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Refinements in Acute Dietary Exposure Assessments for Chlorpyrifos

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Food pesticide residue data are used by the U.S. Environmental Protection Agency (EPA) to determine potential dietary risk from chronic and acute exposures. An acute dietary risk assessment determines the pesticide exposure resulting from a single-day consumption of food, and uses stepwise refinement of residue estimates to better judge actual exposures. All exposure refinements use estimates of the fraction of crops treated and food residues measured increasingly closer to the point of actual food consumption, without changes in the pesticide uses. Exposure distributions at all levels of data refinement were extremely right skewed. At the highest level evaluated, estimated exposures at the 99.9th percentile were 0.00087 mg/kgBW/day compared to 0.2648 mg/kgBW/day at the tolerance level for children 1−6 years, theoretically the highest-exposed population sub-group. The estimated exposure at the 99.9th percentile of the U.S. population was approximately twice the exposure at the 99th percentile and 33 times the exposure at the 90th percentile. This evaluation showed the calculated exposure at the highest tier of assessment was 300 times lower than the tolerance level assessment for children 1−6 years at the 99.9th percentile. Reduction in exposure estimates between these tiers was due to a combination of the following factors: food residue measurements in a specially designed market-basket study, government-sponsored monitoring data, probabilistic methodologies, market share information, and food processing data. This case study demonstrates that an improved understanding of the uncertainties of acute dietary exposure from pesticides is possible by using well-established statistical tools and applying them to comprehensive exposure information, including residue monitoring data, consumption data, and pesticide use information.

KEYWORDS: Chlorpyrifos; food residues; tolerances; exposure assessment; dietary exposure

INTRODUCTION

The process of dietary risk assessment of pesticides considers chronic and acute exposures to the U.S. population and sensitive population sub-groups. Acute dietary risk assessments estimate the exposure and risk following consumption of pesticide residues in food or water for a single day's food consumption, whereas chronic assessments estimate exposures and risk from food consumption over a period of weeks to years.

The U.S. Environmental Protection Agency (EPA) has established procedures for acute dietary risk assessment for use in the re-registration of pesticides, and continues to explore acute dietary policy in the implementation of the Food Quality Protection Act (FQPA) (*1*). The accuracy of any dietary assessment is dependent upon the toxicology data, chemical residue information, and consumption data that are used. The current approach of the EPA Office of Pesticide Programs (OPP) is to use a tiered approach for acute dietary risk assessment that proceeds from very conservative assumptions about food residues, to inclusion of more realistic residue values measured closer to the point of consumption. The process is designed to match the level of resources used to the level of concern (*2*). As the assessment progresses through the tiers, additional data and effort are necessary to estimate acute dietary exposures. At each tier of assessment, acute dietary exposure is calculated as the product of the amount of pesticide residue on a food item multiplied by the amount of the food item consumed by an individual each day (*2*). Acute dietary risk can then be estimated on a population basis by dividing the exposure value by the acute reference dose to yield a percent of reference dose (RfD). Current EPA OPP policy and guidance modifies the RfD for estimation of dietary risk by dividing the RfD by any additional safety factor mandated by the FQPA from concerns regarding special sensitivities to infants and children. This modified RfD is referred to as the population-adjusted dose (PAD). The results of acute dietary risk assessments are used by OPP as a risk management tool to ensure food treated with a pesticide will not pose an unacceptable risk to human health. Emerging policy within EPA intends to further clarify the rationale and procedures for tiered acute dietary risk assessment.

Critical to any acute dietary assessment are residue and consumption data. Extensive field studies that measure potential food residues are required by regulatory agencies prior to allowing the use of a pesticide on crops. Such field studies

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quantify the terminal residues of the pesticide on plant tissues that could be consumed, directly or indirectly, by the U.S. population. Such residues are measured under conditions of the maximum proposed application rate and the shortest interval between application and harvest (*3*). Ultimately, these data are used to establish enforcement standards (tolerances) and to estimate dietary risk. Additional residue measurements come from special government monitoring programs and market-basket surveys sponsored by the registrant.

