Our Children's Toxic Legacy

How Science and Law Fail to Protect Us from Pesticides

Second Edition

John Wargo

1998

Yale University Press New Haven and London

sample sizes should support efforts to estimate pesticide exposure. This frequency would probably capture significant changes in diets due to variables such as marketing, health advisories, and advances in food-processing technologies.

Third, EPA should pay special attention to the contamination of liquids. Children, especially infants, consume much more liquid per unit of body weight than do adults. This tendency means that children could be exposed in significant amounts to pesticides in drinking water—especially because tap water is normally added to processed liquids such as concentrated fruit juices and infant formula. Families living in rural areas where pesticides and fertilizers have been heavily applied, and where water is derived from shallow wells, should therefore have their water tested for the most commonly used compounds. In addition, institutions that manage community water supplies should be certain that residue tests are employed that can detect compounds historically used within watersheds surrounding the supply: many of the pesticides used in agriculture and allowed to remain as residues on food are not monitored in community drinking water supplies. Sampling designs should also be carefully structured to detect "pulses" of contamination that may follow periods of heavy pesticide application such as preemergent herbicide use during the spring, or when heavy rains follow droughts.[26]

Fourth, the accuracy, efficiency, and effectiveness of pesticide exposure estimates—and of the regulations that are based on them—have been compromised by the fact that authority to manage pesticides has been fractured among EPA, USDA, and FDA. Each agency has used a different food coding system designed for different purposes. USDA has collected data for nutrient analyses; FDA collected residue data to find violations of allowable residue levels; and EPA has used its own coding scheme to estimate food intake and associated pesticide exposures. Promises of improved interagency coordination and improved environmental monitoring following the release of the NAS study *Pesticides in the Diets of Infants and Children* have been largely unkept because budget shortfalls increasingly constrain research efforts. EPA bears responsibility because it has never admitted the scale of monitoring required to know and manage the mixture of pesticides it has allowed to be dispersed into the food and water supplies we all encounter daily.[27]

CHAPTER 10

Averaging Games

Simplification of Exposure and Risk

Since its founding in 1970, EPA has judged the safety of individual pesticides independent from one another. Moreover, EPA has lacked the legal authority to deny registrations or tolerances based on judgments that available substitutes pose lesser risks—a constraint rationalized by an uncertain understanding of the relative toxicity among possible substitutes.[1] The complexity of estimating exposure for even single pesticides further narrowed the agency's attention and resources toward single chemicals. The result has been a highly incremental, segmented form of regulation, and one that has often focused on single crop uses of single pesticides.[2]

The averaging of risk has played an exceptionally important role in the history of EPA's pesticide regulatory behavior. As EPA granted or adjusted pesticide tolerances during its first several decades, it assumed an average level of food intake across the entire population and an average level of food contamination by pesticide residues. The agency also projected that exposure occurred evenly across a seventy-year life span, which led to its average lifetime cancer risk estimates for the entire U.S. population. The analyses became more refined during the mid-1980s as the agency developed the capacity to examine age-related food intake and exposure patterns. But, as explained in chapter 9, even by 1995 the age groupings EPA examined were broadly defined—children ages one to six and ages seven to twelve—and these groupings were not related to shorter and earlier periods of physiological vulnerability such as those described in chapter 8.

By 1992, EPA acknowledged that childhood exposure and risk estimates had never caused tolerances to be adjusted or registrations to be revoked.[3] By neglecting to consider variations in diet and pesticide residues across age groups, EPA had little understanding of whether the thousands of tolerances it oversees afforded protection for children. In fact, the legal standard for tolerance-setting—which permitted them to balance risks against benefits—did not require that a limit guarantee protection.[4]

This chapter explores the effects that averaging methods may have on the ways that risks are characterized. As this discussion reveals, many forms of averaging have been used by the agency, each of which has effectively lowered estimates of risk. Averaging together food consumption and detected

residue statistics trivializes most risks. Further, these averages cast public attention away from minorities bearing significant risks.

An alternative method of exposure and risk estimation that does account for variance in the distribution of risk is presented here, using the widely used fungicide benomyl as an example. This approach considers the distribution of exposure and risk among children in yearly age classes and provides a necessary introduction to the problem of managing pesticide mixtures, which follows in chapter 11.

Benomyl: A Case Study

Benomyl, or Benlate, is a systemic fungicide manufactured by E. I. du Pont Corporation. Since its introduction in 1972, it has become one of the most widely used fungicides within a chemical family known as benzimidazoles. Benomyl is effective in preventing more than 190 different fungal diseases. It acts as a protective surface barrier and penetrates plant tissues to arrest infections. Benomyl is applied as a seed treatment, transplant dip, and foliar spray, and it is registered for use on more than seventy crops in fifty countries, including imported foods such as bananas and pineapples. In the United States, benomyl is registered for use on a wide variety of crops, and nearly seventy-five food and feed tolerances for it exist.

