Agrichemical and Environmental News

A Monthly Report on Pesticides and Related Environmental Issues

January 2002 • Issue No. 189 • http://aenews.wsu.edu

Necessity Is the Mother of Invention:

EPA Unveils Preliminary CRA on OPs

Dr. Allan S. Felsot, Environmental Toxicologist, WSU

"The problem is that science has not kept pace with policy in this area." So suggested an EPA regulator regarding the fact that water quality standards for industrial effluents may be set below plausible analytical detection limits (9). I was reminded of this statement as I pored over the EPA's hot-off-the-presses ***Preliminary Cumulative Risk Assessment [CRA] of the Organophosphorus Pesticides*** (15). None of the toxicology and risk assessment books lining my shelves discusses how to cumulate exposure and risk from multiple chemicals. But the pace of science was not taken into consideration when policy created a hole that science had to fill. With passage of the Food Quality Protection Act (FQPA) in 1996, Congress mandated EPA to reassess all pesticide residue tolerances mindful of their safety for infants and children. Congress explicitly defined safety as "a reasonable certainty of no harm" that could only be determined if EPA considered the **cumulative** effects from residues with a common mechanism of action and the **aggregated** exposure from all sources (dietary, drinking water, and residential).

EPA moved swiftly in applying existing scientific methodology to determine hazards of the registered organophosphorus (OP) insecticides to infants and children, but new ground had to be broken if exposure was going to be aggregated and cumulated across dietary and non-occupational pathways. Aggregation of exposure seemed quite straightforward and logical. Simultaneously cumulating exposure to multiple OP pesticide residues was more problematic. No one had done it before.

COOPERATIVE EXTENSION
WASHINGTON STATE UNIVERSITY

Cooperating agencies: Washington State University, U.S. Department of Agriculture, and Washington Counties.
Cooperative Extension programs and employment are available to all without discrimination.
Evidence of noncompliance may be reported through your local Cooperative Extension office.

FOR FREE SUBSCRIPTION OR CONTACT INFORMATION, SEE END OF ARTICLE.

Faced with the daunting task of inventing scientific methods to meet the new policy demands, EPA worked diligently to carry out Congress' mandate. Some would say they worked too slowly. In 1999, EPA was sued by the Natural Resources Defense Council (NRDC), who alleged that EPA was not considering cumulative risk and therefore was not meeting the deadlines of the FQPA. During March 2001, the lawsuit was finally settled through a U.S. District Court's issuance of a consent decree. EPA agreed to do what Congress mandated, which it had been doing all along, albeit not quickly enough for everyone. The plaintiffs must have walked away smiling as they pocketed the $40,000 that the Court awarded them for their troubles.

The Evolution of Cumulative Risk Assessment

In its infinite wisdom about toxicological matters, Congress was following the recommendations of the National Research Council (NRC) 1993 report, ***Pesticides in the Diets of Infants and Children*** (4) when they passed FQPA. But attempts to cumulate exposure to multiple OP insecticides predated the NRC's report. The lawyers at the NRDC had commissioned the 1989 report, ***Intolerable Risk***, the progenitor of all the hype about Alar (5). Buried and unnoticed within that report was a seminal section on OP insecticides. That section claimed that children were overexposed to OP insecticide residues because they tended to eat an extraordinary amount of fresh fruits, vegetables, and juices in comparison to adults.

Intolerable Risk was fundamentally flawed in its analysis (not to mention overshadowed by the brouhaha over Alar), but the ideas for how to cumulate exposure to multiple OP residues seemed to have influenced the NRC. NRC, however, moved cumulative exposure assessment two steps forward by considering the probability of eating more than one OP residue at a time and by also considering the possibility of exposure from drinking water.

Just prior to the release of NRC's report, Environmental Working Group (EWG) emerged as the new protector of the food supply from pesticide residues. The group made a name for themselves with exposés showing the co-occurrence of multiple pesticide residues in foods that children ate (18). After passage of the FQPA, EWG bested all other advocacy groups with its 1998 publication of ***Overexposed: Organophosphorus Pesticides in Children's Food*** (19). Hailed as groundbreaking by EWG's fans and friends, the report was essentially a rip-off of what the NRC had already done. But there was a big difference. Whereas the NRC was trying to show how a cumulative exposure assessment should ideally be done, EWG used their analysis to make claims such as one bite of an apple could lead to OP insecticide exposure above safe levels. The scientific community concluded that the EWG report, like the NRDC's earlier attempt, was flawed (1, 20).

To Cumulate or Not to Cumulate: That Is the Question

The FQPA explicitly states that exposure to pesticide residues with a common mechanism of toxicity must be cumulated. The common mechanism of toxicity, known by toxicologists as the mode of action, pertains to two or more pesticide chemicals or other substances that cause a

common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (12). Thus, how a pesticide causes toxicity on the cellular level through interaction with biochemical targets like enzymes or receptors must be known before deciding that chemicals have common modes of action. All OP insecticides inhibit acetylcholinesterase enzyme, the proper functioning of which is necessary for modulation of nerve signal transmission in the central (brain and spinal cord) and peripheral (nerve-muscle interface) nervous system. If you think this seems like sufficient similarity to pronounce this group of pesticides as having a common mode of action, you would be in good company. An independent panel of seventeen scientists determined that, indeed, all OPs have a common mode of action. (3).

