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EXPERT PANEL REPORT

# **A Review of the Science on the Potential Health Effects of Pesticide Residues on Food and Related Statements Made by Interest Groups**

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## EXECUTIVE SUMMARY

This report describes the deliberations and conclusions of a scientific expert panel assembled to evaluate statements made by the Environmental Working Group (EWG) and the Organic Trade Association (OTA) regarding the potential health effects of pesticide residues on food and the nutritional quality of organically-grown food compared to food grown using conventional agricultural methods. The panel was commissioned by the Alliance for Food and Farming, but the sponsor did not participate in the production of this report.

The EWG has recently assembled a list of 47 fruits and vegetables for which they have analyzed publicly-available data to determine the number and magnitude of pesticide residues detected on these commodities. This list includes a subgroup that EWG has termed the “dirty dozen,” asserting that these 12 foods contain the highest levels and/or numbers of pesticides relative to other commonly available produce in the United States, and implying that there are known to be adverse health effects associated with consuming these foods that are due to the presence of these pesticide residues. For example, the EWG states that “The growing consensus among scientists is that small doses of pesticides and other chemicals can cause lasting damage to human health, especially during fetal development and early childhood.” “Small” is not defined. The OTA has made similar statements with a focus on the potential negative effects to children, although it has apparently not conducted any relevant independent analysis of exposure or toxicity data or the epidemiology literature.

The panel has reviewed the materials prepared by the EWG and the OTA and came to the following conclusions:

- The EWG’s list may reflect a relatively accurate ordering of the listing of the 47 commodities from the “highest” to “lowest” levels/numbers of pesticide residues. However, the list is misleading to consumers in that it is based only upon exposure data while remaining silent about available information on the assessment of the toxicity of pesticides presented in the diet, and, as such, does not provide a basis to assess risk. There also is no acknowledgment of the fact that the data show that the residue levels detected are, with very rare exception, below or, more likely, well below, the legal limits established only after calculating the potential total non-occupational exposure that an individual might experience to a pesticide approved for use on an agricultural commodity. Furthermore, it is disconcerting that EWG does not describe its methodology in sufficient detail so that others can duplicate their analysis and independently judge its credibility, particularly given the widespread press coverage that its Shopper’s Guide to Pesticides has received.
- The Panel does not agree with EWG’s assertion that there is a “growing consensus among scientists” that the amount of pesticide residues currently found on food constitutes a significant public health issue. While there will always be some uncertainty associated with evaluating the possibility of small health risks, the available scientific data do not indicate that this source constitutes a significant risk.
- The U.S. EPA’s current process for evaluating the potential risks of pesticides on food is rigorous, and health-protective. The EPA’s testing requirements for pesticides used on food are more extensive than for chemicals in any other use category, and include testing targeted specifically to assess the potential risks to fetuses, infants, and children.
- The currently-available scientific data do not provide a convincing argument to conclude that there is a significant difference between the nutritional quality of organically grown food and food grown with conventional agricultural methods.

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## INTRODUCTION

An expert panel was formed at the request of the Alliance for Food & Farming, a consortium representing growers in California. The panel was formed to evaluate the scientific validity of certain materials prepared by the Environmental Working Group (EWG) and the Organic Trade Association (OTA) regarding the health effects of pesticide residues on food and the nutritional quality of organically grown food versus conventionally grown food.

The panel included five respected scientists from diverse backgrounds, including:

- Dr. Penny Fenner-Crisp, U.S. Environmental Protection Agency, Retired
- Dr. Carl L. Keen, University of California, Davis, Department of Nutrition
- Dr. Jason Richardson, Robert Wood Johnson Medical School, Environmental and Health Sciences Occupational Institute
- Dr. Rudy Richardson, University of Michigan, Environmental Health Sciences
- Dr. Karl Rozman, Kansas University Medical Center, Pharmacology, Toxicology & Therapeutics

Attachment A provides biographical sketches of the panelists. The panel included four toxicologists (Drs. Fenner-Crisp, J. Richardson, R. Richardson, and Rozman) and a nutritionist (Dr. Keen).

The panel was commissioned by the Alliance for Food and Farming, but the sponsor did not participate in the production of this report. The panel met by conference call once to discuss a briefing prepared by the sponsor's consultant and held a meeting in San Jose, California in August of 2009. At the San Jose meeting, three of the panelists participated in person and two participated by teleconference. Representatives of the sponsor observed the meeting, but were not active participants.

An outline of a consensus statement was drafted at the San Jose meeting. Subsequently drafts of this report were distributed to panelists until a final version was agreed upon by all panelists.

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## BACKGROUND

EWG recently distributed an updated “Shopper’s Guide to Pesticides” that lists 47 fruits and vegetables of which the top 12 commodities were shown to have the highest detection rates/numbers of pesticide residues (the “dirty dozen”). The Guide also includes the “Clean 15,” a subset of the 47 commodities which were shown to have the lowest levels/numbers of pesticide residues. The Guide is available in supermarkets across the country and also can be downloaded from an EWG-affiliated website ([www.foodnews.org](http://www.foodnews.org)).

The Guide includes a brief description of the methodology used to construct the list. A related EWG website contains slightly more information on the basis for the list, including a list of published references that were presumably used in its development. The site contains two relevant documents including a “Methodology” piece that presents a cursory description of EWG’s methods for selecting the 47 commodities and a “How to Reduce Exposure” section that includes additional information about health impacts, including a list of citations that EWG alleges supports its claims.