Benomyl captured considerable public attention during the early 1990s because it was one of several compounds that EPA proposed to remove from the market due to its suspected cancer-causing effects. Because the compound concentrates in some foods as they are processed, it is also prohibited from use on these crops by the Delaney clause of FFDCA.[5] Also during this period du Pont was the target of hundreds of lawsuits by farmers and other plant growers who claimed that a reformulation of the fungicide was responsible for widespread plant death and damage. The company has paid more than $500 million in compensation based upon these claims.[6]

EPA based its judgment on benomyl on toxicological evidence that suggests that benomyl is both mutagenic and carcinogenic in laboratory animals. EPA concluded that hepatocellular carcinomas or combined hepatocellular neoplasms occurred in male and female mice at all doses.[7] Tests including a metabolite of benomyl, carbendazim,[8] caused hepatocellular tumors in male mice and hepatocellular adenomas (benign tumors), carcinomas, and combined hepatocellular neoplasms in female mice.[9] The manufacturer contended, however, that increased incidences of liver cancer in mice are confused by a high rate of spontaneous tumor development in both the control group and those exposed. It also points to the absence of a carcinogenic response in two strains of rat and in one strain of mouse, as well as the absence of any indication of a tumor-inducing effect in humans.

Several studies have explored the effects of benomyl on the fetal development of laboratory animals. When fetal rats were treated with benomyl in one study, many craniocerebral anomalies were reported, including hydrocephalus and the growth of cell masses that overgrew and sometimes obliterated subcortical structures of the brain.[10] High doses (125 mg/kg of maternal body weight) produced late fetal death. Other observed systemic malformations included cleft palate and misshapen tails. Finally, benomyl has been linked to an inhibition of the formation of microtubules in the brain that are important to normal early brain development in rats.[11]

There is also evidence that benomyl damages male rats' reproductive organs. Rats exposed over seventy days in another study were claimed to experience a dose-dependent decrease in testicular weight, depressed sperm counts, and lower fertility.[12] By 1984 there was some evidence that these effects may be age-related, because animals treated prior to puberty showed no reproductive organ effects, whereas those treated during puberty experienced at least one of the following: decreased testicular or epididymal weight, decreased epididymal sperm counts, or testicular lesions.[13]

In 1989 carbendazim was found in still another study to have hormonal effects. As exposure to MBC increased, more follicle stimulating hormone (FSH) and pituitary luteinizing hormone (LH) were produced by the body. And following subchronic exposure to benomyl, gonads changed by the contaminant appear to upset hormonal balances by acting on the central nervous system.[14] Reduced fertility may have been caused by testicular swelling; occluded, or blocked, ducts; duct or tubular atrophy; or tissue reduction. These conditions generally appeared to be dose-dependent.[15] In another study, benomyl appeared to cause changes in the chromosomes of somatic cells, and when tested in mice the compound induced chromosome changes in oocytes—immature female reproductive cells.[16]

Estimating Childhood Exposure

Methods of estimating exposure and associated risks have long been confused by the absence of current, high-quality data and by the dispute over appropriate ways of combining food, residue, and toxicity data. Given these limitations, EPA has relied upon computer models that project the magnitude of exposure, its distribution in the human population, and its toxicological significance. The choice of data sets for food intake, residue, chemical use, and toxicity can thus have dramatic effects on exposure and risk estimates. Similarly, the selection of a method for combining and presenting these data may have broad implications for exposure and risk forecasts.

Benomyl provides a good case with which to explore these problems, because dietary exposure may come from as many as seventy-five different

food sources, each of which is permitted by tolerance to contain benomyl residues in the marketplace.[17] The method presented below considers the exposure of children ages one through five to benomyl on numerous foods that they reported eating. Intake values for each child are combined with average residue values for each food to create an exposure estimate for each child. Rather than assigning some average level of exposure to a broadly defined age group, it identifies the probable exposure of each child.

As demonstrated in the previous chapter, children consume more of fewer foods than adults, especially during the first few years of life, and particularly fruits, juices, and some vegetables.[18] For any given estimate of pesticide residue levels, this means that differences in exposure among individuals will be driven exclusively by differences in what is eaten. Yet the problem is not this simple; the risk assessor must choose among the different residue data sets that commonly exist for each pesticide-food combination. In many cases, no residue data exist for important foods such as juices or milk, and the analyst is forced to make many assumptions.

This exposure analysis includes far fewer foods than the total number permitted by law to contain benomyl residues. The reason for this simplified approach is that residue data available from FDA's residue sampling program are often of insufficient quality to estimate exposure.[19] FDA does not test all foods that have tolerances, and when it does test, the number of samples is often far fewer than necessary to estimate national exposure. Benomyl posed an additional problem in that it required its own special residue detection test; it was not picked up by common multi-residue scans.[20] Compounds that require extraordinarily expensive individualized tests are far less likely to be tested by FDA than compounds detectable using less costly multi-residue scans. In defense of FDA, they perceive their mission to be the policing of EPA tolerances in the marketplace, not natural exposure analysis. For this reason, along with budgetary constraints, FDA has not restructured its sampling designs to support the types of exposure analyses suggested in this book.

