Impacts of the Food Quality Protection Act on Children's Exposures to Pesticides

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I. Introduction

Substantial evidence gathered over the past half century has shown that environmental exposures in early life can alter patterns of childhood development, and influence life-long health and risk of disease and dysfunction (National Research Council 1984). Among the chemical exposures identified as potentially harmful to early development are: cigarette smoking during pregnancy (Haddow et al., 1998), thalidomide, diethylstilbestrol (DES) (Herbst et al., 1970), lead (Dietrich et al., 2001; Ris et al., 2004), ethyl alcohol (Lupton et al., 2004), ionizing radiation (Newcombe et al., 1971), polychlorinated biphenyls (PCBs) (Jacobson et al., 1996), organochlorine pesticides (Longnecker et al., 1997; Longnecker et al., 2001; Longnecker et al., 2002), methyl mercury (Trasande et al., 2005a), outdoor air pollutants (Trasande et al., 2005b), benzene (Pedersen et al., 2004; Raaschou-Nielsen et al., 2001) and certain other pesticides (Gray et al., 2001), especially the organophosphate insecticides (NRC, 1993).

Prenatal factors and early childhood exposures also play a role in development of disease in later life (Barker 2004a; Barker 2004b; Barker et al., 2005; Barker 2005; Eriksson et al., 2003; Forsen et al., 2004; Kajantie et al., 2005; Syddall et al., 2005). Fetal growth has been linked to risk of cardiovascular function, hypertension, and diabetes in adulthood, and accelerated childhood

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growth is related to subsequent risk of breast cancer in women (Ahlgren et al., 2003; Ahlgren et al., 2004), as well as to impaired glucose tolerance in adulthood. There are almost certainly additional etiologic associations, some subtle but nonetheless important across a large population, between the environment, pre- and perinatal exposures, and disease in children.

Progress in identifying the environmental causes of disease has been slow and incremental. Reasons include the fact that most studies have:

- Examined relatively small populations of pregnant women and their offspring;
- Focused on one chemical at a time;
- Lacked the statistical power needed to examine interactions among chemical, social, and behavioral factors in the environment, and gene–environment interactions; and
- Suffered from the brief duration of follow-up.

Previous discoveries of environmental exposures that influence children's health and development have produced significant gains for disease prevention. Examples include reductions in the use of alcohol and tobacco during pregnancy (Lumley et al., 2004), minimization during pregnancy of diagnostic X-rays, and removal of lead from gasoline (Grosse et al., 2002). Evidence is presented in this symposium suggesting that the major changes in regulation called for in the Food Quality Protection Act (FQPA) have begun to reduce infant and child exposures to OP insecticides, resulting in tangible improvements in reproductive outcomes and children's health.

Changing Patterns of Disease in American Children

Patterns of illness have changed substantially in the past century among children in the United States and other industrial nations (see Centers for Disease Control statistics at http://www.cdc.gov/nchs/hus.htm). Infant mortality has declined. Life expectancy has increased. With notable exceptions such as HIV/AIDS, infectious diseases have receded as the leading cause of illness and death.

Today the major illnesses confronting children in the United States are a group of chronic conditions, including a number of psychosocial and behavioral conditions termed the "new pediatric morbidity" (Haggerty 1995). These include:

- Asthma -- the leading cause of hospitalization and school absenteeism, asthma more than doubled in incidence between 1980 and 1996 (Centers for Disease Control 1998).
- Childhood and young adult cancers, such as acute lymphocytic leukemias, brain cancer and testicular cancer -- the incidence rates of these malignancies have increased by 10 percent (Shu et al., 1995), 40 percent (Schechter 1999) and 68 percent respectively (Devesa et al., 1995), over the past 15 to 30 years, despite declining mortality.