EWG’s “dirty dozen” list is as follows (starting with the “worst”):

1. Peach
2. Apple
3. Bell pepper
4. Celery
5. Nectarine
6. Strawberries
7. Cherries
8. Kale
9. Lettuce
10. Grapes (imported)
11. Carrot
12. Pear

EWG’s “Clean 15” includes (starting with the best):

1. Onion
2. Avocado
3. Sweet corn
4. Pineapple
5. Mango
6. Asparagus
7. Sweet peas
8. Kiwi
9. Cabbage
10. Eggplant
11. Papaya
12. Watermelon
13. Broccoli
14. Tomato
15. Sweet potato

EWG assembled the list by analyzing databases of pesticide residue measurements collected by the U.S. Department of Agriculture (USDA) in its Pesticide Data Program (PDP) and the Regulatory Monitoring Program and Total Diet Study of FDA’s Center for Food Safety and Applied Nutrition.

Within the EWG’s report, the discussion of the putative health effects of pesticide residues is very limited, and thus difficult to critically evaluate. The only reference to this topic is the introductory paragraph in the Shopper’s Guide where EWG states:

“The growing consensus among scientists is that small doses of pesticides and other chemicals can cause lasting damage to human health, especially during fetal development and early childhood. Scientists now know enough about the long-term consequences of ingesting these powerful chemicals to advise that we minimize our consumption of pesticides.”

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The above statement does not include any citations, thus complicating a direct evaluation of its relevance with respect to the amounts of residues that have been reported to be present on the foods listed on the dirty dozen list.

Another statement in the “How to reduce exposure” piece states that:

“Even in the face of a growing body of evidence, pesticide manufacturers continue to defend their products, claiming that the amounts of pesticides on produce are not sufficient to elicit safety concerns. Yet, such statements are often made in the absence of actual data, since most safety tests done for regulatory agencies are not designed to discover whether low dose exposures to mixtures of pesticides and other toxic chemicals are safe, particularly during critical periods of development. In general, the government demands, and companies conduct, high dose studies designed to find gross, obvious toxic effects. In the absence of the appropriate tests at lower doses, pesticide and chemical manufacturers claim safety since the full effects of exposure to these mixtures of chemicals have not been conclusively demonstrated (or even studied).”

The most relevant points in this section are the contentions that studies do not exist on low doses of pesticides and pesticide mixtures, both of which are addressed later.

The “How to Reduce Exposure” piece also raises issues associated with increased vulnerability of children and criticism of the Environmental Protection Agency’s (EPA’s) regulation of pesticides.

Similar to EWG, the Organic Trade Association (OTA) has made statements about the health effects of pesticide residues. The OTA focuses on the potential effects of these residues on children<sup>1</sup>:

“In the past decade, research and analysis has shown that children may be much more at risk than adults for pesticide exposure, and may suffer greater harm to health and development from exposure. Yet standards for safety and tolerance limits for these chemicals rarely include adequate consideration of risks to children.

Recent laws now mandate factoring in these risks and re-evaluating safety limits, but the wheels of re-evaluation have turned very slowly. [Note: OTA infers that this task has not been completed. However, it is in error here. The re-evaluation of existing tolerances mandated by FQPA in 1996 was completed in 2008]. Organic foods, therefore, may be especially important to more fully protect children from the risks of exposure, even when pesticide levels in foods are within existing legal limits.

Why are children at greater risk? First, they ingest more food and water per pound of body weight than adults, so any exposure is greater in proportion to their size. Second, these chemicals may be more harmful to developing organs and bodily systems, including neurological and reproductive systems, than they are to mature bodies.

In a study published in May 2002 in *Food Additives and Contaminants*, organic foods were shown to have significantly lower pesticide residues than conventionally

<sup>1</sup> See <http://organicitsworthit.com/environment.html>.

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grown foods (for a number of reasons, such as persistent residues in soil that last for many years, some organic foods may still show residue).

Other studies show the environmental benefits of organic agriculture to air, soil and water, lowering the total toxic burden to our ecosystems. As demand for organic foods continues to grow, more farmers are likely to view organic methods as a viable and marketable option, helping to stabilize supply and price.

It adds up to an evolving landscape that increasingly allows for--and makes a compelling and credible case for--including organic foods in children's diets whenever possible. As concerned parents, teachers, administrators and food service professionals create and insist on innovation and reform in school lunch programs, organic foods make sense as part of the picture."

Regrettably, citations to scientific studies were not provided in the above to support these statements, complicating their critical evaluation.

OTA has an additional document on pesticide exposures and children that focuses on studies that find lower pesticide exposures for those that have organic diets and cites several studies that conclude that there health effects associated with pesticide use for farm workers.

### **CHARGE TO THE PANEL**

The panel was asked to address the following issues:

1. The basis for the EWG ranking of the commodities by pesticide residue levels/ numbers to come up with the list of 47 fruits and vegetables, including the "dirty dozen."

2. The link between pesticide residues on fruits and vegetables, and health effects, including:
  - a. Scientific evidence linking pesticide residues and health effects
  - b. The adequacy of the U.S. regulatory system for protecting against harmful levels of pesticide residues, including effects to infants and children.
3. The evidence that organic foods have a greater nutritional quality than conventionally-grown foods.