Those foods chosen for the exposure analyses had FDA residue data of sufficient quality existed and are normally eaten by children. These foods include apples, apple juice, bananas, cherries, grapes, oranges, orange juice, peaches, pears, pineapples, plums, strawberries, and tomatoes.[21]

The Danger of Averages

Exposure to a pesticide residue is normally computed by multiplying the amount of food intake by the expected concentration of the contaminant. For example, to estimate the national average exposure to benomyl on apples, one would simply estimate the average intake of apples (0.45 grams/kilogram of body weight/day) and then calculate the average residue level on those apples (0.16 ppm). These two figures can then be multiplied to produce an average exposure estimate from a single chemical and a single food. This simplified approach is the one used by EPA for the past two decades to estimate average dietary exposure to carcinogens. The product, however, captures none of the variance in either food intake or residue concentration. As demonstrated in chapter 9, for example, one-year-olds may consume on average as much as fifteen to twenty times more apple juice than do adults.

The problem is far more complex than that just described, because we are really interested in estimating exposure to benomyl residues from all potential food sources. In this case, mean intake of each food may be multiplied by mean detected residue levels for each food; the sum of the resulting exposures for each food will give an average exposure to benomyl for all foods. This method, however, still does not capture any of the differences in either the food-intake or residue data.

To account for variance in dietary patterns and levels of contamination, distributions can be summarized by simply ranking all values between lowest and highest. Given any distribution, the ninetieth-percentile value is exceeded by only 10 percent of the sample; a 99 percent percentile value is exceeded by only 1 percent of the sample. Food intake and residue data have been combined in different ways to produce exposure estimates by EPA, depending on the type of toxic effect which is being explored. To estimate exposure to a carcinogen, for example, EPA commonly chose to average food intake values and multiply them by average residue values for each food. The resulting exposure estimates are then summed across foods as just described.

An even more conservative approach would be to combine ninetieth-percentile food-intake levels with ninetieth-percentile residue levels. One would initially suspect this method to produce even higher exposure estimates than those produced by multiplying both mean food intake and mean food residue values, and that the product would significantly exceed normal exposure. This approach might be appropriate if the quality of residue or food intake data has been diminished by sampling problems. For example, confidence in the FDA residue data is diminished both by the small sample sizes of residue tests and by the purpose for the data's collection. If FDA is legally responsible only for determining if a tolerance has been exceeded, it has no incentive to report levels beneath the tolerance. The FDA data sets contain many "non-detections" that therefore demand careful interpretation.[22]

Summary statistics of food intake and residue levels may be combined in different ways to produce exposure estimates. Mean food intake for children between ages one and six are combined with mean and ninetieth-percentile residue values to produce the exposure values presented in figure 10–1. A

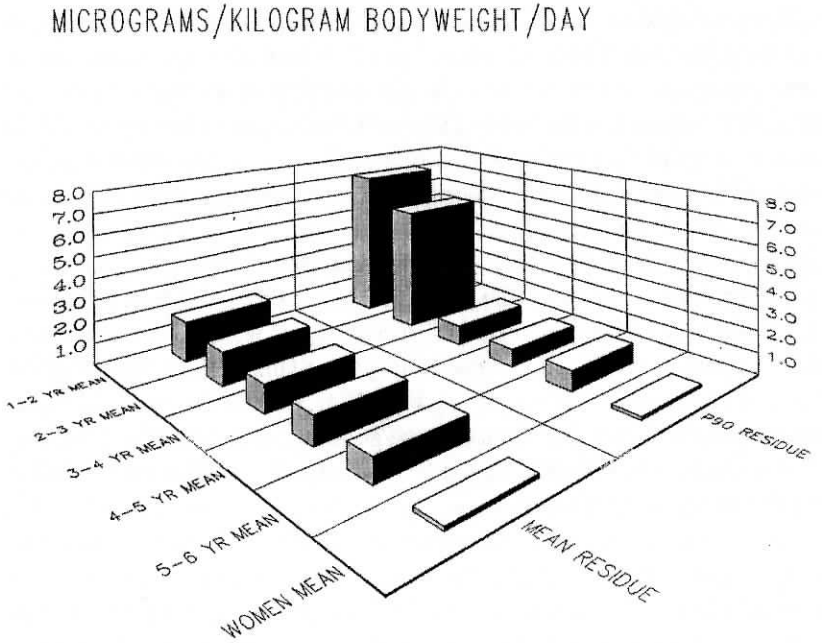

Figure 10–1. Benomyl exposure: the simple case. In this case only mean food intake is combined with mean and ninetieth percentile residue values to produce exposure estimates. Residue values are derived from FDA residue data sets from 1988 and 1989. Food intake data are derived from the USDA CSFII, 1985–86.

modest decline in exposure is seen as children reach age six, whereas women's exposure is significantly less, almost by a factor of ten.

The effect of using ninetieth-percentile food-intake levels to estimate exposure is demonstrated in figure 10–2, which also contains the data presented in figure 10–1. If we assume that the probabilities of eating more than the ninetieth-percentile level for each food considered is a physical impossibility—simply because no one can eat that much food—and that the probability of benomyl contaminating *each* of these foods at the ninetieth-percentile level is very close to zero, these estimates might be thought of as extremely conservative.