Many of the other classes of pesticides, especially among the herbicides and fungicides, cause adverse effects only at comparatively high doses by nonspecific mechanisms that result in systemic toxicity after prolonged exposure. Thus, it is unlikely they can be concluded to have common mechanisms of toxicity. Nevertheless, EPA has already set its sights on several common-mechanism groups, including carbamate insecticides (e.g., carbaryl, aldicarb, methomyl) and triazine herbicides (atrazine, simazine).

How to Cumulate

Prior to the December 2001 release of its preliminary CRA for OP pesticides, EPA issued for comment a guidance document that laid out the fundamental processes for conducting a CRA (13). This document included a cumulative dietary exposure assessment of three “anonymous” OP insecticides to illustrate CRA principles. By November 2000, EPA released a CRA case study of twenty-four OP pesticides, each identified anonymously by letter codes (14). After consideration of feedback from the public, including advocacy groups like Consumers Union, and its own Scientific Advisory Panel (SAP), EPA released a revised guidance document (16).

Assuming that a determination of a common mechanism of toxicity already has been made for a group of pesticides, a CRA is developed by following four general steps:

- Determine **realistic exposure scenarios** leading to co-occurrence of pesticide residues.
- **Combine residues** from multiple pesticides into a single dose for each exposure scenario.
- Determine **magnitude of exposure**.
- Compare magnitude of exposure to a predetermined benchmark of toxicity (**risk characterization**).

In addition to requiring that multiple pesticides with common toxicity mechanisms be cumulated from any one pathway of exposure, CRA also requires aggregation of all non-occupational (i.e., residential) exposures with dietary and drinking water exposure. Indeed, EPA recommends that prior to a CRA, single chemicals go through an aggregate risk assessment. EPA recently also released its revised guidelines for conducting aggregate exposure and risk assessment (17).

Based on years of monitoring food residues and observing U.S. marketing practices, EPA assumes the food supply contains a constant incidence of pesticide residues throughout the

year. Residues in drinking water and at residences, however, are likely to be seasonal. Indeed, as illustrated in Figure 1, a distribution of possible exposures exists for each day of the year, and all must be summed on a daily basis to yield a total exposure per day. Although OP insecticides may have both agricultural and urban uses, the likelihood of co-occurring residues (and thus exposure) is far less than 100%. Undoubtedly it would be highly precautionary to assume a constant exposure every day from every source, but EPA is rightly moving to greater reality in risk assessment.

Realistic Exposure Scenarios

Dietary Exposure

The source of residue data for the dietary exposure scenario mostly came from the U.S. Department of Agriculture (USDA) Pesticide Data Program (PDP) studies conducted during 1994-2000 (7). These data are supplemented for meats using residue figures from the Food and Drug Administration (FDA) Total Diet Study program (8). For foods that are processed or are a combination of several commodities (e.g., pizza is wheat, tomatoes, and cheese), processing and translation factors are used to adjust the residues to reflect the foods as eaten.

The potentially exposed population is taken from the USDA's CSFII (Continuing Survey of Food Intake by Individuals) database for the years 1994-1998. The database contains individual consumption records for over 20,000 people recorded on a two-day period. The database also contains records for over 5000 children under the age of nine years old. On the basis of the CSFII, EPA divided exposed populations into the following age groups: 1-2, 3-5, 20-49, and >50 years old.

A realistic CRA must account for the likelihood that any one food will have more than one OP residue. For example, apples and apple juice are consumed in proportionally large amounts by kids, and they also contribute significantly to dietary OP insecticide exposure compared to other foods. The USDA PDP database shows that over 36% of apple samples and 28% of apple juice samples had two or more pesticide residues of some kind. However, only 22% of apples and 2% of juice samples had two or more OP residues (Figures 2 and 3). Thus, the likelihood of a child being exposed to apple products containing two or more pesticides with a common mode of action on any one day is quite small and even further diminished by the fact that 56% and 79% of apple and apple juice samples, respectively, contained no detectable OPs (Figures 2 and 3).

Drinking Water Exposure

Much less data are available about residues in water than in food. When EPA assesses risk for single chemicals, it often uses computer simulations of pesticide behavior in soil and water to estimate high-end residues in drinking water. However, concentrations are often unrealistically high when compared to actual monitoring data in the USGS National Water Quality Assessment

Project (2). When cumulating, this kind of error can multiply, resulting in a gross overestimation of exposure.

The objective of CRA is to examine exposure to two or more OP residues within a restricted period of time. Unfortunately, existing water monitoring data does not sufficiently account for daily fluctuations in residues nor does it necessarily include all OPs used in an area over multiple years. Because data for a CRA is needed on a daily time step, EPA uses computer simulations to estimate the residue concentrations. The pesticide behavior model PRZM (Pesticide Root Zone Model) is used to estimate runoff to surface water and leaching to groundwater. The simulation model EXAMS (Exposure Analysis Modeling System) is used to predict behavior of residues in surface water.