This study describes a tiered acute dietary risk assessment using data for chlorpyrifos, a widely used organophosphate insecticide. Chlorpyrifos (*O*,*O*-diethyl-*O*-(3,5,6-trichloro-2-pyridinyl)phosphorothioate) has been registered since 1974 for use on food crops. It is currently approved for application on more than 40 crops in the U.S. Available pesticide residue data for chlorpyrifos in the United States are highly comprehensive, thus affording an opportunity to investigate the methods used to refine dietary risk estimates.

The tiered process of acute dietary risk assessment is described in detail by the EPA in their Acute Dietary Exposure Assessment Office Policy (*2*). The policy begins with a tolerance level assessment for each crop for which the pesticide product has an approved use, and proceeds to refined estimates of exposures by using food residues measured close to the point of consumption. The assumptions used in a tolerance level assessment serve as a screening tool to obviate further consideration of those pesticides for which there are clearly no risk concerns (*4*). This first tier of assessment assumes that every acre of each crop listed on the pesticide label is treated and the pesticide residues occur at the tolerance levels. Further tiers include estimates of the fraction of the crops that are treated with the pesticide, effects from food processing (washing, peeling, and cooking, etc.) on residue levels, and the random chance of eating food with specific residues. Each subsequent refinement requires more data and more effort to estimate the actual food residues at the point of consumption. The most refined estimates require widespread food residue monitoring data, food processing studies, and a thorough understanding of the use patterns and market share of the pesticide. These highly refined assessments are seldom conducted because they require monitoring data, or extensive market-basket surveys (MBS) which involve collection and analysis of food samples from supermarkets and other food distribution centers in a manner that adequately represents the entire population. However, for established pesticide products such as chlorpyrifos, such assessments are highly appropriate for estimation of acute dietary risk. The market-basket residue surveys and monitoring data realistically estimate the magnitude of pesticide residue on food as it is purchased by the consumer, because samples are taken closer to the point of consumption, and more accurately represent actual patterns of use and food distribution than measurements from a typical field trial. For each level of assessment, the food residue information is coupled to specific, daily consumption records for the entire U.S. population, and certain population sub-groups. Because comprehensive residue data are available for chlorpyrifos, including government-sponsored monitoring data and market survey data, it is amenable to acute dietary risk assessment at all tiers. Therefore, chlorpyrifos is considered here as a case study for evaluation of acute dietary risk assessment procedures.

MATERIALS AND METHODS

Dietary Exposures. Dietary exposure is calculated using a simple algorithm:

$$E_i = (R_i \times C_i \times P_i) \div 1000 \quad (1)$$

$$E_t = \sum E_i \quad (2)$$

where E_i is the exposure from the pesticide on food i (milligrams/kilogram body-weight/day, mg/kgBW/d), R_i is the chemical residue on food i (micrograms residue/gram food, μg/g), C_i is the daily consumption of food i (grams food/kilogram body-weight/day, g/kgBW/d), P_i is the probability of consuming a certain residue on food i on a single day, and 1000 converts micrograms of residues to milligrams. The total daily exposure E_t is the sum of exposures from all foods consumed on a single day. Total daily exposures were summarized in an empirical probability distribution. All exposure values reported here were calculated as the exposure for 99.9% of those exposed according to U.S. EPA policy (*4*, *5*). For a tolerance level assessment, R_i was the tolerance value, P_i was 1, and C_i was the daily food consumption for food i. For estimates that did not use Monte Carlo simulations, the probability (P_i) of eating a certain food residue was the fraction of the total crop acres that were treated based on market estimates.

The dietary exposure evaluation model (DEEM, version 7.075), a commercially available software package, was used to estimate exposure to chlorpyrifos via food consumption by the general U.S. population and certain subgroups. The model combined the consumption data and residue data for a given pesticide to analyze dietary risk (*6*). For higher tiers of assessment, DEEM developed a conditional, joint probability function from the individual pesticide residues and the food intake information.

Monte Carlo type analyses randomly sampled food residues to predict the likelihood of exposures on individual days. The DEEM model did not follow a typical Monte Carlo sampling process in that it did not randomly sample all foods, but rather allowed samples only as specified by the individual dietary records. The model began by choosing individual 1, day 1, and food 1, then randomly selected a residue value for food 1. The resultant exposure was calculated, then food 2 was evaluated. All exposures from food consumed by individual 1 on day 1 were summed before proceeding to day 2, day 3, etc. The process was repeated for all individuals and all commodities to derive daily exposure estimates for the population. The residue values for a commodity were multiplied by food consumption quantities for each participant in the survey. Every individual and every food in the consumption survey was evaluated. The resultant distribution properly considered the joint probability of food consumption by limiting the analysis to those exactly specified by the individual food diaries for each individual for each day. Typically, 1200 Monte Carlo iterations, representing 1200 eating events per food for each individual, were used for an assessment. Preliminary investigations showed that this number of random samples was sufficient to reach convergence to a consistent exposure estimate.