Surprisingly, the combination of ninetieth-percentile residue levels with ninetieth-percentile food intake values may produce results, not anticipated by the earlier figures. For some single foods consumed by three-, four-, and five-year-olds, for example, ninetieth-percentile exposure levels are *zero,* lower than the combination of mean residue with mean food intake. This phenomenon occurs in cases where a high proportion of residue testing results are reported as zeros. If more than 90 percent but less than 100 per-

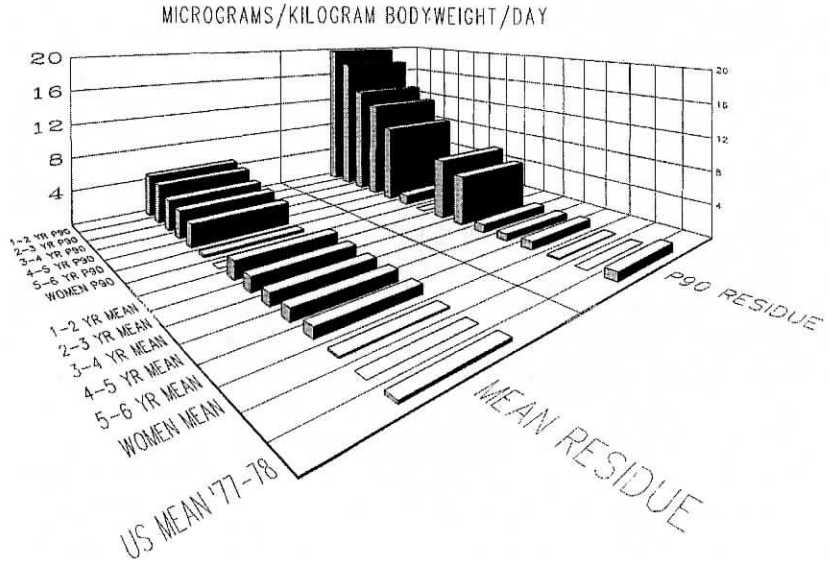

Figure 10–2. Benomyl exposure scenarios, including ninetieth percentile residue levels. These exposure estimates include those contained in figure 10–1. In addition, ninetieth percentile food intake values were used to estimate exposure.

cent of the tests are reported as zeros, then mean residue levels will be higher than ninetieth-percentile residue levels. The same effect may also be common for foods that are rarely consumed. The figures presented above do not capture this possibility, because children consume moderate or large quantities of most of the foods analyzed. Thus the use of summary exposure statistics such as ninetieth-percentile values to represent the upper limit of exposure levels may offer a false sense of security.

Tolerance levels for residues are then used to calculate the exposure allowed by regulation, presented in figure 10–3. Whereas tolerance-level contamination is rarely detected in any residue monitoring surveys, this figure demonstrates that exposures at the legal limits are ten to one hundred times higher than what is predicted using detected FDA residue data. It is important to emphasize at this point that all of the exposure analyses presented so far provide no information concerning the magnitude of risk posed, because they remain divorced from any toxicological data.

A Richer Perspective: Exposure Distributions

An alternative to combining summary residue and food intake statistics is to use detailed data about individuals' diets. This method permits exposure to be estimated for each individual and the expression of age-class exposures

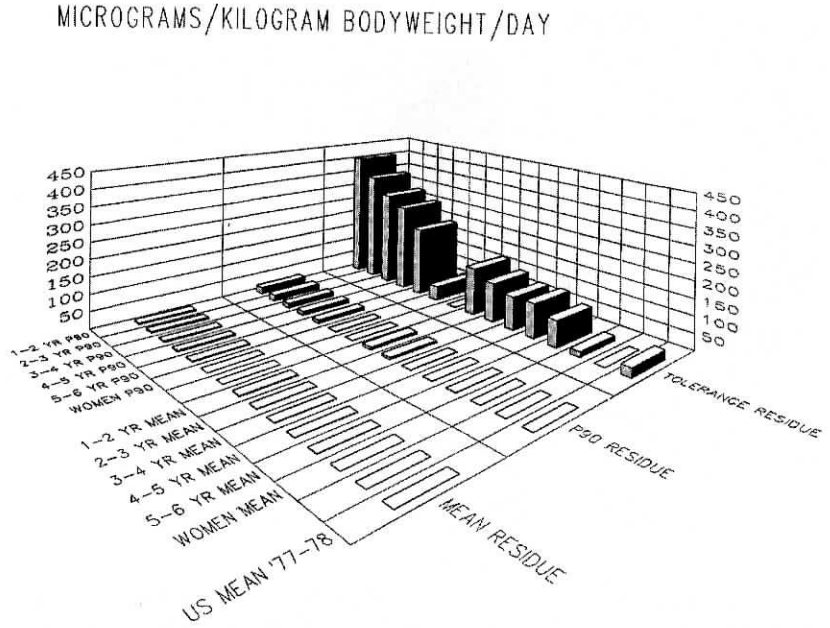

Figure 10–3. Benomyl exposure scenarios if tolerance-level residues are assumed. The exposure estimates of figures 10–1 and 10–2 are dwarfed by the estimates produced if legally allowable, or tolerance-level, residues are assumed. Although the Delaney Paradox study was severely criticized for estimating risk by assuming that residues remained on foods at the tolerance level, it seems reasonable to ask whether tolerances protect children and others from exposures that pose significant health risks.