To improve the accuracy of modeling, EPA has refined its analyses to consider regional trends in pesticide usage based on the twelve Farm Resource Regions defined by the USDA. These regions depict common geographical specializations in farm commodities. The pesticide behavior simulation models can account for everything from application and cropping practices to weather to physicochemical properties of the pesticide. EPA considers typical application rates (available from the USDA National Agricultural Statistics Service) and percent of crop acres treated rather than maximum use rates and assumptions that all registered crops are treated.

The exposure scenario chooses the most vulnerable surface and ground water resource in each of the twelve regions and uses its water as the drinking water source. For example, the Pacific Northwest is called Region 12, and its most vulnerable area for surface water contamination is the Willamette Valley. Thus, that location became the de facto water resource for the entire region. PRZM-EXAMS then models each OP pesticide crop combination for input residues. Residues in water are estimated on a daily basis but they are compared to residues from actual monitoring data to ensure a realistic exposure scenario.

Residential Exposure

Residential exposure has been another black hole in exposure assessment. Very little monitoring takes place in realistic residential settings. EPA has developed standard operating procedures for conducting residential exposure assessments (10) and applies these principles to CRA. As with water, EPA considered regional patterns in pesticide use based on the twelve Farm Resource Regions. In the absence of direct monitoring data, EPA estimates exposure from homeowner application and exposure to “bystanders” who may come in contact with a treated area either inside or outside of the home.

One source of information for residential exposure is a compendium of occupational exposure scenarios known as the Pesticide Handler Exposure Database (PHED). This database provides information about unit exposures to pesticides for each pound or gallon applied (expressed as milligrams of pesticide per pound or gallon). Another source of information is the Exposure Factors Handbook (11). The handbook is a database with distributions for a myriad of different parameters needed to calculate exposure given an estimated residue in the residential

environment. For example, the handbook provides for each age group percentile breathing rates, body weights, and surface areas of body parts. If a person is playing outside on a lawn, the handbook gives information about the time likely to be spent in an activity for different ages.

Ideally, residential estimation procedures should also account for very unique exposure scenarios such as living in a community with area-wide mosquito control, spending time on golf courses, or having a pet on which flea control products are used. These practices would occur regionally as well as seasonally depending on the incidence of the pests. For the preliminary CRA, however, EPA did not consider exposure from flea control, but the agency indicated that a preliminary study of exposures from the use of pet flea collars was comparatively negligible.

How to Combine Residues

Each exposure scenario will have an associated database of pesticide residues. Because individual OPs have different potencies (i.e., toxicities), they cannot be simply added together. For example, methamidophos (Monitor) has an acute oral LD50 of 13 mg/kg, but malathion's LD50 is 5700 mg/kg. (LD50 refers to the median lethal dose to 50% of test animals, extrapolated to account for human size.) If each of these two pesticides left an equal residue of 1 ppm on food, it would present a different likelihood of hazard. Thus, EPA had to develop a method to normalize the magnitude of each OP residue to the same potency scale.

EPA solved this problem by mathematically constructing a dose-response curve for brain acetylcholinesterase inhibition in female rats following at least twenty-one days of oral dosing with increasing amounts of each OP (expressed as mg/kg). All of this information was available in the manufacturers' data packages submitted to EPA for consideration of registration. The data were fit to an exponential model that allowed estimation of a benchmark dose causing no more than a 10% difference in acetylcholinesterase activity from the non-dosed group of rats. This dose, called the BMD10, represents the Point of Departure (PoD) on the dose response curve because the change in response (i.e., acetylcholinesterase inhibition) can be definitely tied to an exposure dose. Effects may occur below the PoDs but have not been directly measured and their magnitude has a higher degree of uncertainty.

After deriving the BMD10 doses, the next step was to express the potency for acetylcholinesterase inhibition by each of the OPs relative to one of the OPs known as the index chemical. Methamidophos was chosen as the index chemical because of the completeness of its toxicity database. Division of the BMD10 for the index chemical by the BMD10 for any one of the OPs yielded a ratio called the Relative Potency Factor (RPF, formerly known as a Toxic Equivalency Factor). For example, the BMD10 for azinphos-methyl (AZM) is is 0.90 mg/kg/day, and the BMD10 for methamidophos (METH) is 0.08. Thus, the RPF associated with AZM is 0.08/0.90 or 0.09 (Table 1).

To change all residues into methamidophos equivalent residues (i.e., index equivalent residues), the residue concentration for each OP in a matrix (e.g., food, water, home lawn) was multiplied by the RPF. Using the example above, each AZM residue value in the USDA PDP

database would be multiplied by 0.09, effectively changing the residues into methamidophos equivalents but now having a magnitude nearly one-tenth of the actual AZM concentration (Table 1). The RPFs in relation to the LD50s and the corresponding transformation is illustrated in Table 1 for the tolerances of five compounds registered on apples.