### **CHARGE QUESTION #1 - IS THE BASIS FOR SELECTING THE "DIRTY DOZEN" SCIENTIFICALLY SOUND?**

EWG briefly describes its methodology for selecting the list of 47 fruits and vegetables, including the "dirty dozen" on the "Methodology" portion of its Shopper's Guide to Pesticides webpage. Data from the U.S. Department of Agriculture (USDA) Pesticide Data Program (PDP) and the Food and Drug Administration's (FDA) Pesticide Regulatory Monitoring and Total Diet Study Programs were used as the basis for characterizing the numbers and levels of residues of pesticides on the commodities. EWG focused on the 47 fruits and vegetables that were "reported eaten on at least one tenth of one percent of all 'eating days' identified in the 1994-1996 USDA food consumption survey and with a minimum of 100 pesticide test results from the years 2000 to 2007." EWG considered six measures of contamination on commodities:

1. Percent of samples tested with detectable pesticides
2. Percent of the samples with two or more pesticides
3. Average number of pesticides found on a sample
4. Average amount of all pesticides found

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5. Maximum number of pesticides found on a single sample
  6. Number of pesticides found on the commodity in total

EWG assigned each commodity a score of 1 to 100, with 100 being the worst. However, the details on how the scoring for each of the six measures was integrated into a composite score are not provided. Thus, the scores cannot be readily reproduced.

It is also unclear if EWG weighted the six measures in any way. However, an ideal weighting would place more emphasis on the concentrations of the residues that were detected, which appears to only be a part of criterion #4. Merely detecting a residue does not provide an adequate scientific basis for judging whether or not there are potential health effects.

The Panel attempted to reproduce the EWG assessment, using the USDA PDP and FDA Pesticide Residue Monitoring Program<sup>2</sup> data from 2000-2007. If one were to assemble a list of the commodities with the highest rankings, giving equal weight to each of the six measures, the ordering of the 47 commodities on the EWG list appears reasonable, although a few differences could occur with different (and equally arbitrary) assumptions.

The Panel's principal criticism of the list is that there was no attempt to consider the toxicity profile of individual pesticides or to assess risk. Characterization of potential *risk* is the key to understanding if there should be any public health concern about health effects due to the presence of pesticide residues in food. In addition to having information on the levels/numbers of pesticides on the commodities, it is

necessary to consider information on the toxicity of the pesticides. A more scientifically-sound approach would be to integrate the data on the levels of residues (more than in just one of six measures) with data on toxicity of the detected pesticide(s). As it stands now, the EWG "dirty dozen" provides no basis to assess or understand the potential for risk.

Furthermore, given the widespread media attention devoted to the list, it is disconcerting that EWG has not to date shared its algorithm with the scientific community or the public or subjected it to an outside expert peer review, as it often demands of the regulatory agencies whose activities it tracks.

## **CHARGE QUESTION #2 - IS THERE A SCIENTIFIC LINK BETWEEN PESTICIDE RESIDUES ON FOOD AND HEALTH EFFECTS, AND IS THE U.S. REGULATORY SYSTEM ADEQUATE FOR LIMITING HARMFUL LEVELS OF PESTICIDES ON FOOD?**

### **Background**

This section addresses the scientific evidence on the question of whether pesticide residues on food are harmful to human health and the related question of the adequacy of the U.S. regulatory system for limiting harmful levels of pesticides on food.

The Environmental Working Group (EWG) has made several claims about health effects as part of their "dirty dozen" campaign. One key quote from EWG's materials is:

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<sup>2</sup> <http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/Pesticides/ResidueMonitoringReports/ucm125187.htm#fig1-06>.

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“The growing consensus among scientists is that small doses of pesticides and other chemicals can cause lasting damage to human health, especially during fetal development and early childhood. Scientists now know enough about the long-term consequences of ingesting these powerful chemicals to advise that we minimize our consumption of pesticides.” (EWG, undated)

In addition, EWG argues that toxicity testing required by EPA for pesticides is “not designed to discover whether low dose exposures to mixtures of pesticides and other toxic chemicals are safe, particularly during critical periods of development.” (EWG, undated)

The Organic Trade Association (OTA) focuses on potential effects for children and argues that EPA’s toxicity testing requirements are inadequate: “Yet standards for safety and tolerance limits for these chemicals rarely include adequate consideration of risks to children.”<sup>3</sup>

## **General Science of Pesticide Residue Health Studies**

Little published research directly addresses the potential health effects of exposures to pesticide residues in the diet. For example, epidemiologic studies that compare populations with different levels of pesticide dietary exposures are lacking. The vast majority of studies to date that have examined the potential for health effects resulting from pesticide exposure in children are in populations with higher (and, primarily, non-dietary) exposures than the general population, including children of farm workers and pesticide applicators (Arcrury et al., 2007; Eskenazi et al., 2004), as well as children exposed through repeated indoor pesticide

application (Berkowitz et al., 2004). Of these studies, most have focused on the organophosphate pesticides (e.g. chlorpyrifos and diazinon) and found that the levels that these populations were exposed to were much higher than the general population. Based on data from NHANES, the median level of the primary metabolite of the pesticide chlorpyrifos, TCP, in the urine is 1.7 µg/L, whereas median levels of TCP in the more highly-exposed populations are 45%, 94%, and 341% greater than the NHANES values (Arcrury et al., 2007; Eskenazi et al., 2004; Berkowitz et al., 2004). This comparison suggests that the predominant sources of exposure in these studies are from non-dietary sources.