to be presented as a distribution.[23] I prepared this analysis for each of five age groups (each of which spanned one year). The results were then plotted as the distribution presented in figure 10–4.[24]

This method fully captures the differences in eating habits among people, although it neglects the variance within individuals that occurs.[25] In addition, because this distribution was prepared for a compound that EPA believed poses some cancer risk, residue data were summarized as mean values.[26] Representing exposures in this manner facilitates rapid identification of the sample proportion estimated to fall above any known toxicologically significant dose. The exposure scale may be adjusted by a potency factor and may be time-weighted to estimate the cancer risk accumulated during the year of exposure.[27]

Interpretations So Far

It is clear that summary statistics can provide an incomplete and potentially deceptive representation of pesticide exposure patterns. However, each alternative presented above is valuable for different reasons. The combination of

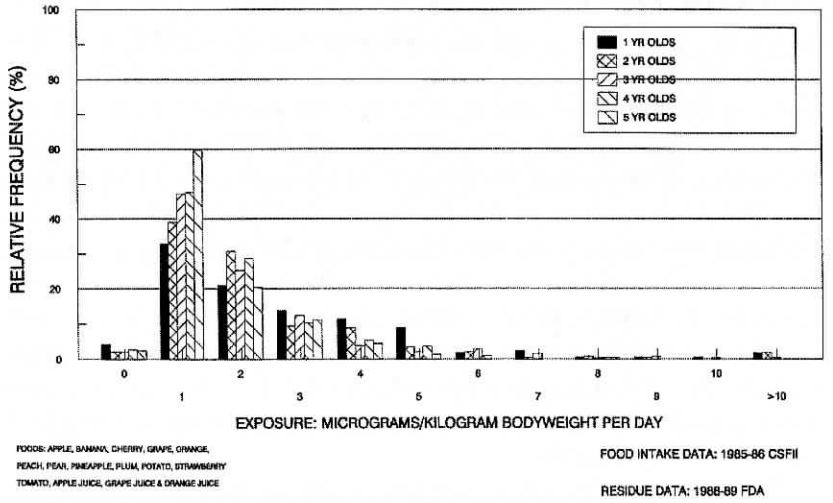

Figure 10–4. Childhood exposure to benomyl: distributional approach. Many more children were estimated to be exposed to benomyl than not. Less than 5 percent of children ages one to five received no benomyl exposure, according to this very conservative estimate.

summary statistics provides a fairly efficient method for detecting rough magnitudes of exposure and risk. One can clearly determine if residues at the tolerance level pose health risks, and depending upon the quality of data, combining food-intake data and pesticide residue information in summary statistics provides a general outline of likely exposure distributions. Yet these statistics can be deceptive; both the food intake and residue distributions tend to be highly skewed, creating a condition in which the ninetieth-percentile is often either less than the mean value or zero.

The population distribution method, by contrast, provides a more complete picture of possible exposures, particularly when the groups studied are delineated by year of age. One can quickly see if thresholds of acceptable exposure have been breached, and exposures can be translated into annualized risk estimates or proportions of the acceptable daily intake. But one should not conclude that the exposure estimates presented in this case are accurate. Use of other residue data sets, including field trial and market-basket data, can yield significantly different results. Also, considerable uncertainty surrounds the estimates of residues in processed foods such as juices, which are consumed in great amounts by small children. The sensitivity of exposure and risk estimates to varying assumptions regarding the magnitude of residues is tested in the following section, where I again rely on the distributional method just described.

Residue "Monkey Business"

Given the problems associated with available pesticide residue data described here and in chapter 4, I have chosen to compare six different scenarios of childhood exposure. In all six I use the same food intake data, but then I explore the effects of incorporating six different residue data sets. These residue data include (1) du Pont field trial results, (2) the results from a du Pont Corporation market-basket survey, (3) FDA compliance and surveillance data for the years 1988 and 1989, (4) National Food Processors' Association (NFPA) data provided by corporate members, (5) data collected in raw food testing by a private residue-testing laboratory, and (6) exposures legally permitted by tolerances in place as of 1993. The sampling designs vary significantly among these types of residue data, as do the sample sizes and analytical methods. Sample sizes and the number of positive detections are compared in table 10–1.

The primary purpose of the comparisons is to analyze the differences in exposure estimates that result from the use of alternative residue data sets. The analyses that follow test the hypothesis that exposure estimates—along with associated risk estimates—are sensitive to the source of residue data. Each of the residue data sets is described briefly below.

