5	0.7	396
Azinphos-methyl	2	8	26	85	—	—
Benomyl	0.0005	0.04	0.8	68	2	143
Bifenthrin	0.0008	0.2	0.02	12	0.2	100
Bromoxynil	0.02	2	—	—	—	—
Captafol	0.0002	0.007	1	142	1	145
Captan	0.0001	0.07	0.2	92	1	432
Chlorothalonil	0.0007	0.06	1	1,046	2	1,726
Chlorpyrifos	0.001	1	—	—	—	—
Clofentezine	—	0.002	—	—	—	—
Cyanazine	0.003	23	—	—	—	—
Cycloate	0.0002	0.08	—	—	—	—
Cyhexatin	1	48	2,667	114,667	—	—
Cyromazine	<0.0001	0.006	0.1	8	0.02	1
Daminozide	0.004	0.08	0.2	4	3	47
Dichlorvos (DDVP)	—	0.5	—	520	—	520
Dichloropropene	0.005	0.02	—	—	—	—
Difflubenzuron	0.003	0.1	—	—	—	—
Dinocap	0.003	0.3	—	—	—	—
Diquat dibromide	0.001	0.2	0.5	119	—	—
EPTC	0.006	0.03	1	6	—	—
Ethoprop	0.001	1	67	11,333	—	—
Flucythrinate	0.007	7	0.5	565	—	—
Folpet	0.02	0.1	31	249	108	871
Londax	—	0.005	—	—	—	—
Mancozeb	0.0008	0.05	3	174	11	575
Mevinphos	0.05	0.1	—	—	—	—
Molinate	0.005	0.2	12	540	—	—
Monocrotophos	0.2	1	800	4,200	—	—
Myclobutanil	0.0002	0.002	0.2	2	—	—
Oxydemeton-methyl	0.03	2	57	3,080	—	—
Paclobutrazol	—	0.003	—	5	—	—
Paraquat	0.002	0.3	0.4	88	—	—
Propargite	0.01	0.06	—	—	—	—
Triadimefon	0.002	0.4	—	—	—	—
Triadimenol	0.01	0.1	0.01	0.1	—	—

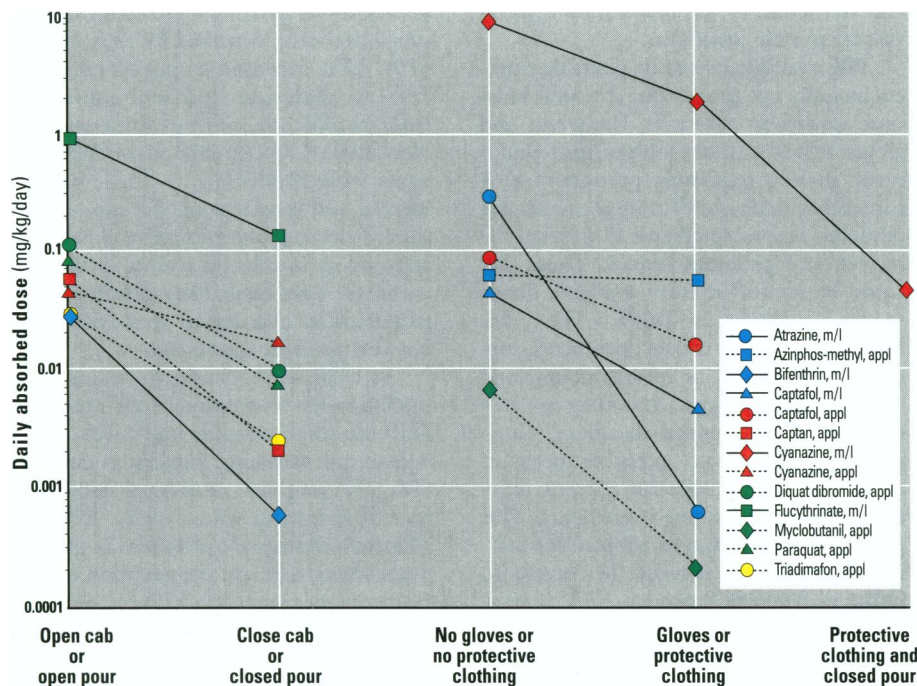
<sup>a</sup>Numbers in bold are those classified as high priority in this analysis.