The lack of published literature on health effects arising directly from pesticide residues in food would seem to be evidenced in the fact that neither EWG nor OTA cite a single study that specifically examines exposure via this pathway. Most of the studies that EWG and OTA cite address exposures as a consequence of occupational activities or in environments at/near application sites (e.g., Andersen et al., 2008; Garry et al., 2002; Hoppin et al., 2006). These scenarios generally result in exposures substantially greater than dietary exposures. For example, in EPA’s chlorpyrifos risk assessment, the Agency estimates that the short-term dermal exposure for an aerial applicator to be 50 µg/kg/day with an absorbed dose of 1.5 µg/kg/day, assuming a 3% dermal absorption (EPA, 2006). The estimated inhalation exposure is 0.7 µg/kg/day for a total dose estimate of 2.2 µg/kg/day. By comparison, the estimated chronic dietary exposure is 0.0008 µg/kg/day and the estimated acute dietary exposure is 0.02 µg/kg/day. Thus, the estimated occupational exposure estimate is between 100-3000 times higher than the estimated dietary exposure. Given that EPA uses the 99.9th percentile for acute dietary exposure estimates and the 50th percentile for chronic dietary and occupational exposure estimates, the higher end of the range (3000) is likely the more accurate.

<sup>3</sup> See <http://organicitsworthit.com/environment.html>.



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Only one study cited by EWG is centered on dietary exposure (Petersen et al., 2008), but it focuses on polychlorinated biphenyls (PCBs) and methyl mercury (neither of which are pesticides) and only secondarily addresses occupational exposure to pesticides. Other studies cited by EWG focus on non-pesticides such as PCBs, phthalates and dioxins (Lundqvist et al., 2006; Stewart et al., 2008; Swan et al., 2005).

There is a substantial literature on the health benefits of consuming fruits and vegetables. Numerous published studies show that the consumption of fruit and vegetable-rich diets is associated with a reduced risk for high blood pressure; reduced risk of heart disease, stroke, and probably some cancers; and a lower risk of ocular and digestive problems<sup>4</sup> (e.g., Law et al., 1998; Liu and Russell, 2008; Joshipura et al., 1999; Appel et al., 1997).

Individuals who consume large amounts of fruits and vegetables likely have higher dietary consumption of pesticides, compared to individuals with lower fruit and vegetable consumption<sup>5</sup>. Of course, the research showing the positive effects of fruit and vegetable consumption does not shed much light on the question of whether or not the presence of low levels of pesticide residues may detract from, or have no impact on, the beneficial effects of consuming these foods. However, it strongly supports the hypothesis that some of the alleged adverse effects of dietary consumption of low level pesticide residues are not of the same scale as the beneficial effects of consuming fruits and vegetables; otherwise, the adverse effects from dietary pesticide consumption would be evident in these studies.

## EPA's Regulatory Process

While there is little scientific literature that directly addresses potential adverse effects from pesticide exposures in the diet, the safety of the U.S. food supply with respect to pesticide residues can be evaluated by examining EPA's regulatory process.

Some of the most important points about EPA's regulatory process include:

- EPA requires more toxicity testing for pesticides used on food than any use category of chemicals.
- The development of toxicity reference levels for pesticides representing a "reasonable certainty of no harm" includes the incorporation of uncertainty factors that serve to achieve this regulatory standard. Typically, assessments include at least a 10-fold uncertainty factor for extrapolating from animals to humans, and a 10-fold factor for intraspecies variability, unless empirical data are available to show a different factor better reflects the data at hand. Furthermore, EPA, when establishing tolerances (the legal limits on foods) must include an additional 10-fold safety factor for infants, children or fetuses unless there is convincing evidence that a different factor is appropriate.
- As a default, cancer risk is evaluated using a linear, no-threshold model and a 1 in a million acceptable risk level, unless the available data support the use of a margin-of-exposure approach.
- For acute exposures, EPA bases the assessment on the 99.9th percentile of exposure for different subpopulations, which is greater than the percentiles typically used in risk assessments in other EPA programs.

<sup>4</sup> <http://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/vegetables-and-fruits/>.

<sup>5</sup> It is true that an organic diet will lead to lower pesticide residue consumption. However, only a relatively small fraction of the population consumes only organic food and many of the studies showing the benefits of fruits and vegetables contain subjects for which organic diets were not available for most of their lives.

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- EPA is obligated to assess the aggregate risk to a single pesticide from all dietary and non-occupational exposures when deciding whether or not to approve a new or continued use on a single commodity.
  - EPA also must evaluate the combined risk associated with pesticides and other substances to which the general population may be exposed that have a common mechanism of toxicity using cumulative risk assessment methods. To date, the members of groups of organophosphate, N-methyl carbamates, chlorotriazine, and chloracetanilide pesticides have been assessed. A large group of synthetic pyrethroid insecticides are currently undergoing evaluation.

In accordance with the mandates of the Food Quality Protection Act of 1996, EPA's updated risk assessments have resulted in the reduction of use rates, numbers of allowable uses, and the cancellation of all registrations of many chemicals and product formulations.

The U.S. Department of Agriculture (USDA) manages a monitoring program which measures levels of pesticide residues on a wide variety of foods. The Pesticide Data Program (PDP) data indicate that pesticide residues measured on domestic and/or imported commodities rarely exceed EPA tolerances, and, generally, are one or more orders of magnitude below the legal limit. In 2007, residues exceeding the EPA tolerance were detected in only 0.4% of 11,683 samples (USDA, 2008). While it would be desirable to further limit the already small number of samples that have residues exceeding tolerances, it is important to note that the toxicity of a pesticide does not factor into establishing a tolerance, and the tolerance level represents an exposure that is often substantially less than levels shown to cause effects in animal testing.