Food Industry Residue Levels

The National Food Processors' Association routinely collects data from its member organizations. These data include the sample, chemical, food, detected residue if any, and the limit of detection. The suitability of this information for national exposure and risk assessment, however, is questionable for several important reasons. First, the data were not collected according to any uniform sampling plan; instead, sampling strategies were defined differently by member corporations. Moreover, because the randomness of the survey methods is uncertain, the data's representativeness of residues likely to be found in the nation's food supply remains ambiguous. The only cases of positive benomyl detection used in the analysis were values detected by NFPA in apples and apple juice. It is important to recognize that since this study was completed, NFPA has standardized its testing protocols, providing for more reliable data for the purpose of risk assessment.

Market-Basket Residue Levels

Du Pont conducted a market-basket survey to examine residue levels in the marketplace. The sampling design of a market-basket survey is particularly important because the results can be dramatically affected by regional patterns of chemical use and food distribution. A properly designed market-basket survey is very valuable because it obviates the need to make complex assumptions regarding the effects on residues of food processing, as well as regional variations in pesticide use and food distribution.

Table 10–1. Residue Scenarios: Number of Samples (S) and Number of Positive Detections (D)

	FDA		DP FT		DP MB		NFPA		Private lab	
	S	D	S	D	S	D	S	D	S	D
Apple	134	35	138	122	26	5	67	25	127	65
Apple juice	—	—	—	—	—	—	29	16	—	—
Apricot	—	—	—	—	—	—	6	0	19	5
Banana	72	8	—	—	—	—	4	0	—	—
Bean	5	0	35	29	30	3	19	0	38	10
Blueberry	—	—	—	—	—	—	—	—	14	3
Carrot	—	—	—	—	—	—	—	—	12	1
Celery	—	—	—	—	—	—	—	—	24	4
Cherry	21	5	—	—	—	—	7	0	4	1
Cucumber	—	—	—	—	—	—	6	0	4	1
Grape	27	12	71	65	11	4	—	—	11	5
Nectarine	14	8	18	5	—	—	—	—	39	14
Orange	6	0	18	13	12	12	1	0	6	1
Orange juice	1	0	—	—	—	—	2	0	—	—
Peach	26	13	82	72	15	1	15	0	81	44
Pear	23	1	15	14	24	6	—	—	—	—
Pineapple	25	18	—	—	—	—	1	0	7	4
Plum	21	10	—	—	—	—	—	—	28	18
Raisin	—	—	—	—	—	—	13	0	—	—
Raspberry	14	0	—	—	—	—	2	0	17	6
Rice	—	—	—	—	—	—	6	0	—	—
Squash	4	0	—	—	—	—	4	1	—	—
Strawberry	30	2	—	—	—	—	6	0	16	11
Tomato	20	0	35	23	25	1	—	—	—	—
Watermelon	5	0	—	—	—	—	3	0	—	—
Wheat	—	—	—	—	—	—	12	0	—	—

Key: FDA = Food and Drug Administration; DP FT = Du Pont Field Trial; DP MB = Du Pont Market Basket; NFPA = National Food Processors Association

Among seven foods analyzed, a total of 143 samples were tested; of these, thirty-two (22 percent) had residue levels above the limit of quantitation. Juices were not sampled. This low percentage is similar to that found by the NFPA, but approximately 50 percent lower than the percentage positive found by the more focused sampling design of the private testing laboratory.

FDA Surveillance Residue Levels

Only FDA surveillance sampling results were used in this analysis, and these data were used only if sample sizes exceeded twenty for any individual food. These small sample sizes make any attempt to estimate exposure highly suspect; this problem also often confronts EPA when it attempts to judge pesticide risks. Whereas benomyl is registered for use on more than seventy foods, FDA residue data—pooled for 1988 and 1989—had sample sizes that exceeded twenty for only ten foods listed in table 10–1. Among the twenty-six foods, 448 samples were tested, and 112 of these (25 percent) had residues reported above the detection limit.

These data demonstrate that FDA focused its scarce monitoring resources on fresh rather than processed foods. For example, apple juice was not sampled, and orange juice was sampled only once. This observation is particularly important because these two juices are among the foods most consumed by young children. These findings also raise an important question about the reasonableness of testing only a few samples of single foods—for example, five of beans, six of oranges, and four of squash. Although there may be a rationale for focusing monitoring resources on suspected violators, the usefulness of FDA's surveillance data for developing national estimates of pesticide exposure from food is limited at best.

The disadvantages of these data for estimating exposure to pesticides include (1) extremely limited sample sizes for most foods for which pesticide tolerances have been established, (2) the absence of regional or seasonal stratification in sampling design, (3) the fact that residue concentrations are diminished by FDA's procedure of blending slices from different pieces of food, (4) the realization that detection limits in some cases may have been set only to detect tolerance violations, and (5) the fact that sampling of processed foods is extremely limited compared with raw agricultural commodities—a situation that forces complex assumptions regarding the effect of processing on residues for each food. The primary advantage of FDA data is that it is the only sampling scheme that is applied uniformly across the nation's food supply.