Dose-response curves for dermal and inhalation exposures that are relevant for assessing residential exposure are not as well developed as those for oral exposures. Thus, the EPA examined the dose-response database to yield a concentration equivalent level (CEL), defined as the lowest dose giving a maximum of 15% inhibition of brain acetylcholinesterase relative to the control (non-dosed) animals. The RPFs for residues subject to inhalational or dermal exposure were calculated similarly as for the oral BMD10s, again using methamidophos as the index chemical.

Magnitude of Exposure

Once all of the residues regardless of exposure pathway were changed to equivalents of the index chemical, then all co-occurring equivalents were summed together to yield one equivalent residue. An example of the basic calculation is shown in Table 1 for five OP insecticides that have tolerances on apples. All chemicals as methamidophos equivalents are added together when they co-occur to yield the cumulative index equivalent residue.

EPA calculated the exposure from any pathway by multiplying the cumulative index equivalent residue by the amount of food eaten (weight of food and volume of water consumed) or the degree of residential contact (e.g., surface area of lawn or carpet contacted or volume of inhaled air). The calculations are actually probabilistic because they use the entire distribution of residue and consumption or contact data. EPA uses a proprietary exposure model called DEEM (Dietary Exposure Evaluation Model) to reflect the probability of eating food containing one or more pesticide residues. The calculations start with the first person in the CSFII database and multiply the amount of each food consumed by a randomly selected cumulative index equivalent residue associated with the specific food item. For each consumption record, the process of randomly selecting an index equivalent residue and multiplying is repeated many times to obtain a distribution of index equivalent exposures.

Although food residues and thus exposures are comparatively homogeneous from day to day, drinking water and residential exposures can vary widely depending on time of year and weather. Thus, cumulative index exposures are determined on a daily time step. Furthermore, by grouping likely drinking water and residential exposures according to the twelve Farm Resource Regions, peak seasonal use of products could be easily accommodated based on regional weather, cropping, and pest occurrence patterns. EPA was able to eliminate unlikely combinations of OPs from the calculations, thereby conserving computer resources. To handle the daily computations, EPA adopted the proprietary model CALENDEX to integrate all exposure scenarios across time.

Risk Characterization: Exposure vs. Benchmark Dose

All of the exposure information was assembled and organized by percentiles of exposure for each pathway (see Table 2 for an example of dietary exposure). For example, the 50th percentile represents a cumulative OP exposure that is 50% greater (or lower) than the rest of the exposures in the population. For acute dietary risk assessments of single chemicals, EPA had been examining exposure at the 99.9th percentile. At this percentile, only 0.1% of the population had exposures greater than the calculated value.

Bear in mind that a computer simulation generates all of the exposure data by randomly and repeatedly selecting individual pesticide residues and consumption values from a large database. Thus, the exposures are theoretical for a population rather than an individual and are prone to greater error as the percentile increases. The only way to check whether exposure at the higher percentiles is real is to conduct actual studies with humans. Such a reality check was conducted for chlorpyrifos individually in an aggregate risk assessment of chlorpyrifos users (6). Modeled exposures at the 99th percentile predicted well the results observed in a study that biomonitored approximately 1000 individuals for urinary metabolites of chlorpyrifos.

For the risk characterization of individual chemicals, EPA has been comparing the estimated dietary and drinking water exposures with the Reference Dose (RfD). The RfD benchmark is derived by applying a safety factor of 100 to the acute or chronic oral No Observable Adverse Effect Level (NOAEL). If children are determined to be extraordinarily sensitive to a pesticide, an extra threefold to tenfold safety factor is applied to reduce the RfD to the Population Adjusted Dose (PAD). For dietary exposure, EPA would characterize risk as acceptable (i.e., a reasonable certainty of no harm) if exposure was less than 100% of the RfD or the PAD.

EPA characterizes risks for individual chemicals in the residential setting by examining the ratio between the dermal or inhalational NOAEL and the estimated exposure. The ratio is called the margin of exposure (MOE) and EPA expresses no concern when its magnitude is 100 or greater (300 or 1000 where children's sensitivity is an issue.)

For the preliminary CRA, EPA calculated MOEs on a daily basis for food, drinking water, and residential cumulative exposures in each of the twelve Farming Resource Regions. Instead of using the oral NOAEL as a basis of comparison, EPA used the methamidophos PoD (i.e., the BMD10s) specific to each route of exposure. They also calculated the aggregate cumulative exposure for the entire U.S. population. The latter information was presented as a three-dimensional graph for the percentile of each day's exposure and the corresponding MOE (Figure 4).

Pertinently, EPA chose not to comment on the significance of the magnitude of the MOEs nor on the appropriate percentile of exposure at which to calculate the MOE. It seems that CRA is just too new of a tool and characterizations made for individual chemicals may not be properly applicable to cumulative assessments based on a common mode of toxicity. For example, EPA has made no decision as to whether extra FQPA safety factors should be considered in

determining the significance of the MOE because the toxicological basis for grouping chemicals by a common mechanism may be entirely different than the basis for determining that children are extraordinarily sensitive.