## Summary Conclusions for Charge Question #2

The Panel's summary conclusions include:

1. Pesticide residues on food represent a small exposure compared to occupational exposure. There are no studies that specifically link pesticide residues in the diet with health effects. Those epidemiologic studies that posit a link to health effects evaluate populations living in primarily agricultural environments and who are also exposed via other pathways. However, even these studies are insufficient to establish causal relationships. The exposures of these subjects are primarily from pathways in addition to food, with these pathways accounting for much higher levels of exposure. These studies are not capable of assessing any contribution that pesticide residues *in the diet* may make to the risk of exposure to these substances.
2. EPA has adopted a public health protective approach to ensure "a reasonable certainty of no harm" (the legal standard mandated in FQPA) from consuming pesticide residues on food. It incorporates the most sophisticated, data-rich set of risk assessment methods that EPA conducts. Contrary to OTA's assertion, the process explicitly considers infants, children and pregnant women and has an added layer of protection for these subpopulations. While there will always be some uncertainty associated with evaluating the possibility of small health risks, the available scientific evidence shows that EPA's process is appropriately and adequately health-protective.
3. EWG states that there is a "growing consensus among scientists" "that small doses of pesticides and other chemicals can cause lasting damage to human health, especially during fetal development and early childhood." If "small doses" is understood to mean the doses one receives from pesticide residues in food, this statement is not supported by the existing scientific evidence.

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4. The EWG has provided a list of scientific publications to justify their claims about health effects of pesticide residues. None of the papers cited differentiated dietary exposures from other pathways. Therefore, none of the studies is sufficient to draw a conclusion that there are adverse health effects associated with pesticide residues on food.
  5. EWG states “Scientists now know enough about the long-term consequences of ingesting these powerful chemicals to advise that we minimize our consumption of pesticides.” The Panel agrees that pesticide intake should be limited; it is the opinion of the Panel that EPA does a sound job in limiting it to levels meeting the “reasonable certainty of no harm” FQPA standard.
  6. EWG implies that toxicity tests are inadequate. In contrast to this idea, the Panel notes that EPA requires more data for pesticides residues on food than for chemical in other use categories. Contrary to EWG’s assertion, these studies must include at least one dose that shows no effects. If the study results do not reveal a no-effect level, then either the study must be repeated until a no-effect level is identified or have an additional uncertainty factor applied to the lowest dose showing minimal effects, yielding a surrogate no-effect level. There is also a requirement for developmental neurotoxicity testing, designed to assess the potential for neurological effects on developing fetuses and children, for those pesticides known or suspected of possessing neurotoxic potential.

### **CHARGE QUESTION #3 - IS THERE A DIFFERENCE IN THE NUTRITIONAL QUALITY OF ORGANICALLY-GROWN FOOD COMPARED TO FOOD GROWN USING CONVENTIONAL AGRICULTURE?**

There is a perception among many consumers that organically-grown food is nutritionally superior in some respects to food grown with conventional agriculture. Two hypotheses have been put forward to explain the potential differences. One hypothesis is that conventionally-grown plants have more nitrogen available to them through the use of synthetic fertilizers. As a consequence, the resources of the plants are diverted towards supporting growth resulting in a decrease in the production of plant secondary metabolites such as organic acids, polyphenolics, chlorophyll, and amino acids, all of which may have some nutritional benefit (Winters and Davis, 2006). Another hypothesis is that organic production methods lead to greater stresses on plants. A stressed plant then may expend more resources in the synthesis of its own chemical defense mechanisms, which, in turn, may yield substances which would not have positive nutritional effects (Winters and Davis, 2006).

Generally, controlled studies have shown mixed results. Some support the conclusion that organic production methods lead to increases in nutrients. Other studies show no demonstrable differences. A recent analysis conducted by the London School of Hygiene & Tropical Medicine provides a comprehensive review of the available literature (Dangour et al., 2009). The authors identified 46 studies with sufficient documentation and quality upon which they performed a systematic review. Eleven nutritional categories were evaluated. The nitrogen content of conventionally-grown plants was higher, and the phosphorus and titratable acidity levels were higher for organically-grown plants. These differences were considered biologically plausible due to

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differences in fertilizer use (nitrogen and phosphorus) and ripeness at harvest (titratable acidity). There was no difference for the remaining eight categories, including some key ones, including Vitamin C, phenolic compounds, magnesium, calcium, potassium, zinc, total soluble solids, and copper. The authors concluded that:

“The current analysis suggests that a small number of differences in nutrient content exist between organically and conventionally produced foodstuffs and that, whereas these differences in content are biologically plausible, they are unlikely to be of public health relevance.”

The authors encourage more research in this area.

The Scientific Status Summary on Organic Foods from the Institute for Food Technologists (IFT) echoes the conclusions of the London review (Winters and Davis, 2006). The IFT Summary discusses a variety of issues surrounding organic foods, including: (1) levels of pesticides, (2) nutritional value, (3) naturally occurring toxins, and (4) microbiological safety, and includes a summary of a number of key studies comparing organic and conventional foods with respect to nutrient levels.

The IFT Summary states:

In some cases, organic foods may have higher levels of plant secondary metabolites; this may be beneficial with respect to suspected antioxidants such as polyphenolic compounds, but also may be of potential health concern when considering naturally occurring toxins. Some studies have suggested potential increased microbiological hazards from organic produce or animal products due to prohibition of antimicrobial use, yet other studies have not reached the same conclusion. Bacterial isolates from food

animals raised organically appear to show less resistance to antimicrobial agents than those food animals raised conventionally.