Residue Levels Provided by a Private Laboratory

A private testing laboratory certifies for some grocery manufacturers—and, in turn, grocers and consumers—that marketplace produce is free from detectable levels of certain pesticides. The lab tested 447 samples for benomyl residues (almost identical to FDA's 448 samples for 1988 and 1989). Among these, 193 (43 percent) had residues above the detection limit. By contrast, the NFPA tested 203 samples and found only 42 cases (20.6 percent) where residues exceeded the limit of quantitation. The distinction in findings may have several explanations. First, the private lab focuses its sampling on produce and sources of produce where a compound of concern has been detected. Benomyl's status as a B2 (probable human) carcinogen has caused them to test extensively for the compound. Second, the private lab tested a different but overlapping set of foods than did NFPA. Residues were detected most frequently on apples, peaches, and plums. The highest percentage of residue detections above the limit of quantitation in NFPA sampling was found on apples (37 percent) and apple juice (55 percent). The private lab did not test any apple juice, which raises questions regarding the appropriateness of using any single residue data set for estimating national levels of pesticide exposure.

Residue Levels Detected in Field Trials

Du Pont Corporation submitted a substantial body of residue data in 1989 to EPA to support continued registration of benomyl. These data are extremely important because the application rate and detected residue level for each sample of raw agricultural commodity were carefully recorded and sample sizes for single raw commodities were often large enough to permit statistical analyses. Unfortunately, residue tests were much less frequently conducted for processed foods made from benomyl-treated raw foods; this absence of information has forced complex assumptions to be made regarding residue fate. Another limitation of field trial data is that detected levels are likely to be far higher than those found in market-basket surveys due to uneven use of the compound around the country. Du Pont tested a total of 412 samples. Of these, 343 (83 percent) contained residues above the detection limit. This discovery suggests that if treated crops are tested, residues will likely be detectable. Moreover, du Pont's analyses were conducted under the assumption that only ten foods are consumed.[28]

Residues at Tolerance Levels

Although benomyl is allowed by law to be used on more than seventy foods, exposure analyses were conducted assuming tolerance level residues on only fifteen foods in order to permit reasonable comparison with the residue data sets described above. Tolerance-level residues permit exposures roughly one to two orders of magnitude above those residue levels detected using these other residue data sources.[29]

Interpretations

Exposure estimates for children based upon the six different residue scenarios are presented in figure 10–5.[30] Variation in the shape of the distributions demonstrates the importance of using judgment when selecting residue data to estimate exposure. Several conclusions may be drawn from the analyses. First, the level of childhood exposure varies widely depending upon the residue data set chosen for analysis. In this case, field trial data yields the highest exposure estimates, followed by data from private testing labs, FDA data, market-basket data, and finally, NFPA data. The comparison across exposure estimates is made difficult by the fact that there is some variation in the foods that were included in the scenarios (as determined by the availability of adequate sample sizes). As mentioned earlier, this problem routinely confronts EPA as well.

Second, the interpretation of "nondetections" is most important when they comprise the majority of any residue data set, as they do in the case of the FDA and NFPA data. The influence of nondetection interpretations also depends on the level of consumption of the food in question, as well as on the potency of the chemical of concern.[31] Third, assumptions regarding food-processing effects have a dramatic influence on exposure estimates for children—especially when one considers that children consume large amounts of liquids such as apple juice, orange juice, grape juice, and milk. EPA's requests for data on residues in processed foods should thus target foods consumed most by children, including processed juices, which are increasingly supplied by corporations in tropical nations.

Fourth, EPA's use of "percent acreage treated data" to adjust exposure and risk estimates often reduces estimates by 80–90 percent. This approach is another form of exposure and risk averaging. It is extremely important that these data be explicitly excluded from the exposure estimates and examined openly and critically before their use. If employed, one must acknowledge that exposure and risk are averaged across the country, even though regional patterns of pesticide use and food distribution could cause local populations to be regularly exposed well above average levels. Fifth, any conclusion regarding which foods are "riskiest" may be falsely governed by the pool of foods used to conduct the risk assessment. For example, if only five foods from a market-basket survey are deemed to have sample sizes large enough for exposure and risk assessment purposes, whereas fifteen foods from a field-residue survey are considered sufficient, the relative ranking of riskiest foods will differ significantly between the two data sets.

Finally, and perhaps most importantly, childhood exposure to pesticides should be represented as distributions, calculated from individual food intake