**Table 2.** Maximum and minimum acute and chronic doses as a percentage of the relevant toxicological measures for harvesters<sup>a</sup>

Pesticide	Absorbed daily dose as % of estimated human LD <sub>50</sub>		Lifetime absorbed daily dose as % of RfD		Added lifetime cancer risk/1,000,000	
	Min	Max	Min	Max	Min	Max
Abamectin	<0.0001	0.0005	—	—	—	—
Amitraz	—	0.04	—	<b>108</b>	—	<b>135</b>
Azinphos-methyl	0.2	<b>9</b>	22	<b>892</b>	—	—
Benomyl	0.0002	0.003	0.4	4	0.8	<b>9</b>
Bifenthrin	0.03	0.05	1	2	<b>11</b>	<b>20</b>
Captafol	<0.0001	0.002	1	<b>168</b>	1	<b>172</b>
Captan	0.002	0.01	4	18	<b>17</b>	<b>84</b>
Chlorothalonil	<0.0001	0.04	0.7	<b>133</b>	1	<b>219</b>
Chlorpyrifos	0.0002	0.05	—	—	—	—
Cyhexatin	—	<b>5</b>	—	<b>18,267</b>	—	—
Dinocap	0.01	0.05	—	—	—	—
Flucythrinate	0.007	0.07	0.06	6	—	—
Folpet	0.007	0.07	26	<b>274</b>	<b>91</b>	<b>959</b>
Mancozeb	0.0006	0.009	3	90	<b>11</b>	<b>297</b>
Mevinphos	0.008	0.6	—	—	—	—
Monocrotophos	1	<b>4</b>	<b>7,200</b>	<b>21,600</b>	—	—
Myclobutanil	0.002	0.006	2	9	—	—
Oxydemeton-methyl	0.006	0.2	19	<b>176</b>	—	—
Paclobutrazol	—	<0.0001	—	0.02	—	—
Paraquat	0.005	0.005	—	1	—	—
Phosmet	0.2	<b>3</b>	70	<b>325</b>	—	—
Propargite	0.002	0.006	—	—	—	—
Triadimefon	0.002	0.05	—	—	—	—

<sup>a</sup>Numbers in bold are those classified as high priority in this analysis.



**Figure 1.** Reduction in the daily absorbed dose given different protective measures for mixer/loaders (m/l) and applicators (appl).

EPA has jurisdiction over regulation of pesticides in the agricultural workplace.

OSHA retains jurisdiction in certain areas but has not taken any substantive action. OSHA has adopted a hazard communication standard for chemical hazards in the workplace, but pesticides subject to labeling under FIFRA are exempt (65). OSHA also sets standards for air contami-

nants in workplaces and establishes requirements for how employers must provide and employees must use personal protective equipment, but agricultural operations are exempt (66,67).

EPA has determined that its 1974 regulations are inadequate to protect workers (68). The 1974 regulations prohibit spraying of workers, prohibit reentry to agricul-

tural operations “until sprays have dried or dusts have settled,” set reentry intervals for 12 pesticides, require protective clothing for entry of treated areas, and require “appropriate and timely” warnings (64).

EPA adopted expanded worker protection regulations in August 1992 (68). Employees in farms, forests, nurseries, and greenhouses and those who mix, load, or apply pesticides are included. Because EPA does not have authority to directly regulate workplaces or establish occupational standards, the regulations are largely implemented by requiring manufacturers to include their substantive requirements on the labels of pesticides (69). The regulations were to be implemented in April 1994, but the effective date has been delayed until 1995 (70).

In new regulations, reentry intervals are established for all pesticide products based on acute toxicity and range from 12 hr for some restricted-use pesticides to 48 hr. Verbal notice or posting of sprayed areas is to be provided to workers. Personal protective equipment is required for handlers, depending on the acute toxicity of the pesticide formulation (Table 3). Employers must provide the equipment and ensure that it is used correctly. Washing facilities are required. EPA separately proposed but has not yet adopted a standard for hazard communication that would require pesticide safety training for all workers and access to information on products (71). These regulations differ from most of EPA’s regulatory program in that they do not depend on reviews of individual pesticides.