While many studies demonstrate these qualitative differences between organic and conventional foods, it is premature to conclude that either food system is superior to the other with respect to safety or nutritional composition. Pesticide residues, naturally occurring toxins, nitrates, and polyphenolic compounds exert their health risks or benefits on a dose-related basis, and data do not yet exist to ascertain whether the difference in the levels of such chemicals between organic foods and conventional foods are of biological significance.”

It is important to state that the nutrient levels in natural plants can vary for a wide variety of reasons. It is plausible for plants grown under different conditions, such as conventional versus organic agriculture, to have different nutritional qualities. However, there is no convincing reason to believe that any one production method is consistently superior in regard to nutrition. This is borne out by the available data which shows mixed results regarding systematic difference between foodstuffs grown with conventional versus organic agriculture.

It is also notable, as the IFT review details, that there is no convincing evidence of greater microbiological risk associated with organic food, as some have suggested. The microbiological risk may be more related to the quality of the production method and the prevention of contamination than from the particular production method used.

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## **ATTACHMENT A - BIOGRAPHICAL SKETCHES OF THE PANELISTS**

### **Dr. Penny Fenner-Crisp**

Dr. Fenner-Crisp served as the Executive Director of the ILSI Risk Science Institute (RSI) from December 2000 until August 2004, following a 22-year career at US EPA. Her duties at EPA included nearly 12 years serving in several capacities as the Senior Science Advisor, Deputy Director and Director of the Health Effects Division of the Office of Pesticide Programs. Earlier assignments included serving as the Director of the Health and Environmental Review Division (HERD) of the Office of Pollution Prevention and Toxics (OPPT) and Senior Toxicologist in the Health Effects Branch of the Office of Drinking Water (ODW). She played key roles in the development of many EPA risk assessment policies and practices primarily related to human health and was involved in the activities of several international organizations as an expert on several WHO IPCS working groups, as a member of the WHO Expert Panel of the Joint Meeting on Pesticide Residues for nine years and as the lead U.S. Delegate to several workgroups of the OECD test guidelines program. In April, 2000, she received the Agency's highest award, the Fitzhugh Green Award, for her contributions on behalf of EPA to its international activities.

Dr. Fenner-Crisp received her Ph.D. in Pharmacology from the University of Texas Medical Branch in Galveston and is a member and former officer of several professional scientific societies including of the Society of Toxicology and the Society for Risk Analysis. She has been a Diplomate of the American Board of Toxicology since 1984 and served on its Board of Directors from 2001-2005. She served on EPA's Endocrine Disruptor Methods Validation Subcommittee from 2001-2004 and the Strategic Science Team of the American Chemistry Council's Long-range Research Initiative from 2002-2005. Currently, she is a member of the Board of Directors of the Midwest Center for Environmental Science and

Public Policy, the Drinking Water Committee of EPA's Science Advisory Board and EPA's National Pollution Prevention and Toxics Advisory Committee. She also is a member of the National Academies of Sciences expert group charged with conducting a review of the Worker and Public Health Activities Program administered by the Department of Energy and the Department of Health and Human Services.

### **Dr. Carl L. Keen**

Dr. Carl L. Keen is the Mars Chair in Developmental Nutrition, Professor of Nutrition & Internal Medicine, and a Nutritionist in the Agricultural Experiment Station at the University of California at Davis. Dr. Keen received his B.S. and Ph.D. degrees in Nutrition from the University of California, Davis. Dr. Keen's research group has four main areas of focus. The first concerns the influence of diet on embryonic and fetal development. A significant proportion of birth defects are the consequence of embryonic and fetal malnutrition. A thesis in the laboratory is that the correction of suboptimal nutritional deficiencies during early development should result in a marked reduction in pregnancy complications. The second research theme in the group is the study of gene-nutrient interactions, with an emphasis on how subtle changes in cell nutrient concentrations can influence the expression of select genes. The third major research theme in the group is the study of how diet influences oxidant defense systems and cellular oxidative damage. The fourth area of research in the laboratory is on the effects of diet on the development and progression of vascular disease. A current hypothesis in the laboratory is that the putative cardiovascular health benefits associated with plant food-rich diets can be attributed in part to their flavanol content. Dr. Keen's group has over 600 peer-reviewed scientific papers in the above areas.

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### **Dr. Jason Richardson**

Jason Richardson, M.S., Ph.D. is an Assistant Professor in the Department of Environmental and Occupational Medicine at Robert Wood Johnson Medical School and Resident Member of the Environmental and Occupational Health Sciences Institute. He received his M.S. and Ph.D. degrees from Mississippi State University where he conducted research on mixtures of organophosphate pesticides and the developmental neurotoxicity of organophosphates during critical periods of development. He then completed postdoctoral training in Molecular Neuroscience and Neurotoxicology at Emory University. His research at EOHSI focuses on the role of environmental exposures during development and how such exposures interact with genetic susceptibility to produce neurological disease.