Food Consumption Data. Food consumption data from the USDA Continuing Survey of Food Intakes by Individuals (CSFII) conducted from 1989 through 1992 (*7*−*9*) were used in this assessment. The 1989−1992 CSFII had 10,383 participants, each with three complete days of intake records. The survey also contained information on general health information such as food and nutrition intake. Each CSFII represented a stratified area probability sample of individuals residing in households in the U.S. The surveys, designed by the USDA, measured dietary intake of all individuals in survey households for a continuous three-day period. Households and individuals were surveyed in all four seasons and on all days of the week. The USDA developed statistical weights that were applied to the data to estimate representative consumption rates for the U.S. population (*10*). The food consumption data, i.e., foods as consumed, were translated into raw agricultural commodities and their food forms using recipe translation files contained within the DEEM software. For example, if a person reported consumption of apple pie, the model evaluated exposure to a pesticide via the ingredients of the pie such as apples, sugar, wheat flour, leavening agents, animal fat, spices, water, etc. (*6*). The CSFII data for the years 1989 to 1992 were used for all assessments.

Food Residue Data. For the tolerance level assessment (tier I), the food tolerance values used were as reported in 40 CFR 180.342 and

40 CFR 185.1000 (*11*). Field residue values, where samples are collected directly from the field, were from required field studies submitted as a part of the pesticide registration package submitted to the U.S. EPA (*3*). Approximately 390 residue data points from field trials on 47 crops were used in the analysis. In total, 204 foods were included in the acute exposure analysis.

In the higher levels of assessment, market-basket survey data for chlorpyrifos were used in the analysis when available. A market-basket survey measured residues of chlorpyrifos on samples of apples, applesauce, apple juice, fresh orange juice, tomatoes, peanut butter, whole milk, ground beef, and pork sausage. The survey collected random food packages in a stratified sample from 200 grocery stores across the U.S. in 1993 and 1994 (*12*). These food items were selected because of their expected high consumption by infants and children, and the potential for high residue levels, based on use patterns. The food samples were collected at retail outlets selected from a national database of more than 95,000 supermarkets, superettes, and convenience stores. Sampling of the stores was weighted so that each store's probability of selection was proportional to its sales volume, geographical region, and urbanization status. Therefore, the residues measured were statistically representative of 84% of the food sales in the U.S. sold in supermarkets. Residues of chlorpyrifos in ground beef were used to represent cattle meat and byproducts, goat meat and byproducts, and sheep meat and byproducts. A total of 1,649 residue data points was available from the chlorpyrifos market-basket survey for use in the assessment. Because residues were measured on composite samples, residues on individual fruit were estimated.

Because the acute dietary assessment focused on single servings, the data for single servings (single fruits) of apples and tomatoes were imputed from composite samples (five apples, four tomatoes) that had been collected in the chlorpyrifos market-basket survey. The imputing process generated a set of single-serving residues from each composite sample equivalent in distribution to the actual residues on the single fruits if they had been measured according to current EPA policy (*13*).

For imputation, the distribution of the composite samples was first determined to be a log-normal distribution with a mean and variance estimated from the composite samples. The central limit theorem states that the mean of individual observations and the mean of small samples, drawn from the same distribution, will be the same. The theorem also states that the relationship between the variance of individual observations (s^2) and the variance of small samples (S^2) of size n are related as shown in eq 3.

$$S^2 = s^2/n \tag{3}$$

For apples, five single-serving values were randomly generated from a log-normal distribution with the mean the same as the value of the composite residue and variance $\sqrt{5}$ times that of the variance of the composites. The mean of five samples also was equivalent to the composite residue representing ±1%. A similar approach was used for tomatoes using four fruit per composite. Because the log-normal distribution could generate values with no upper limit, imputed residue values were truncated to tolerance values of 1.5 ppm for apples and 0.5 ppm for tomatoes. The procedure followed here differed from current EPA policy which does not allow for truncation of imputed residues to tolerance values.

