Methods for Quantifying Dietary Risk from Residues of Pesticide Active Ingredients, Metabolites and Isomers Found in Food

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INTRODUCTION

Pesticide dietary risk assessments are often made more complex by the environmental fate of pesticide residues on or in food. A full accounting of potential risks requires analysis of the various metabolic breakdown products and isomers associated with a given parent compound – the active ingredient actually sprayed on the crop or applied to a field before or at planting. Dealing with these complexities forms a major part of the challenges faced by the Office of Pesticide Program's residue chemistry branch.

As EPA's dietary risk assessment methods have become more sophisticated, the agency has done a more thorough job of assessing the metabolic breakdown pathways of pesticide residues found on food. In some cases, the agency has requested separate toxicity data on metabolites or isomers of particular concern. In addition, the EPA has also asked the USDA's Pesticide Data Program (PDP) to modify its analytical methods to provide separate data on certain metabolites, isomers, and active ingredients.

Since its inception, the PDP program has evolved in many ways. Analytical methods have become more sensitive, quality control procedures have been refined, the range of crops tested has grown, and the number of pesticides and their metabolites and isomers included in the program has increased. Most changes have been in response to direct requests from EPA for more refined data to incorporate in its FQPA-driven dietary risk assessments.

New Challenges

Since its inception in the early 1990s, the PDP has tested over 60,000 samples of fresh fruits and vegetables, juices, processed foods, grains, and milk. One of the valuable applications of the extensive pesticide residue database that has now been compiled is assessing trends in the frequency, level, and relative risks of pesticides found in food. Consumers Union has developed a Toxicity Index for this purpose, which is based on PDP data in conjunction with mammalian toxicity data from EPA. (See the report "Do You Know What You're Eating?" for Toxicity Index methodology and applications to the 1994-1998 PDP results, accessible at http://www.ecologic-ipm.com/findings_CU.html).

A full accounting of pesticide dietary risk levels in a given food must encompass residues of metabolites and isomers, in addition to parent compounds. Over the years, however, the PDP has changed how it reports the residues stemming from application of a given active ingredient (or "parent" compound). In general, the PDP has been more thorough in recent years in testing and reporting results for major metabolites and isomers. But significant differences are encountered in the PDP database over time in how testing was carried out and results reported. Accordingly, in calculating relative risk levels over time and assessing trends, whether using CU's Toxicity Index methodology, EPA's cumulative risk methods, or any other dietary risk assessment program, a method must be developed for reconciling differences in the way residue data are reported.

This technical appendix sets forth the decision criteria used by Consumers Union in its analytical work with the 1999 PDP dataset. In both our 1997 report ("Do You Know What You're Eating?") and 1998 report ("Update: Pesticide Residues in Children's Foods"), we calculated Toxicity Index scores by pesticide food combination for domestically grown food, as well as for imports by country of origin. In the 1998 report, our basic tables covered 1994-1998, using current EPA reference doses, some of which had changed since our 1997 analysis. Our 1999 report will cover 1994-1999, and will incorporate changes in reference doses as well as changes in the way metabolite and isomer residue data were utilized. For this reason, there will be some differences in the toxicity index values reported in the tables produced in our 1999 report in contrast to our earlier reports.

Scope of the Problem

The table "Quantifying Risk from Dietary Exposure to Pesticide Active Ingredients, Metabolites and Isomers Found by USDA's Pesticide Data Program" (see hot link on website for table) includes all parent pesticide compounds, metabolites, and isomers included in the PDP database in at least one year since 1994. The first check box indicates whether the chemical is a metabolite and the second column, whether the active ingredient is a parent compound of a PDP-identified metabolite.

The next two boxes identify chemicals that are isomers or impurities. These designations are taken directly from the listing of each of the 155 chemicals in Appendix E. of the 1999 PDP report. The last column under the heading "Chemical Identity" lists the parent compound of each metabolite and isomer. The next six columns indicate whether any residues were reported by the PDP in program years 1994-1999.

In calculating CU's Toxicity Index value for active ingredients, metabolites and isomers, we use the most recent EPA chronic Population Adjusted Dose (the chronic Reference Dose divided by any additional safety factor called for by the FQPA's 10-X provision). The column "Tox Data Source" shows the source of cPADs for each active ingredient, metabolite or isomer. In some cases, EPA may have or estimate cPADs specific to a given metabolite or isomer, and in such cases, we will use that data instead in estimating metabolite/isomer TI values. The last column reports the cPAD value

currently in our database linked to the active ingredient in the column "Tox Data Source," reflecting EPA's latest publicly announced cPADs.