**Regulation of priority pesticides.** The success of the reregistration process in addressing priority pesticides has been limited. EPA allows products registered before November 1984 to stay on the market until they are tested, and test results are reviewed in a process called “reregistration” (72). EPA has grouped pesticides for reregistration into four groups (Table 4). The categories are supposed to reflect the potential for health or environmental risks, with “A” pesticides representing the highest potential risk and “D” the lowest. To date, about 13% of pesticides subject to reregistration have reached the final stage of review (73). Almost half of these are from the D group. In a recent study, the General Accounting Office concluded that EPA will not meet the current deadline of 1998 to complete the reregistration process (74).

Of the 24 priority pesticides identified in this study, 23 are subject to reregistration because they were on the market in 1984 (bifenthrin being the exception.) None of the 23 has received approval for reregistration, though daminozide has reached the final stage before reregistration. Four have been canceled by EPA or

**Table 3.** Personal protective equipment requirements by toxicity category from the U.S. EPA worker protection regulations

Toxicity type	Acute toxicity category			
	I	II	III	IV
Dermal/skin irritation	Coverall, long sleeves, long pants	Coveralls, short sleeves, short pants	Long sleeves, long pants	Long sleeves, long pants
	Chemical-resistant footwear	Chemical-resistant footwear	Shoes	Shoes
	Chemical-resistant gloves	Chemical-resistant gloves	Chemical-resistant gloves	No requirement
Inhalation toxicity	Respiratory protection	Respiratory protection	No requirement	No requirement
Eye irritation	Protective eyewear	Protective eyewear	No requirement	No requirement

their manufacturer (Table 4). Of the remaining 19, 17 are category A, and 2 are category B.

**Special review of pesticide active ingredients.** FIFRA authorized EPA to conduct "special reviews" to assess particular risks of pesticides, whether they have been fully approved or not (75). EPA has used this process infrequently in recent years; a 1993 report by the EPA inspector general indicated that no new special reviews had been initiated in four years (76). Half of the 24 priority pesticides have undergone or are undergoing special review (Table 4). Four are currently under special review (aldicarb, atrazine, dichlorvos, oxydemeton-methyl, with atrazine in "pre-special" review). Six have undergone special review in the past without being canceled (alachlor, amitraz, benomyl, captan, cyanazine, and daminozide). Two were canceled by agreement with their manufacturers during or after a special review (77).

In this study, eight priority pesticides were identified because of acute toxicity. Of these, only aldicarb has been subject to a special review for acute effects. The review began in 1984 and is ongoing. Fifteen of the priority pesticides were identified in this analysis because of chronic effects. Of these, captafol and cyhexatin were canceled due to chronic effects. Another two, dichlorvos and oxydemeton-methyl, are in special reviews, which began in 1984 and 1987, respectively. Special reviews for two others, amitraz and cyanazine, were completed.

Twelve priority pesticides were identified in this analysis due to potential carcinogenicity. Of these, eight (alachlor, amitraz, atrazine, benomyl, captafol, captan, daminozide, and dichlorvos) have been subject to special review or are currently undergoing special review for cancer effects. Captafol was canceled because of carcinogenic effects. The review ofalachlor resulted in adoption of significant worker protection measures, including warnings, personal protective equipment requirements, and use of closed systems. Use of

dust masks was required with benomyl. With two other cases, amitraz and captan, no actions were taken to protect workers. The pending reviews were initiated in 1988 or 1984 (77).

**Personal protective equipment, technological controls, and use restriction for active ingredients.** In addition to adopting general requirements such as the worker protection regulations, EPA may adopt requirements such as personal protective equipment (PPE), technological controls, and restriction of use to certified applicators for specific pesticides.