For food items not sampled in the chlorpyrifos market-basket study, residues were obtained from a chlorpyrifos residue database created from residue field trial data collected over the past 27 years and reviewed and accepted by the EPA. Residue field data that supported the current chlorpyrifos label, and had the maximum application rate and frequency combined with the shortest interval from application to harvest were used to give the most conservative measure of food residues and the resulting dietary exposure estimate. After decomposition of composite samples to impute single-serving residues, and inclusion of field trial data as necessary, more than 3000 residue data points were incorporated into the market basket assessment.

Monitoring Data. Residue monitoring data collected as part of the USDA's Pesticide Data Program (PDP) and FDA's pesticide residue surveillance program were used whenever available. PDP data were preferred because samples were collected at food distribution centers according to a statistical protocol to ensure representation across the entire U.S. FDA samples were collected from grocery stores or supermarkets four times per year, one from each of four geographic regions. Three cities from each region were sampled. In the refined exposure assessments reported here, PDP data from surveys reported in 1994 through 1997 (*14*) and FDA data from 1992 to 1997 were used (*15*). Samples that were reported as having nondetectable residues were given a value of one-half the average limit of detection (LOD) across all samples according to current EPA policy (*13*, *16*). Estimates of the percent of crop acres treated were used to convert an appropriate number of samples with nondetectable residues to true zero values in place of $^1/_2$ the LOD. In some cases, residues from one commodity were used to represent other commodities with similar agronomic use patterns according to current policy (*17*). Examples of such surrogating of residues include the use of fresh oranges to represent all citrus, green beans to represent all succulent beans, cucumbers for squash and pumpkins, and broccoli for all *Brassica*. PDP residues were not adjusted for percent crop treated because the distribution of residues was assumed to represent the national distribution. Composite samples of apple and tomato were decomposited to single-serving residues using the method of Allender (*18*). For apples, the 425 detectable residues, each containing an estimated 15 apples, were decomposited into 1000 samples. For tomatoes, 109 samples with detectable residues were decomposited to represent 1000 single tomatoes. A total of 23,500 measured residue values were used from the PDP, FDA, and market basket surveys.

Treatment of Nondetectable Residues. For field and market basket data, residue values reported as below the limit of detection (LOD) were assigned $^1/_2$ the value of the LOD. Residue values reported as less than the limit of quantitation (LOQ), but greater than or equal to the LOD were assigned $^1/_2$ the LOQ according to current EPA policy (*16*). When PDP or FDA monitoring data were used, the number of LOD residues reported for each commodity was set equal to zero on the basis of estimates for the percentage of the crop not treated. For example, if the residue data set contained 100 samples with nondetectable residues, and market share was 10%, then 10 of the residues were given the value of $^1/_2$ LOD, the remaining 90 samples were given the value of true zero.

Estimates of the Percent Crop Treated. The probability of encountering food items treated with chlorpyrifos was determined using market data obtained by the Dow AgroSciences marketing research function and the EPA Biological and Economic Analysis Divisions (BEAD) of OPP (*19*). The EPA values were estimated from 1987 to 1993 data collected by Doane Marketing Research, Inc. Dow AgroSciences gathered values that are more recent from Doane for 1995 and 1996. The EPA and Dow AgroSciences estimates were similar where market share was relatively unchanged over the past 10 years. For those cases where the Dow AgroSciences data and the EPA data were not similar, the values were averaged to ensure the most recent marketing research data were included. Such averages were used to account for shifts in product use due to changes in pest pressure and competitive pest management technologies. For Monte Carlo simulations, the probability of foods not treated with chlorpyrifos was included by augmenting the field trial data with the appropriate number of zeroes based on market share (percent of crop treated). This did not effect actual residue levels in a sample, only the random chance of sampling a given residue. However, residues from the market-basket survey and government-sponsored monitoring programs were not adjusted for market share because the probability of encountering samples with residues of chlorpyrifos was inherent in the sampling process. In the latter case, use data were used to determine the number of residue samples reported as having nondetectable residues that should be considered as not treated and with zero residues.