Decision Rules

With a few exceptions noted below, Toxicity Index values are calculated for pesticide active ingredients, metabolites, and isomers as if each were a separate chemical. In estimating total TI scores for a given food, the TI values for parent compounds and their associated metabolites and/or isomers are assumed to be additive.

The simplest case is an active ingredient with a single reported metabolite. In cases where the PDP reports residues of both the parent compound and the metabolite in the same food, CU calculates toxicity index values both the parent and the metabolite. The toxicity data for the parent is used in calculating the metabolite TI value, unless EPA has data specific to the metabolite. As noted above, in aggregating TI scores across all residues found in a food, the parent compound and metabolite TI scores are treated as additive.

Residues of acephate and its metabolite methamidophos are reported separately. It is not possible to determine which portion of methamidophos residues are caused by the metabolic breakdown of acephate in contrast to residues from the direct (legal or illegal) application of methamidophos.

Many pesticide metabolites have also been registered as an active ingredient and applied as a parent compound. Examples include dimethoate and its metabolite omethoate, and aldrin and dieldrin. In cases where there are no active U.S. registrations of the metabolite, we treat the chemical (e.g., omethoate or dieldrin) as a metabolite of its parent compound.

In cases with two or metabolites of an active ingredient, a separate TI value is reported for each, along with the parent compound. The toxicity data for the parent compound is used in calculating metabolite TIs.

In some cases, PDP reports the residues found of a stable metabolite of the parent compound, and no data on the parent itself. For example, benomyl is reported as carbendazim. In such cases, TI values are based on the frequency and mean of carbendazim residues, coupled with parent compound toxicity data. **[Help is sought from EPA in determining in which cases there are cPADs available for metabolites and isomers].** In reporting PDP findings and TI values for such cases, we use the nomenclature "carbendazim (benomyl)" in our 1999 report.

Sometimes PDP reports residue data on an active ingredient in a way that encompasses several isomers and/or metabolites of the active ingredient. Permethrin is an example. In 1994-1997, PDP reported residues of "permethrins," encompassing both the cis and trans isomer of permethrin, as well as other isomers. **[Martha Lamont and PDP staff – is that a correct statement? Is it generally known what percent of total**

permethrins are accounted for by the cis and trans isomer?]. In 1998-1999, PDP reported residues of "Total Permethrins" and "Permethrin cis" and "Permethrin trans." But in both 1998 and 1999, PDP tested far fewer samples for "Total Permethrins" than for the cis and trans isomer. In 1999, there were 893 samples of seven foods tested for "Total Permethrins" and 5,526 samples of 14 foods tested for both the cis and trans isomer of permethrin. Not surprising, the percent positive for "Total Permethrins" and the cis and trans isomer are very similar in individual foods.

Interestingly in 1999 results, the sum of the means of the cis and trans isomers of permethrin was between a half and two-thirds the mean residue of "Total Permethrins." Accordingly, it appears that the cis and trans isomers of permethrin account for as much as two-thirds of all permethrin isomers. **[Correct way to state this?]** Likewise, the value of CU's Toxicity Index for the cis plus trans isomer generally accounts for half to two-thirds of the TI value for "Total Permethrins" (when the toxicity data for permethrin is used in estimating cis and trans TI values).

Since "Total Permethrins" appears to be a more comprehensive measure of residues and risk, we will base TI values on "Total Permethrins" residue data in cases where PDP tests 100 or more samples of a given food for "Total Permethrins." We will report TI values based on the percent positive and mean residue levels reported for "Total Permethrins", even when there are 600 or more samples tested for both the cis and the trans isomer. But when analyzing permethrin residues by country of origin, cases will arise where there are less than ten samples of "Total Permethrins" tested of a given food, below CU's cut-off for minimal sample size to estimate a TI value. In such cases, we will use data for permethrin cis and permethrin trans isomers if there are more than 10 samples tested of the food from a given country. In a few cases, this will introduce a modest bias in our results when comparing TI scores for a food grown in the U.S. in contrast to imports. Domestic TI values based on "Total Permethrins" will be somewhat higher, other things equal, than imported TI values based on the sum of permethrin cis and trans TI values.

Endosulfan is another active ingredient that has posed challenges for the PDP and EPA over the years. In 1994-1995, PDP reported residues just for "Endosulfans," presumably encompassing all isomers. In its 1996-1999 reports, tables include residues of "Endosulfan I," the isomer "Endosulfan II," and the metabolite "endosulfan sulfate." In all cases, essentially the same number of samples was tested for each endosulfan isomer and metabolite.

We assume that the "Endosulfans" data reported in 1994-1995 is roughly comparable to the sum of the two isomers and one metabolite of endosulfan reported in program years 1996-1999. In calculating TI scores, we use the toxicity data for endosulfan for its two isomers and metabolite, and sum the TI values for each in aggregating TI values for a given food.