Despite EPA's lack of comment about what the CRA means in terms of OP insecticide risk, they did describe the pathways of exposure that contributed most to the calculated MOEs. First, drinking water contributed very little to the cumulative exposure. Drinking water exposures were at least tenfold lower than exposures from food. Naturally, if a specific food contributed disproportionately to residues because of its high incidence of occurrence of a single OP (for example, azinphos-methyl on apples), than food exposure would tend to give a low MOE when all residues are cumulated. In general, however, adults had MOEs greater than 100 at the 99.9th percentile, but the children's MOE was about 50 (Table 2).

Most useful was the conclusion that residential exposure, not drinking water or food, accounted for the lion's share of exposure and thus tended to significantly push up the MOEs. Inhalation of the OP insecticide DDVP (Vapona) from hanging home-use anti-pest strips was responsible for the greatest residential exposures along with indoor crack and crevice treatments. Among children, the age-characteristic behavior of putting the hands in the mouth was the overwhelming factor driving the magnitude of exposure.

Stay Tuned for Details on the Storm

Frankly, I found the preliminary CRA to be a well crafted, state-of-the-art invention that has made a giant leap in science policy. To me, it seemed that EPA bent over backwards to make the exposure scenarios as realistic as possible. OPs like chlorpyrifos and diazinon with canceled or soon-to-be withdrawn residential uses were not considered in the CRA, forestalling an unrealistic assessment of exposure. The United States was broken into regions that more accurately portrayed cropping and use practices. EPA replaced reliance on assumptions about residues and consumption (or contact) with actual distributions of these parameters. If any pesticide registrant wants even more realism, then I would advise them to put their money where their mouth is. More monitoring and carefully designed experiments, especially with regard to drinking water residues and residential exposures, should help lower the exposure outcomes and thus raise the MOEs even further.

I especially appreciated that EPA refrained from specific conclusions about the meaning of the daily MOEs and from choosing any specific percentile of exposure to examine. In my opinion, they used the preliminary CRA for the best good, namely, deciding what is contributing to the greatest exposure. Such information can be used to craft better risk mitigation strategies.

But I see storm clouds rising. Based on comments submitted after EPA's pilot case study of the twenty-four anonymous OPs (14), I predict the environmental advocacy groups will be all over EPA like fleas on a dog. For the same reasons that I liked EPA's approach to interpreting the CRA, the EAGs will scold EPA for its noncommittal and refusal to incorporate extra safety factors, which they will perceive as lack of action on OPs altogether.

But that's the beauty of democracy, isn't it? Everyone has a say. So, if you want to throw in your two cents, I encourage you to download the preliminary CRA and then submit your comments to EPA by March 8, 2002.

Editors Note: For information about submitting comments, contact EPA staff member Karen Angulo (703-308-8004 or angulo.Karen@epa.gov).

Dr. Allan S. Felsot is a frequent contributor to Agrichemical and Environmental News ***and a member of its editorial board. He can be reached at*** afelsot@tricity.wsu.edu ***or (509) 372-7365.***

References

1. Barraj, L. M., B. Petersen, and J. R. Tomerlin. 1998. Report on cumulative dietary risk assessment of organophosphorus insecticides is flawed. Reg. Toxicol. Pharmacol. 28:67-68.

2. Larson, S. J., R. J. Gilliom, and P. D. Capel. 1999. Pesticides in streams of the United States—Initial Results from the National Water Quality Assessment Program. US Geological Survey Water-Investigations Report 98-4222 (downloaded December 2000 from http://water.wr.usgs.gov/pnsp/)

3. Mileson, B. E., J. E. Chambers, W. L. Chen, W. Detttbarn, M. Ehrich, A. t. Eldefrawi, D. W. Gaylor, K. Hamernik, E. Hodgson, A. G. Karczmar, S. Padilla, C. N. Pope, R. J. Richardson, D. R. Saunders, L. P. Sheets, L. G. Sulatos, and K. B. Wallace. 1998. Common mechanism of toxicity: a case study of organophosphorus pesticides. Toxicological Sciences 41(1):8-20.

4. National Research Council (NRC). 1993. Pesticides in the Diets of Infants and Children, 133 pp. Natl. Acad. Press, Washington, DC.

5. Natural Resources Defense Council (NRDC), 1989. "Intolerable Risk: Pesticides in our Children's Food." New York, 1989.

6. Shurdut, B. A., L. Barraj, and M. Francis. 1998. Aggregate exposures under the Food Quality Protection Act: an approach using chlorpyrifos. Regulatory Toxicology & Pharmacology 28(165-177).

7. U.S. Department of Agriculture Pesticide Data Program Annual Summaries (1994-2000). http://www.ams.usda.gov/science/pdp

8. U.S. Food and Drug Administration. Center for Food Safety and Agpplied Nutrition: "Pesticides, Metals, Chemical Contamiants & Natural Toxins." http://vm.cfsan.fda.gov/~lrd/pestadd.html

9. U.S. Environmental Protection Agency. 1994. Draft of National Guidance for the Permitting, Monitoring, and Enforcement of Water Quality-Based Effluent Limitations Set Below Analytical Detection/Quantitation Levels. March, 22, 1994. Washington, DC.