Processing Factors. Processing factors were incorporated into the dietary risk assessments to account for dissipation or concentration of residues as the raw food is processed into various food fractions such as juice, puree, or oil (*20*). The processing factors, calculated as the ratio of the residue value in the processed commodity to that in the raw food, were computed for several food items from results of processing studies performed according to EPA protocols. Processing studies with sugar beets, citrus, field corn, cotton, grapes, onion, peanut,

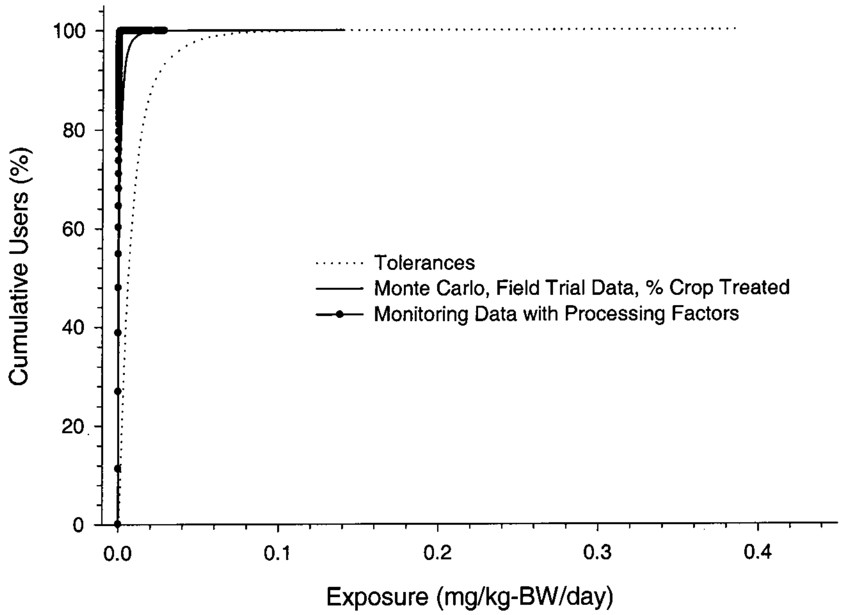

Figure 1. Cumulative exposure distributions for chlorpyrifos at three levels of data refinement for the U.S. population.

plums, sorghum, soybean, sunflower, tomatoes, and wheat were available for chlorpyrifos. In the absence of processing data, default adjustment factors were used that assume residues were concentrated in the processed food commodity. The default adjustment factors were based on percent yield tables (*21*).

For foods such as poultry and eggs, secondary residues can occur in animals because of consumption of feed stuffs containing residues of chlorpyrifos (e.g. alfalfa forage, hay, and seed). These were identified by (a) determining the chlorpyrifos dietary burden from each feed stuff, (b) determining the total dietary burden (TDB) from a diet composed entirely of the highest contributing feed stuffs, and (c) converting the TDB value to residue values (*3*).

RESULTS AND DISCUSSION

Estimates of pesticide-specific dietary risks must include information on the amount of food consumed by individuals, the amount of pesticide present at the point of consumption, and the toxicological significance of those residues. A critical component of the process is the estimation of levels of pesticides present in foods (*22*). Approaches to estimate exposures can range from purely theoretical to data intensive. For example, a theoretical estimate would assume all residues are present at a predetermined (e.g., tolerance) level. Estimates with increasing levels of data requirements include field residue measurements, actual "dinner plate" measurements for large numbers of individuals (*23*), and inclusion of large amounts of monitoring and population consumption data. Each level of data refinement requires substantially more data and a better understanding of the actual use patterns for a pesticide. The simplest approach to exposure assessment, and the most conservative, is to assume tolerance level residues are present on all foods. Although not a safety standard, such a tolerance approach sets an upper, legal, limit for residues on individual foods, and provides an efficient method to identify those pesticide uses with no exposure concerns. The assumption of maximum legal residues generally represents a large exaggeration of the actual levels encountered by consumers (*22*).

For acute dietary assessments, approaches must also be considered that estimate exposures due to individual food consumption patterns. It is impossible to know precisely how much food every individual in the country consumes, either over a lifetime, or on a single day (*24*); similarly, it is impossible to know how much residue each specific food item contains. As a result, the U.S. EPA has used Monte Carlo methods to estimate different levels of exposure as a result of differences in food consumption and residues based on the local and national distribution of consumption and residue data.