PPE available for use by pesticide workers includes eye protection, chemical resistant aprons or coveralls, footwear, and gloves as well as more sophisticated equipment, such as respiratory protection. EPA sometimes adopts PPE requirements for pesticide active ingredients during special reviews or registration reviews. Those that could be identified from available documents are shown in Table 4. They are recorded in special review documents, registration standards, or records maintained by product managers, but they are not tracked in any central database. Consequently, there is no accessible means to comprehensively identify current label requirements for active ingredients. PPE requirements may also be adopted for individual product formulations (M. Yanchulis, Office of Pesticide Programs, EPA, personal communication). Because there may be hundreds of formulations of a single active ingredient, this information is difficult to compile. As noted previously, EPA included provisions for PPE, based on the route of exposure and acute toxicity of products, in its 1992 worker protection regulations (Table 3) (68,78). These requirements were originally scheduled to take effect in April 1994, but the effective date for provisions related to reentry intervals and certain label requirements was extended by Congress until January 1995 (70).

EPA may also require use of technological controls for individual pesticides, though this approach has received less

emphasis than PPE. EPA has occasionally required technological controls for specific active ingredients. As for PPE, there is no central data source to identify the controls. Technological control requirements that can be identified from review of documents for special review pertaining to active ingredients are shown in Table 4. EPA did not adopt provisions for technological controls, unlike PPE, in its 1992 worker protection standards.

EPA may classify a pesticide as restricted to use by certified applicators. Such pesticides may be sold only to persons certified to apply them. This is believed to reduce exposure because certified applicators are more likely to follow requirements for application, protective equipment, and hazard communication. Of the 22 priority pesticides still in use, 10 (45%) have had all or most all uses restricted (Table 4).

**Case studies: regulatory response to toxic pesticides.** We reviewed two pesticide active ingredients, aldicarb and oxydemeton-methyl, more closely as examples of how EPA addresses occupational exposures.

Aldicarb has the highest value for acute toxicity of any pesticide in this study. Its acute toxicity and cholinesterase-inhibiting properties were identified by EPA in 1984 (79). EPA initiated a special review in 1984 to address groundwater contamination by aldicarb, noting occurrences in New York. Gaps in data on worker exposures were identified. A 24-hr reentry interval and requirements for use of long-sleeved clothing and protective gloves were adopted as interim measures until more complete data could be submitted. The manufacturer also agreed to restrict use to certified pesticide applicators.

In 1988, EPA identified cholinesterase inhibition at low exposure levels, acute toxicity for small animals and birds, and a widespread poisoning incident as concerns (80). EPA proposed restrictions within 300 feet of drinking water wells. EPA has adopted a strategy for pesticides in groundwater which relies on the adoption of state management plans (80). EPA has indicated aldicarb will be addressed under this process (Housenger J, Office of Pesticide Programs, EPA, personal communication).

Aldicarb was identified again in 1993 as one of the five pesticides of greatest concern to EPA for acute health risks to workers as part of a larger review of 83 pesticides. Rather than addressing this issue through the special review process, EPA required manufacturers to obtain national data on poisonings attributed to aldicarb from poison control centers (81). The notice was issued in July 1993 (82). The data received last winter are under review at EPA but are not available to the public. No action has been taken as of September

1994 (First J, Office of Pesticide Programs, EPA, personal communication).

Oxydemeton-methyl has the highest estimated lifetime absorbed daily dose as a percentage of reference dose of the pesticides in special review that are still on the market. The reregistration process for oxydemeton-methyl began in the mid-1980s. EPA required studies of teratology and reproductive effects, and reentry and exposure data for mixers, loaders and applicators involved in ornamental uses. Studies done in 1986 for the California Department of Food and Agriculture (CDFA) identified male reproductive effects as a concern, according to the EPA reregistration document. [In December 1986,

CDFA suspended all home-use products, restricted use to licensed applicators, and required use of full body protection and closed systems. Oxydemeton-methyl is one of four pesticides for which such precautions were adopted (83).]

A special review was initiated in 1987 for oxydemeton-methyl (84). In 1993, the product manufacturer requested that the registration be canceled. EPA issued a notice of voluntary cancellation in March 1994 (85). The manufacturer decided not to conduct the tests necessary to support continued review of the chemical. EPA indicated in its notice that it expected to cancel the product in June 1994. However, another manufacturer expressed interest in

manufacturing the chemical and asked EPA for extensions on the deadlines for submission of required exposure and toxicological studies. Because the deadlines for submission of test results have not been met, EPA has the authority to suspend the product. However, such a decision would be subject to appeal, and the manufacturer indicated it would not pursue the matter if the chemical was suspended. Growers also contacted EPA to express concerns about cancellation of oxydemeton-methyl (Schnaubelt L, Office of Pesticide Programs, EPA, personal communication).