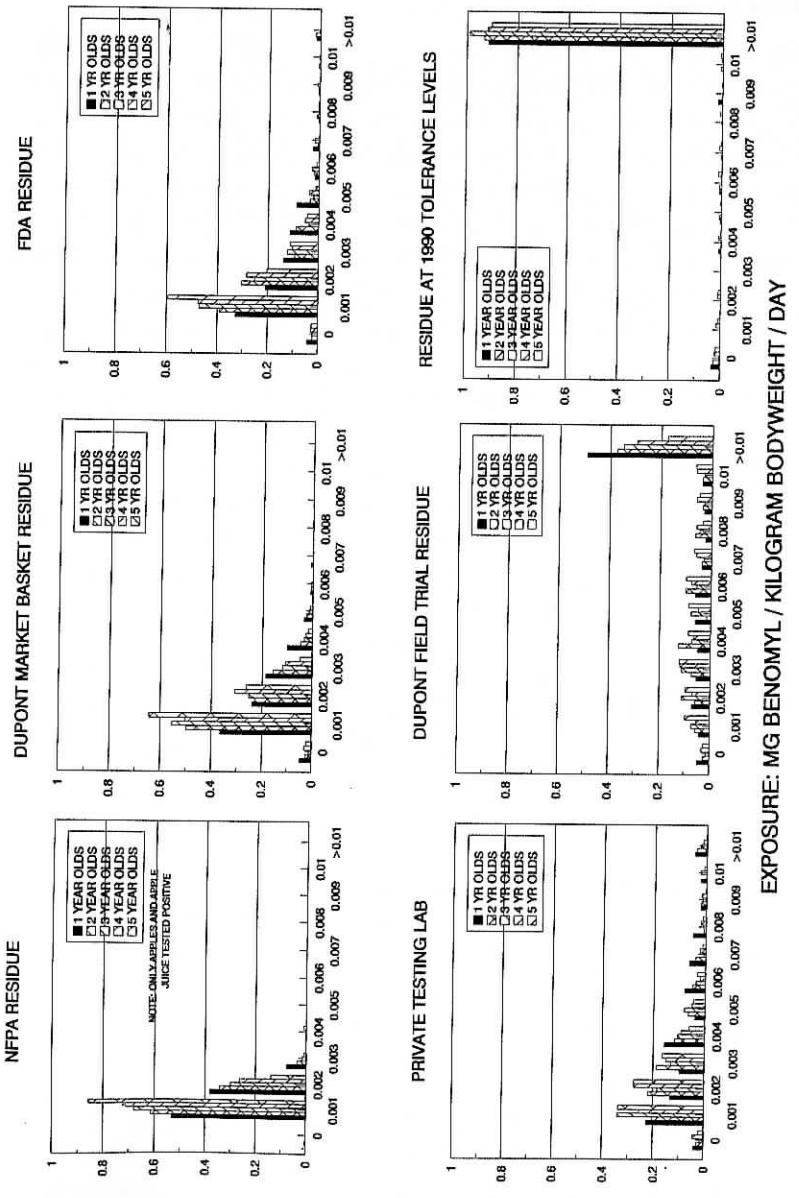

Figure 10–5. Which residue data set should EPA use to estimate exposure and risk? A comparison among six alternatives. These exposure estimates are derived from the five residue surveys described in table 10–1. In addition, exposure is estimated assuming that residues are found on foods at legally allowable, or tolerance, levels. Tolerance-level residues produce the highest exposure estimate, followed by manufacturer field trial results, followed by private testing lab results. Exposure estimates were lowest in National Food Processors' Association residue data, followed by manufacturer's market-basket and FDA data. Which should be used as a basis for tolerance-setting and registration decisions?

data: summary statistics can obscure important high levels of exposure. Although in the case presented above I employed individual food intake data, I combined it with average residue data to estimate exposure. In the following chapter, a method to estimate exposure to complex mixtures of pesticides in foods is suggested—one that relies on full distributions of both dietary and residue data and thereby provides the richest possible image of exposure and risk distribution.

CHAPTER 11

The Complex Mixture Problem

Since its inception, EPA has been overwhelmed by questions concerning the toxicity, exposure, and risks posed by single pesticides. This situation has prevented the agency from examining the distribution and effects of pesticide mixtures in the diet and other environments. By constraining questions to consideration of single pesticides, and by averaging their risks as demonstrated in the previous chapter, pesticide dangers often appeared trivial—and this conclusion has rationalized EPA's choices to grant tens of thousands of tolerances and registrations to manufacturers. If EPA instead asked how a single pesticide contributes to risks posed by other pesticides—or, better still, other types of toxins—we would build a system of knowledge that would permit the most significant threats to environmental health to be identified and managed.

This licensing behavior in the absence of understanding the collective risks posed by mixtures has created a risk assessment problem of extraordinary proportions. To effectively protect public health, the agency must know the likelihood that combinations of pesticides might appear as residues in the marketplace. Because a single pesticide may contribute to several types of toxic effects, forecasting the risks posed by complex mixtures of toxins in the diet is one of the most perplexing analytical problems facing the agency.

In this chapter, I summarize research on the health effects of a class of insecticides that have often damaged the human nervous system. I also describe a method to estimate childhood exposure to mixtures of organophosphate insecticides, which was reported in the 1993 NAS publication *Pesticides in the Diets of Infants and Children.* The method was developed by Richard Jackson of the U.S. Centers for Disease Control, Daniel Krewski of Health and Welfare Canada, and me.[1]

During the last several decades of the twentieth century, EPA permitted roughly fifty organophosphate insecticides to remain as residues in the food supply. Many of these chemicals have the common neurological effect of inhibiting enzymes known as cholinesterases (ChE's), which are necessary for the normal transfer of signals among nerve cells. If EPA regulates these insecticides individually, what is the collective risk they pose? The purpose of this chapter is to develop an approach to answering this question, rather than to provide a definitive estimate of the hazard posed by the specific mix-