Table 1. Exposure Estimates (mg/kgBW/d) at Different Percentiles of the Distribution: Tolerance Values vs Monitoring Data

population group		50%	90%	97.5%	99%	99.9%
U.S.	tolerance	0.006277	0.02264	0.0455	0.06319	0.1166
	monitoring	0.000002	0.000011	0.000039	0.000086	0.000450
children 1–6 years	tolerance	0.02421	0.05948	0.0876	0.1130	0.2648
	monitoring	0.000005	0.000026	0.000087	0.000167	0.000867

Percentile of Exposure. The current EPA Office of Pesticide Programs policy is to use estimates of exposure at the 99.9th percentile for calculating a threshold of concern for acute exposures when probabilistic methods are used to model the population exposure distribution (*24*). Figure 1 is a graphical comparison of the chlorpyrifos exposure distributions for the U.S. population, for three levels of data refinement. The exposure distributions are extremely right skewed (i.e., with a long tail to the right). Using residue values at the tolerance level, the exposure estimates at the 99.9th percentile were approximately two times higher than the exposures at the 99th percentile for the U.S. population in general, as well as for children ages one to six years (Table 1). When residue monitoring and processing factors were included, the exposure estimates at the 99.9th percentile were approximately five to seven times higher than the exposures at the 99th percentile. Because both food consumption and the residue monitoring distributions are right skewed, the resulting product is also a right-skewed distribution. Whether the CSFII food consumption dataset, or the residue data sets are statistically robust enough to support such exposure values, calculated at the 99.9th percentile, has been questioned (24). Because it is the current policy of the EPA Office of Pesticide Programs to use exposure estimates at the 99.9th percentile for tiers III and IV, this percentile of exposure will be used in this paper for comparisons among all levels of exposure refinement.

Residue Data Sources and Exposure Estimates. Measurements of food residues can come from several different sources.

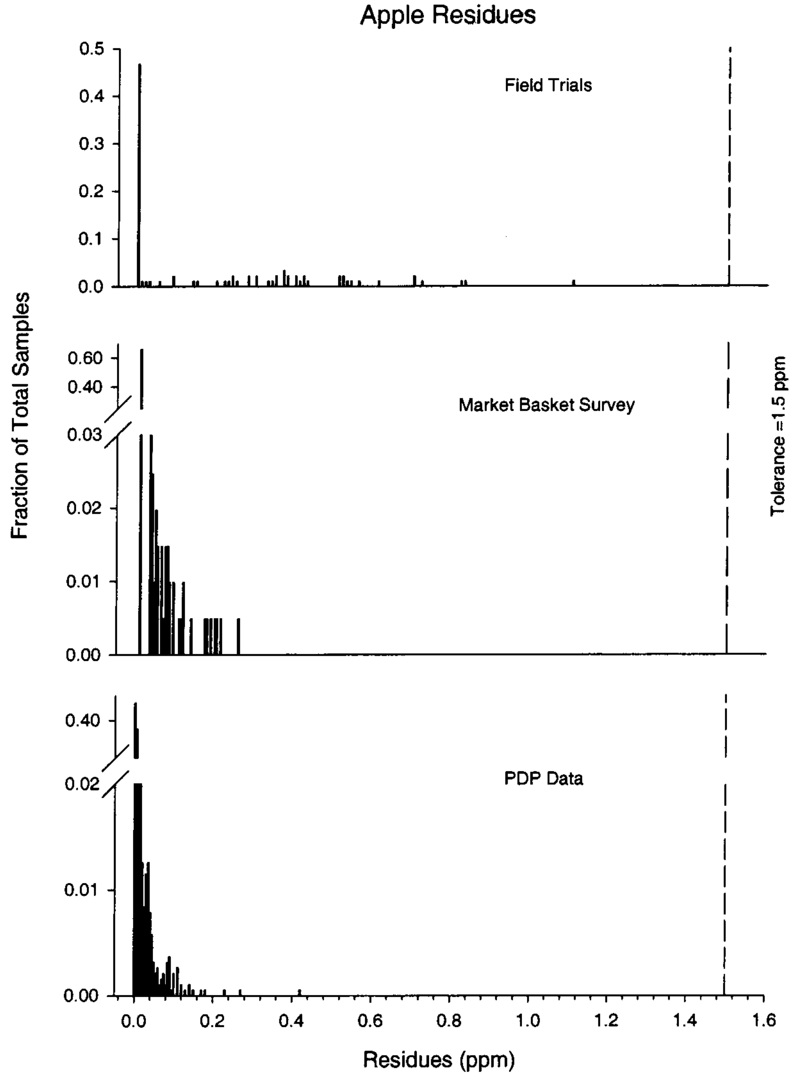

Figure 2. Comparison of apple tolerance values to residue values measured in field trials, a market-basket survey, and USDA's Pesticide Data Program.