As of September 1994, EPA has elected to enter negotiations with the manufacturer, seeking commitments for risk reduction

**Table 4.** Regulatory status for high priority pesticide active ingredients

Pesticide	Acute toxicity category <sup>a</sup>	Acute dose <sup>b</sup>	Chronic dose <sup>b</sup>	Cancer risk <sup>b</sup>	RR category	SR	Reason for SR	Worker protection SR	Length of SR (years)	Restricted use	Reason for restricted use
Alachlor	II	—	—	X	A	Yes	Cancer	Restricted use, closed mixing, loading	3	Yes	Cancer risks
Aldicarb	I	X	—	—	A	Pending	Acute toxicity	No action	10+	Yes	Accident history
Amitraz	III	—	X	X	A	Yes	Cancer	No	2	Yes	Cancer risks, dietary
Atrazine	III	—	—	X	A	Pending	Cancer; worker risks	No action	5+	Yes	Worker exposures, groundwater
Azinphos-methyl	I	X	X	—	A	No	—	—	—	No	—
Benomyl	IV	—	—	X	A	Yes	Chronic effects; mutagen	Dust masks	5	No	—
Bifenthrin <sup>c</sup>	II	—	—	X	na	No	—	—	—	Yes	Nontarget species
Bromoxynil	II	X	—	—	B	No	—	—	—	No	—
Captafol	IV	—	X	X	na	Yes; manufacturer canceled	Acute, chronic, cancer	na	2	na	na
Captan	IV	—	—	X	A	Yes	Cancer	No	9	No	—
Chlorothalonil	I,II	—	X	X	A	No	—	—	—	No	—
Cyanazine	II,III	X	—	—	A	Yes	Chronic effects	Warnings and protective equipment	3	Yes	Chronic effects
Cyhexatin	III	X	X	—	na	Yes; manufacturer canceled	Chronic effects	na	<1	na	na
Daminozide	III	—	—	X	A	Yes	Cancer	No action	8	No	—
Dichlorvos (DDVP)	I	—	X	X	A	Pending	Cancer, chronic effects	No action	10+	No	—
Diquat dibromide	II	—	X	—	A	No	—	—	—	No	—
Ethoprop <sup>d</sup>	I	—	X	—	A	No	—	—	—	Yes (2)	Acute toxicity
Flucythrinate <sup>e</sup>	I	X	X	—	B	No	—	—	—	Yes	Nontarget species
Folpet	II	—	X	X	A	No	—	—	—	No	—
Mancozeb	IV	—	X	X	A	No	—	—	—	No	—
Molinate	II,IV	—	X	—	B	No	—	—	—	No	—
Monocrotophos	I	—	X	—	na	No; manufacturer canceled	—	—	—	Yes	Nontarget species
Oxydemeton-methyl	II	X	X	—	A	Pending	Chronic effects	No action	7+	Yes	Chronic effects
Phosmet	II	X	X	—	A	No	—	—	—	No	—

Abbreviations: RR, reregistration; SR, special review; na, not applicable.

<sup>a</sup>The acute toxicity categories for the pesticide are as follows: I, LD<sub>50</sub> ≤ 50 mg/kg; II, 50 mg/kg < LD<sub>50</sub> ≤ 500 mg/kg; III, 500 mg/kg < LD<sub>50</sub> ≤ 5000 mg/kg; IV, LD<sub>50</sub> > 5000 mg/kg.

<sup>b</sup>X in a column indicates that the pesticide was selected as a high priority for that effect.

<sup>c</sup>Bifenthrin is restricted for emulsifiable concentrates.

<sup>d</sup>Ethoprop is restricted for some products and some uses.