10. U.S. Environmental Protection Agency. 1997a. Standard Operating Procedures (SOPs) for Residential Exposure Assessments;" draft document. December 19, 1997. Office of Pesticide

Programs, Office of Prevention, Pesticides, and Toxic Substances, U.S. EPA. Washington, D.C. http://www.epa.gov/pesticides/trac/science/trac6a05.pdf

11. U.S. Environmental Protection Agency. 1997b. Exposure Factors Handbook. Volume 1, General Factors; Volume 3, Activity Factors. Office of Research and Development, National Center for Environmental Assessment. U.S. EPA, Washington, D. C. http://www.epa.gov/ncea/exposfac.htm

12. U.S. Environmental Protection Agency (1999a), Guidance for Identifying Pesticide Chemicals and Other Substances That Have A Common Mechanism of Toxicity, Fed. Reg. 64:5796-5799. http://www.epa.gov/fedrgstr/EPA-PEST/1999/February/Day-05/6055.pdf

13. U.S. Environmental Protection Agency. 2000a. Proposed Guidance on Cumulative Risk Assessment of Pesticide Chemicals that Have a Common Mechanism of Toxicity. Public Comment Draft. Office of Pesticide Programs, Office of Prevention, Pesticides, and Toxic Substances. U.S. EPA, Washington, D.C. http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-30/6049.pdf

14. U.S. Environmental Protection Agency. 2000b. Cumulative Risk: a Case Study of the Estimation of Risk from 24 Organophosphate Pesticides. Released November 9, 2000. Office of Pesticide Programs, Health Effects Division (7509C). U.S. EPA, Washington, D.C. http://www.epa.gov/fedrgstr/EPA-PEST/2000/June/Day-30/6049.pdf

15. U.S. Environmental Protection Agency. 2001a. Preliminary Cumulative Risk Assessment of the Organophosphorus Pesticides. Released December 3, 2001. Office of Pesticide Programs, U.S. EPA. Washington, D.C. Downloaded report and appendices December 5, 2001 via http://www.epa.gov/pesticides

16. U.S. Environmental Protection Agency. 2001b. Guidance on Cumulative Risk Assessment of Pesticide Chemicals that Have a Common Mechanism of Toxicity. Office of Pesticide programs, Office of Prevention, Pesticides, and Toxic Substances, U.S. EPA. Washington, D. C. http://www.epa.gov/oppfead1/trac/science/

17. U.S. Environmental Protection Agency. 2001c. General Principles for Performing Aggregate Exposure and Risk Assessments. Final. December 2, 2001. Office of Pesticide Programs, Office of Prevention, Pesticides, and Toxic Substances. U.S. EPA, Washington, D. C. http://www.epa.gov/oppfead1/trac/science/

18. Wiles, R., K. Davies, and S. Elderkin. 1995. A Shopper's Guide to Pesticide in Produce. Environmental Working Group, Washington, D.C. 46 pp.

19. Wiles, R., K. Davies, C. Campbell. ***Overexposed. Organophosphate Insecticides in Children's Food.*** Environmental Working Group (EWG) (1998). 48 pp. Washington, DC. http://www.ewg.org/pesticides

20. Wilkinson, C. F. et al. 2000. Assessing the risks of exposures to multiple chemicals with a common mechanism of toxicity: how to cumulate? Regulatory Toxicology and Pharmacology 31:30-43.

Table 1. The benchmark dose 10% (BMD10) and relative potency factors (RPF) for OP insecticides registered for use on apples.

Insecticide	LD50 (mg/kg)	BMD10 (mg/kg)	RPF	Tolerance Residue (mg/kg)	Index Equivalent Residue (mg/kg)
azinphos-methyl	4.6	0.90	0.09	1.5	0.133
chlorpyrifos	223	0.83	0.10	1.5	0.145
diazinon	1160	3.43	0.023	0.5	0.012
malathion	5700	326.37	0.0002	8	0.002
methamidophos	13	0.08	1.00	0.05	0.050

Table 2. Estimated percentile of per capita days falling below the calculated exposure (mg/kg/day) of two population subgroups and the associated margin of exposure (MOE) (15). The MOE was based on the BMD10 oral dose.

	1-2 year old		20-49 year old	
Percentile	Exposure	MOE	Exposure	MOE
50	0.000005	15,879	0.000001	58,721
90	0.000100	800	0.000033	2,415
95	0.000176	454	0.000062	1,280
99	0.000499	160	0.000193	415
99.9	0.001541	51	0.000627	127