Table 2. Exposure Estimates (mg/kgBW/d) by Population Subgroup

level of refinement	U.S.	infants	children 1–6 years	children 7–12 years	females 13–19 years	males 13–19 years
tolerances	0.1166	0.3421	0.2648	0.07807	0.05208	0.04937
tolerance + % crop treated	0.06976	0.3418	0.11884	0.06929	0.04092	0.03333
highest field trial residues	0.05162	0.1391	0.1177	0.04159	0.02207	0.02521
highest field trial residues + % crop treated	0.0293	0.1396	0.06121	0.02687	0.01534	0.012599
Monte Carlo, field trial data,% crop treated	0.02436	0.13929	0.041210	0.026729	0.014933	0.011869
market-basket survey, no PDP	0.000908	0.000679	0.001404	0.001092	0.000694	0.000857
monitoring data,no processing factors	0.000484	0.000880	0.000941	0.000641	0.000305	0.000319
monitoring data with processing factors	0.000450	0.000473	0.000867	0.000604	0.000292	0.000307

As part of the pesticide registration process, field residue trials are required for certain foods, or food groups, in order to establish food tolerances. The tolerance is the maximum legal amount of a pesticide allowed on a food item (*22*). Typically, the tolerance is set slightly higher than the residues measured in field trials to accommodate the maximum residues under the maximum application rates, various weather conditions, and the shortest preharvest interval. Figure 2 shows a comparison between the chlorpyrifos tolerance value, field residues, and monitoring data for fresh apples. The field residue data were adjusted to include the estimated percent of crop treated. Without this adjustment, the field residue data appeared normally distributed, representing the variability between crops grown under controlled conditions at multiple geographic locations.

Food tolerance values gave the highest estimated exposures (Table 2). Estimated chlorpyrifos exposure to the U.S. population, based on tolerances, was 0.1166 mg/kg/day. The highest theoretically exposed population subgroup was children aged one to six years with an estimated exposure of 0.2648 mg/kg/day. Children in the one to six year old sub-population tend to have higher exposures than adults because their body-weight-adjusted consumption is greater, especially for fresh fruit and juices. The tolerance level exposure estimate assumed that every crop acre was treated with chlorpyrifos. When provisions were made for the proportion of crop acres not treated (% crop treated), the exposure estimate for children decreased 45% to 0.11884 mg/kg/day. If, instead of the tolerance value, the highest field residues were used, the exposure estimates further decreased to 0.05162 mg/kg/day and 0.1177 mg/kg/day for the U.S. population and children ages one to six years, respectively. Thus, using the highest measured field trial data, as compared to using tolerance values, reduced the exposure estimates by approximately 55%. Inclusion of that fraction of crop acres not treated further decreased the exposure estimates.

Current EPA policy is that probabilistic analysis techniques such as Monte Carlo can be viable statistical tools for analyzing variability and uncertainty in risk assessments. Such techniques can enhance risk estimates by more fully incorporating available information concerning the range of possible values that an input variable could take, and weight these values by their probability of occurrence (*25*). Because conservative point estimates, such as tolerance values, are sought to ensure worst-case or upper-bound estimates of risk and exposure, without further analysis, the degree of conservatism of such approaches may be hard to determine. Deterministic, or point, estimates may enjoy a precise and/or accurate appearance, and inspire a misleading sense of confidence (*26*). Probabilistic analysis permits the assessment of exposures which result from combinations of the various residue levels and the consumption patterns as defined in the CSFII dataset. The technique randomly samples each probability distribution to produce hundreds or even thousands of scenarios. Each distribution sampled in such a way will reproduce the distribution's shape. The resultant distribution reflects the probability of the values that can occur (*27*). Monte Carlo simulation therefore provides results that are far more realistic than those produced by "what if" scenarios (*27*) using a limited number of residue values.