<sup>e</sup>The registrant for flucythrinate did not pursue registration, and the product has been canceled.

measures (such as incentives for use of closed mixing and loading systems, and restrictions in certain weather conditions) instead of pursuing suspension (Schnaubelt L, Office of Pesticide Programs, EPA, personal communication). If EPA decides to extend deadlines for studies required under reregistration and does not suspend the pesticide, the special review for male reproductive effects would continue, and a position document laying out risks and benefits would be expected in the next year (Poli P, Office of Pesticide Programs, EPA, personal communication).

## Discussion

Data presented here demonstrate the potential for adverse health outcomes from pesticide exposures faced by agricultural workers, with approximately 50% of the pesticides classified as high priority. The strength of this analysis is that dose estimates are based on actual field measurements rather than estimated exposures.

Although the data are the best available, the study has several caveats. The pesticides with available exposure assessments are not a random sample but those identified by the State of California as having the highest potential for adverse health effects. These pesticides would be expected to represent higher risks than a random selection of pesticides.

The consistency of exposure estimates could be improved. There was a large variability among the studies used for the exposure assessments; some were performed by the manufacturer, some were based on surrogate measures, and some were conducted by the State of California. This could affect the quality and comparability of exposure estimates. However, the individual pesticide exposure assessments present a review of existing literature and are peer reviewed by three groups within Cal/EPA. Only five of the exposure assessments used surrogate measures, often in combination with actual measurements. Furthermore, none of the exposure assessments for the 24 priority pesticides was based solely on surrogate measures.

Another contribution to the variability in the dose estimates is the different characteristics of the route of occupational exposures used in the different studies. For example, exposure is affected by pesticide formulation (e.g., granular versus liquid) and application method (e.g., airplane versus tractor). A single exposure assessment can contain studies using different methods of mixing, loading, and application, and different formulations. However, the studies represent the range of observed exposures. Finally, there are no estimates of the statistical distribution of the exposure estimates. Thus, high or low estimates may

or may not represent extreme cases.

Population risks are not estimated because data on the numbers of workers exposed to each pesticide are not available. Moreover, the comparison of dose to LD<sub>50</sub> or RfD is not a true measure of risk because it does not provide a full description of the dose–response relationship. It might be, for example, that an exposure equal to even a substantial percentage of the LD<sub>50</sub> is harmless because the exposure is below a threshold. It would be better to use dose–response data to obtain risk estimates. This would require the reporting of a dose–response curve during the registration or reregistration process.

Although the comparisons of dose to toxicological indices cannot be used as the basis for risk assessment, they can be used to compare the potential for adverse health effects from different pesticides. They can also be used to identify exposures likely to be harmful, as exposures close to the LD<sub>50</sub> are almost certainly harmful and any exposure exceeding the RfD is likely to cause some chronic toxicity in some of the individuals exposed. In this study about half of the lifetime daily dose estimates reported are two to three orders of magnitude above the corresponding RfD.

Finally, basic data necessary for even this limited number of pesticides are not always available. Both toxicological and exposure data for chronic and cancer effects were missing. The LD<sub>50</sub> values were available for all pesticides, RfDs for 39 (95%) were available, and cancer potencies for 25 pesticides (61%) have been estimated. Exposure information was not complete for all job categories. For mixers, loaders, and applicators, estimated lifetime absorbed daily doses for 13 pesticides had not been determined; 23 had not been determined for harvesters, and 31 had not been determined for flaggers. Thus, some pesticides may pose chronic or cancer risks that are not identified.

Exposure information was not complete for all job categories. For example, there were no exposure estimates for harvesters exposed to aldicarb, bromoxynil, daminozide, or dichlorvos. Thus, the potential for even acute health effects from exposure to these pesticides for harvesters could not be determined.

Implementing simple protective measures produced large reductions in exposures to workers. The reduction in exposure associated with the use of protective clothing is consistent with other studies (86). Simple measures, such as glove use, reduced the exposure by an order of magnitude. These differences are based only on glove use and not glove type (though several kinds of gloves were used in these studies, which can affect the exposure esti-

mates). The hands are not necessarily the most important exposure sites. Significant exposure can occur through garment openings and underneath shirt-weight fabrics (87,88). However, using less permeable fabrics can result in thermal discomfort (86). A major disadvantage of using coveralls and less permeable fabrics is that it places the burden of risk reduction on the workers.