### **Dr. Rudy Richardson**

Dr. Richardson is the Dow Professor of Toxicology and Associate Professor of Neurology at the University of Michigan School of Public Health. He received his B.S. (*magna cum laude*) in Chemistry from Wichita State University. Upon achieving Ph.D. candidacy in Chemistry at SUNY Stony Brook, he transferred to Harvard, where he earned the Sc.M. and Sc.D. degrees in Physiology/Toxicology. After postdoctoral work in Neurochemistry at the Medical Research Council Toxicology Unit in Carshalton, England, he joined the University of Michigan as Assistant Professor of Toxicology. Apart from sabbatical leaves at Warner-Lambert/Parke-Davis (now Pfizer) in Ann Arbor and the University of Padua in Italy, Dr. Richardson has been based at Michigan, where he has risen through the ranks to full professor. During 1993-1999 he served as director of the Toxicology Program and in 1998 he was appointed as the Dow Professor of Toxicology. He is board-certified by the American Board of Toxicology (DABT). His research has focused on mechanisms of acute and delayed

neurotoxicity of organophosphorus compounds. Currently he uses kinetics, molecular modeling and mass spectrometry to understand interactions of toxicants with target macromolecules and to develop biomarkers of exposure, toxicity and disease.

### **Dr. Karl Rozman**

Dr. Rozman is a Professor of Pharmacology, Toxicology & Therapeutics at the Kansas University Medical Center. He holds a Ph.D. from the University of Innsbruck in Organic and Pharmaceutical Chemistry. He is a Diplomate of the American Board of Toxicology and a member of many journal editorial boards. Dr. Rozman's research is aimed at elucidating the mechanism of toxicity of chlorinated aromatic hydrocarbons (CAH) and related compounds. The cause of 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced death (and related compounds) in rats is a combination of appetite suppression and inhibition of gluconeogenesis, whereas in mice it appears to be inhibition of gluconeogenesis alone, leading to a lethal hypoglycemia. Currently three lines of research are being pursued: 1) elucidation of the molecular mechanism(s) of action leading to CAH-induced enzyme inhibition; 2) investigation of the subchronic and chronic toxicities of TCDD and its higher chlorinated homologues as well as other heterocyclic analogues such as chlorinated phenothiazines (CPT), and 3) studying female reproductive toxicity of both CAH and CPT. Dr. Rozman has studied chlorinated pesticides extensively such as DDT, hexachlorobenzene, pentachlorophenol, dieldrin, heptachlor, chlordane and more. He has published more than 30 original manuscripts on these topics and has written many book chapters and review articles on chlorinated pesticides as well as on organophosphates.



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## ATTACHMENT B -

### EPA'S REGULATORY PROCESS FOR PESTICIDE RESIDUES ON FOOD

#### Background on Pesticide Regulation

EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). These acts were significantly amended in 1996 by the Food Quality Protection Act (FQPA). FQPA was, at least partly, motivated by the National Research Council's (NRC's) 1993 report "Pesticides in the Diet of Infants and Children," which recommended changes to EPA's risk assessment methods for pesticide residues on food, particularly to provide better protection for infants and children. FQPA called for enhanced stringency in the system of regulation for pesticides and adopted "a reasonable certainty of no harm" standard.

The EPA regulates the residues of pesticides on food commodities using an extensive risk assessment process, with two key elements: (1) characterization of toxicity through an extensive body of required tests, and (2) estimation of dietary exposure through the use of models coupling data on food consumption with data on pesticide residues from field trials, monitoring data, etc.

#### Toxicity Testing

The EPA requires more toxicity data for agricultural pesticides of conventional chemistry than any for other type of chemical. The data requirements for pesticides are detailed in 40 CFR Part 158. The required toxicity tests for these pesticides used on food include:

- Acute oral toxicity – rat
- Acute dermal toxicity
- Acute inhalation toxicity – rat
- Primary eye irritation – rabbit
- Primary dermal irritation
- Dermal sensitization
- Acute neurotoxicity – rat
- 90-day oral – rodent
- 90-day oral – non-rodent
- 21/28 day dermal
- 90-day neurotoxicity
- Chronic oral – rodent
- Carcinogenicity – two rodent species
- Prenatal developmental toxicity
- Reproduction and fertility effects
- Bacterial reverse mutation assay
- *In vitro* mammalian cell assay
- *In vivo* cytogenetics
- Metabolism and pharmacokinetics
- Immunotoxicity

All of these studies are conducted under Good Laboratory Practices (GLP) and the data are reviewed by EPA before they are judged acceptable for risk assessment.

As listed in 40 CFR 158.500, there several other toxicity tests that EPA can conditionally require if needed to refine the risk assessment (e.g., developmental neurotoxicity). Also, many registrants voluntarily conduct additional toxicity studies to refine the risk assessment of their chemicals or to fulfill requirements in other countries. Also, at its discretion, EPA can use open literature data to refine the assessment.

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## **Development of Toxicity Reference Values**

Following the receipt, review and acceptance of the toxicity data by EPA, toxicity reference values are derived for acute and chronic exposure durations, and for lifetime cancer risk, if the pesticide is found to be a carcinogen. EPA uses standard methods to calculate the toxicity reference values, except that they must add an additional 10-fold safety factor to protect children, unless the available data show that some other factor is more appropriate (see below).

The first step in the process is the determination of the point-of-departure for risk assessment. Historically, the point-of-departure was a no observed adverse effect level (NOAEL) from a toxicity study of appropriate duration. However, EPA is moving away from the use of NOAELs when possible, and, instead, deriving benchmark doses (BMDs). As an example, EPA has derived BMDs for cholinesterase-inhibitors, including organophosphates and N-methyl carbamates. To estimate the BMD for this class, EPA first finds whether the brain or red blood cell (RBC) compartments are more sensitive. The BMD for the point-of-departure is usually chosen as the estimated dose that causes a 10% inhibition of either brain or RBC cholinesterase, whichever gives a lower result. This approach is more conservative than other agencies such as the World Health Organization (WHO) which recommends a 20% inhibition for the point-of-departure.