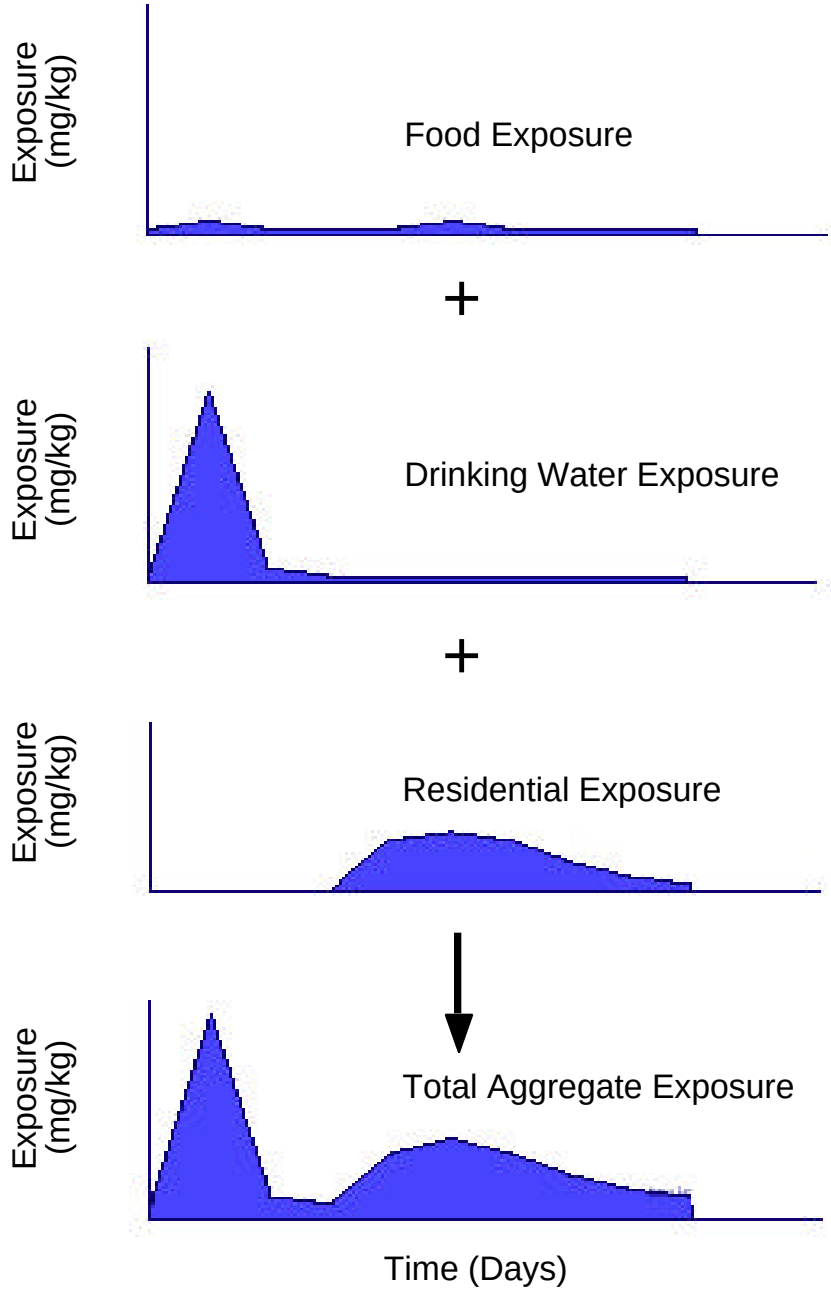

Figure 1. Illustration of aggregate exposure assessment (adapted from reference 17). The distribution of data for food, drinking water, and residential exposure are added together to yield a total aggregate exposure.

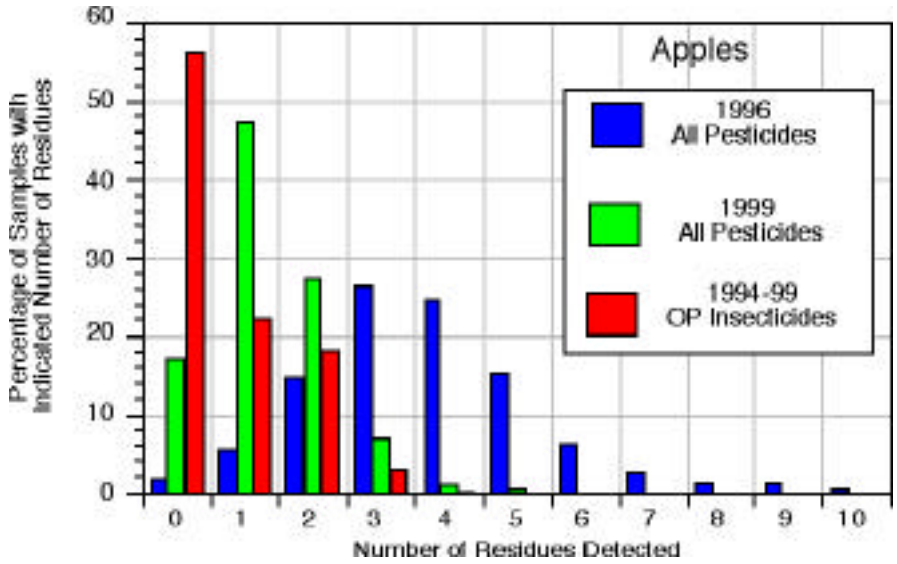

Figure 2. Co-occurrence of pesticide residues in apple samples analyzed in the USDA PDP program.