We found similar reductions in exposure when using technology-based protective measures compared to personal protective equipment. This result is similar to that reported by Rutz and Krieger (87,88) in a review of the exposure studies prepared for the State of California, which compared the exposures from different formulations, handling systems, and application methods. A major advantage of technology-based protective measures is they reduce the burden on workers.

The regulatory system administered by EPA does not appear to be addressing issues identified in this study. The registration and reregistration process relies on case-by-case review of pesticides but is so slow that it has produced few results. None of the pesticides identified as priorities in this study has been found to meet current standards for review (though four have been canceled). Pesticides have remained in use for many years while reviews are pending. Given that the prognosis for completion of the reregistration process is poor, other policy approaches are needed to reduce risks.

The special review process might provide a means to address occupational risks. Several of the priority pesticides, particularly those with a higher than *de minimis* risk of cancer, have gone through special review. However, the reviews were unlikely to result in increased protection for workers. Only three of the nine pesticides subjected to special review because of concerns about cancer resulted in additional protective provisions. For chronic effects, few reviews have been initiated and completed. Only two priority pesticides for chronic effects have undergone special review for chronic effects (two special reviews are ongoing.) There is no evidence this process provides any protection in cases of chronic or acute effects. The duration of the review process is long, averaging 8.5 years. This again suggests that approaches that are not dependent on extensive review of individual pesticides may be an appropriate strategy.

EPA's worker protection regulations would, if implemented, represent an improvement in occupational health policy, as their provisions are not dependent on the pesticide-by-pesticide review processes. However, they have two flaws. Key risk reduction measures are based on acute risks. The proposed personal protec-



tive equipment requirements are generally tied to acute toxicity. This means that significant, preventable exposures to pesticides with chronic or cancer effects may occur without protections. Finally, the regulations are largely implemented through label amendments, which are cumbersome and difficult to monitor.

Case studies suggest that the review of data submitted by manufacturers did not lead to identification of key concerns; important data were generated elsewhere. For example, the aldicarb review focused primarily on groundwater concerns, identified from outside data. For oxydemeton-methyl, data generated by the State of California led to initiation of a special review. The case studies also suggest EPA is using negotiations with manufacturers to implement controls to reduce risk, in light of the long delays and cumbersome processes associated with special review or reregistration.

The use of pesticide labels for adoption and dissemination of regulatory requirements is problematic. Fundamental regulatory requirements are documented only through individual product labels developed and maintained by the manufacturer. There is no computerized or centralized means to obtain information about regulatory requirements, either from a research perspective or a management perspective. Logistical issues appear to constrain the management program.

## Conclusions

The estimated doses of pesticides received by pesticide workers represent significant percentages of standard toxicity measures, especially for chronic endpoints. The potential for chronic illnesses from pesticide exposure is much higher than for acute toxicity for the pesticides examined. The problem is particularly pressing because it affects workers who are often transient and lacking in resources. Although data systems exist in some states for monitoring acute pesticide illnesses, there are no systems for monitoring chronic health effects. Epidemiological studies are needed to assess the health effects from chronic exposures to pesticides.

Current toxicological data on acute and chronic effects are inadequate for computing dose-response curves and risk estimates. EPA should require reporting of dose-response curves for LD<sub>50</sub> values and RfDs so that acute and chronic risks can be determined.

Use of personal protective equipment and technological controls yield reductions in exposure. Because of the limitations on the utility of protective equipment due to potential for heat stress, technological controls may represent a more effective means

to reduce exposures. Closed mixing and pouring systems and closed cabs should be required where pesticides pose health risks to workers. Although risks can be reduced with appropriate clothing and protective measures, even maximum protection may not be enough to protect workers from acute and chronic effects. Because the pesticide-by-pesticide regulatory process is slow and ineffective, emphasis should be placed on development and implementation of worker protection strategies that can be implemented across the board or for large groups of pesticides, based on risks of acute, chronic, and cancer effects.

Finally, it is clear from this analysis that there are large gaps in our knowledge of occupational risks from exposures to pesticides. For now risk assessments are the only method available to evaluate potential adverse health effects from pesticide exposure.

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