EPA applies various uncertainty factors to the point-of-departure, generally including a default 10-fold factor for animal-to-human extrapolation (interspecies variation) and a default 10-fold factor for intraspecies variation. Chemical-specific data, when available, would prompt the application of chemical-specific uncertainty factors. EPA may also apply additional factors for database deficiencies or for extrapolation from subchronic to chronic exposures.

One of the most significant changes mandated in FQPA was the obligation of the agency to apply an additional default safety factor of 10 for the added protection of infants and children. The “FQPA 10X factor” can be adjusted if “on the basis of reliable data, such margin will be safe for infants and children.” As an example, if it can be shown that there is no difference in toxicity for infants and fetuses, compared to adults and there are no database deficiencies, then the FQPA factor may be reduced to as little as 1X.

For cancer risk assessment, as a default, EPA typically uses a linear, no-threshold dose-response model to estimate a unit risk (or potency) factor, based on tumor rates in the animal studies. The unit risk factor can be multiplied by a lifetime average exposure to estimate a lifetime risk. In many cases, depending upon the number and nature of the observed tumor types and number of species showing a positive carcinogenic response, a margin-of-exposure approach to the quantitative risk assessment may be preferred.

## **Exposure Assessment**

EPA estimates dietary exposure to pesticide food residues using residue data collected in field trials, post-harvest, or in market basket surveys, in combination with data on food consumption.

Pesticide registrants obtain registrations for a pesticide on a crop-specific basis. Therefore, for each crop that a pesticide is used on, the registrant must submit field trial data that include measurements of pesticide residues on the commodity following an application at the maximum application rate and minimum

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pre-harvest interval that will be allowed. From the field trial data, a tolerance is established for each crop-pesticide combination. The tolerance represents an upper-bound estimate of the pesticide residue concentration on the crop; the toxicity of the pesticide does not play a role in establishing a tolerance, although it is a factor in whether or not the tolerance is approved. If a food is found with residues exceeding the tolerance or with residues of an unapproved chemical, the food is considered adulterated.

EPA uses residue data from the PDP and FDA's monitoring programs in its higher-tier risk assessments.

EPA characterizes food consumption using USDA's Continuing Survey of Food Intake by Individuals (CSFII). The CSFII is a survey of the food intake of more than 20,000 individuals. These data are used to provide a distribution of the intake of a large range of different food items, and the data are divided into different age and gender categories to derive separate pesticide residue exposures across these categories. Therefore, food intake specific to infants and children are used, as well as women of child-bearing age (a separate risk assessment may be conducted for this subset of adult females if there are reproductive or developmental effects). The software programs used by EPA to perform these calculations contain recipes for processed foods which allow users to estimate the pesticide residues in processed food based on the different ingredients. Also, EPA has published default processing factors which provide estimates of the effect of processing on pesticide residues compared to raw commodities. For higher tiers of risk assessments, registrants may also conduct additional chemical-crop specific processing studies.

There are four tiers of dietary risk assessment, each with increasingly complexity:

1. **Tier 1:** Tolerance levels are used to estimate residue levels; 100% of the crop is assumed to be treated with the pesticide (usually a very conservative assumption); default processing factors.
2. **Tier 2:** Either the tolerance or the highest residue level from the field trial is used (for certain foods, average field trial residues may be used); 100% crop treated; chemical-crop specific processing factors are used.
3. **Tier 3:** The entire distribution of field trial data and/or the PDP survey data can be used and adjusted for the percent crop treated (i.e., the percent of a given crop treated with a pesticide).
4. **Tier 4:** A market basket survey is conducted and used for risk assessment.

The tiering system provides a variety of approaches from easily applied methods to (lower tiers) that give conservative results (i.e., tend to overestimate risk) to more sophisticated methods that require more effort but more closely approximate reality.

In all cases, software is used to estimate the pesticide exposure for each individual or for each population group in the CSFII based on their individual consumption data or on average consumption estimates for the population. The end result is a distribution of exposures for different age groups.

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## Risk Assessment

EPA conducts a risk assessment by comparing the Population Adjusted Dose (PAD) with the pesticide residue dose estimates. The PAD is the reference dose (point of departure divided by uncertainty factors) divided by the FQPA factor. The PAD and RfD are the same if the FQPA factor is reduced to 1X. For an acute risk assessment, EPA takes the 99.9<sup>th</sup> percentile of the distribution across the individuals in the CSFII for each subpopulation and compares that with the acute PAD<sup>6</sup>.

For chronic risk assessment, EPA compares the mean pesticide residue dose estimate with the chronic PAD. For cancer risk assessment (if applicable), EPA estimates a lifetime cancer risk by multiplying the unit risk estimate by the dose estimate or calculates the size of the margin-of-exposure.

If, after all refinements in the risk assessment are complete, there is an exceedance of either the acute or chronic PAD, or if the cancer risk is greater than 1 in a million or exceeds an acceptable margin-of-exposure, adjustments must be made. The adjustments may include a deletion of one or more crops from the label (thus disallowing use on those crops) or a change in the use pattern(s), including the application rate, number of applications, interval between applications, or pre-harvest interval. After the adjustments are made, the assessment is rerun to determine if the “reasonable certainty of no harm” standard has been met. This process is repeated until the standard is met, the use(s) is/are cancelled, or the registration for the chemical is discontinued by the registrant or cancelled by EPA.

<sup>6</sup> Since the Tier 1 assessment is so conservative, a 95<sup>th</sup> percentile is used.