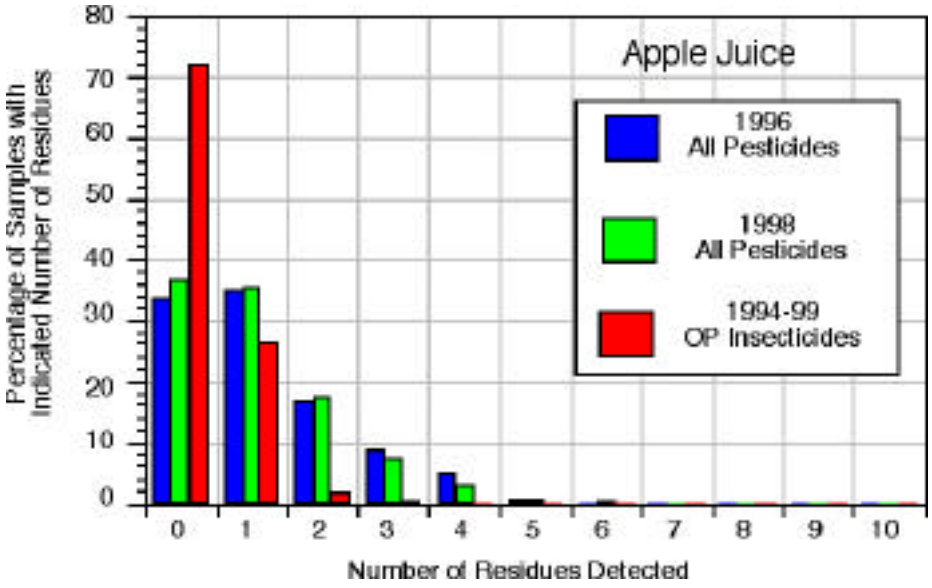

Figure 3. Co-occurrence of pesticide residues in apple juice samples analyzed in the USDA PDP program.

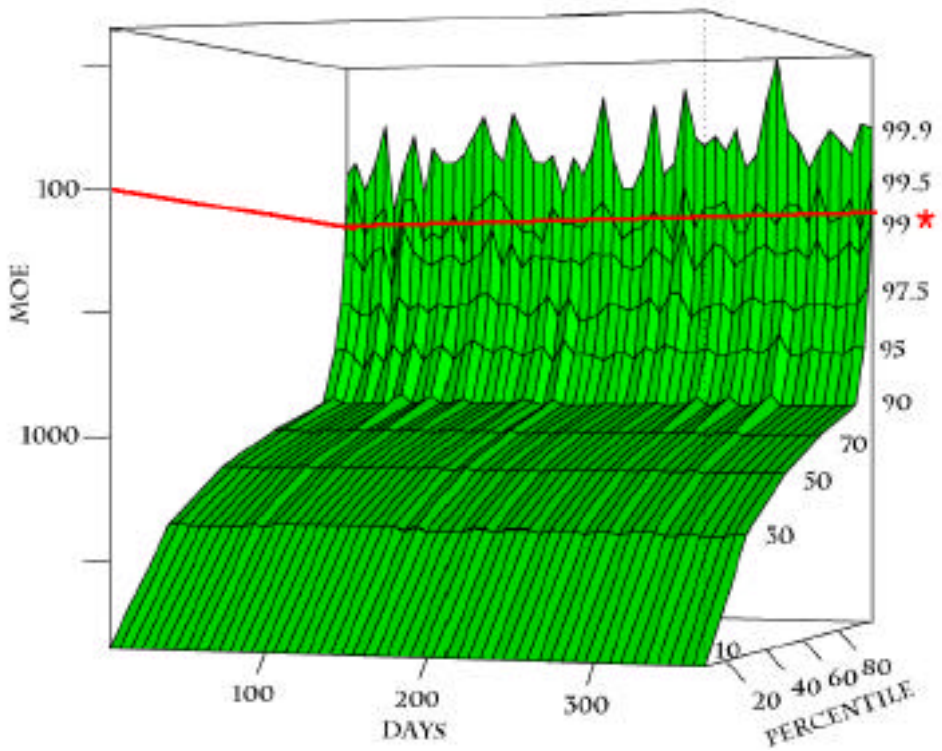

Figure 4. Total cumulative risk from daily exposure to OP insecticides aggregated for food, drinking water, and residential exposure routes (15). The margin of exposure (MOE) represents the difference between the BMD10 for the index OP (methamidophos) and the exposure aggregated for each route. The percentile represents the proportion of the population with exposure on a specific day at or greater than the MOE indicated. For example, on day 365 (the right hand edge of the graph), 99% of the population (red asterisk) has an estimated exposure greater than an MOE of 100 (red line). Thus less than 1% of the population has an MOE less than 100.

FREE SUBSCRIPTION

If you would like to receive monthly e-mail notification when each month's new issue goes on-line, please send an e-mail to majordomo@tricity.wsu.edu. The body of message should read subscribe aenews_dist, and nothing (not even a signature line) should follow the subscribe message.

***AENews* welcomes your comments. Please direct any comments on newsletter content to Catherine Daniels, Managing Editor, (509) 372-7495, fax (509) 372-7491, or cdaniels@tricity.wsu.edu. Comments regarding newsletter format, Web usability, or other general concerns may be addressed to Sally O'Neal Coates, Editor, (509) 372-7378, fax (509) 372-7491, or scoates@tricity.wsu.edu .**