The DEEM software used a modified Monte Carlo approach by randomly sampling from residue values, and stepwise (nonrandomly) analyzed each individual in the CSFII. The resultant joint, discrete, probability distribution provided useful information on the likelihood of exposures to individuals who randomly ate foods containing a range of possible residues. Applying Monte Carlo sampling to chlorpyrifos field trial data gave exposure estimates of 0.02436 mg/kg/day for the U.S. population and 0.04121 mg/kg/day for children ages one to six years. The Monte Carlo estimates at the 99.9th percentile were similar in magnitude to the highest residue (deterministic) calculation. The similarity suggested that the residue data were adequately sampled in such a way that the highest residue value was paired with the highest food consumption value for each commodity. The variability between successive analyses with random seed numbers was less than 2%, further suggesting that the residue data were adequately sampled with 1200 iterations.

Incorporation of Dow AgroSciences market-basket data (*12*) into a Monte Carlo analysis gave a marked reduction in the estimated exposures to chlorpyrifos. For the U.S. population, the estimated exposure was 0.000908 mg/kg/day and 0.001404 mg/kg/day for children one to six years old. The incorporation of residues measured closer to the point of consumption for these nine foods gave a 60−190-fold reduction in exposure estimates. Whereas the field trial data represented the highest residues, the MBS data represent residues resulting from variable application rates, storage times, environmental degradation, and food processing.

Additional residue monitoring data were obtained through the USDA's Pesticide Data Program (PDP, *14*) and the FDA's pesticide monitoring program (*15*). Both of these surveys provided residues on a wider range of foods than was available from the Dow AgroSciences MBS. In addition, certain of the data were surrogated to represent additional foods with similar use patterns and agronomic characteristics (*17*). Following decomposition of composite samples to single servings, the combined MBS, PDP, and FDA data sets contained greater than 23,000 data points. Of the 204 foods included, residue data for figs, dried peas, dried beans, mushrooms, and sugar cane were derived from tolerance values. Data for corn grain, peppermint, spearmint, sunflower, tree nuts, and soybeans were derived from field trails. All other data came from one of the three monitoring data sets. Extensive use of chlorpyrifos residues from large-scale monitoring programs significantly reduced the estimated exposures to all population sub-groups. The estimated exposure was 0.000484 mg/kg/day for the U.S. population, and 0.000941 mg/kg/day for children one to six years old, at the 99.9th percentile. Inclusion of residue reduction factors for wheat baking (0.145), peeling of fruit and vegetables (0.15), and juicing (0.3) where appropriate, gave further reductions in the estimated exposures at the point of food consumption. These processing factors had the greatest impact on the estimated exposures to infants as would be expected from their high consumption of processed grains, fruits, and vegetables.

The exposure estimates presented here compare favorably to estimates published through other analyses. The FDA's Total Diet studies from 1989 and 1990 estimated chlorpyrifos exposures at 0.0000041 mg/kg body weight/day for children aged 14 to 16 years (*28*, *29*). Their exposure estimates are similar to the 50th percentile values given in Table 1. In a recent longitudinal investigation of dietary exposures, MacIntosh et al. (*23*) analyzed pesticide residues in duplicate plate samples at various times of the year. In their survey, chlorpyrifos was detected in 38.3% of the samples. On the basis of measured weights of their duplicate food samples, and self-reported body weights, they estimated a maximum exposure of 0.0002 mg/kg/day and a mean exposure of 0.00000068 mg/kg/day for individuals greater than 10 years old. These values are approximately three to four times lower than the acute exposure values estimated here for 99.9% of the population of children aged 1 to 12 years.

The significant reductions in exposure estimates through refinement in data is remarkable, especially when considering that such refinements were exclusively due to measurements of food residues closer to the point of consumption, and did not include any changes in product use or food consumption patterns. The greatest refinement in the exposure estimate came from a combination of large-scale residue monitoring data, inclusion of market use information, and reduction in residues from food processing. As a result, dietary exposure to chlorpyrifos is well understood, having a comprehensive pesticide residue database that enables review of exposure at higher levels of dietary exposure assessment. This case study demonstrates that an improved understanding and examination of the uncertainties of dietary exposure from pesticides is possible by application of sound and well-established statistical tools to comprehensive exposure information including residue monitoring data, consumption data, and pesticide use information.

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