- Neurodevelopmental disorders, including learning disabilities, dyslexia, mental retardation, attention deficit disorder, and autism – occurrence is more prevalent than previously thought, affecting 5 percent to 10 percent of the 4 million children born in the United States annually (Bertrand et al., 2001; LeFever et al., 1999).
- Obesity and type 2 diabetes -- increasingly important among American children. In 2003, 43 percent of young children entering kindergarten in New York City were overweight or obese (Thorpe et al., 2004).

Beyond childhood, incidence rates of chronic neurodegenerative diseases of adult life such as Parkinson's disease and dementia have increased markedly. These trends raise the possibility that exposures in early life act as triggers of later illness, perhaps by reducing the numbers of cells in essential regions of the brain to below the level needed to maintain function in the face of advancing age. Prenatal and childhood exposures to pesticides have emerged as a significant risk factor explaining impacts on brain structure and health that can increase the risk of neurological disease later in life (Landrigan et al., 2005).

II. Genesis of the FQPA

From the early 1970s through July, 1996 the Environmental Protection Agency (EPA) searched for ways to abide by conflicting statutory provisions in the two federal laws governing the establishment, review, and modification of pesticide tolerances.

The Delaney Clause, a provision in Section 409 of the Food, Drug and Cosmetic Act, prohibited government agencies from knowingly approving a food additive that poses ***any*** level of cancer risk. The Delaney Clause applied to tolerance setting when pesticide residues concentrated in processed or dried foods, because concentrated residues were regarded as food additives. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the statute governing pesticide regulation, called upon the Environmental Protection Agency (EPA) to apply a risk-benefit standard when deciding whether a tolerance could be set covering residues of cancer-causing pesticides, including those known to concentrate in processed food.

To resolve this discrepancy, in 1984 the EPA commissioned a National Academy of Sciences (NAS) review of the conflicting standards and basis for pesticide tolerance setting. This analysis resulted in the 1987 NAS/NRC report *Regulating Pesticides in Food: The Delaney Paradox*. This report called for fundamental changes in federal law and pesticide risk assessment procedures. It also concluded that pregnant women, infants, and children faced unique risks from pesticide exposure, and that existing EPA risk assessment procedures were not taking these unique risks into account (NAS, 1987).

As a logical follow up to the *Delaney Paradox* report, in 1988 the U.S. Congress directed the EPA to request an NAS review of pesticides and risks to children. One of the authors of this report (PJL) was asked to chair the NAS/NRC committee that took on this task. Our committee first met in October of 1988 and our report was released in June 1993 (National Research Council 1993). The major finding of this report was that children are profoundly different from adults in their exposures and vulnerability to pesticides. The report called for fundamental revision of the procedures used to establish pesticide tolerances to account for the unique vulnerability of infants and children.

Pesticides in the Diets of Infants and Children has proven to be a highly consequential Academy report. It stated forcefully the new consensus in the public health community that regulation of toxic chemicals must focus, first and foremost, on protecting infants and children. It led to the creation and refinement of the U.S. Department of Agriculture's "Pesticide Data Program" and to major new EPA research initiatives. It also helped break a political stalemate that had persisted for 20 years.

The legislative debate over the reform of the Delaney Clause had been going on in Washington D.C. since the 1970s. Each year members of Congress supportive of either stricter application of the Clause or its repeal introduced legislative proposals and held hearings. When the 1993 NAS report was issued, the EPA, pesticide industry, and most environmental organizations positively received our findings and recommendations for fundamental regulatory reform. The report provided the foundation for a way to unravel the Delaney Paradox and bring modern science to the assessment and regulation of pesticide risks to infants and children.

The high drama over the reform of the Delaney Clause came to an abrupt end on July 24, 1996 when the House of Representatives passed the Food Quality Protection Act (FQPA) without a single dissenting vote after only a few minutes of discussion. On the next day, the Senate passed the bill on a unanimous consent motion after barely ***one*** minute of discussion.[1]

The *Washington Post* ran a story describing the long process that led to passage of the FQPA in its Sunday edition. The lead paragraph states –

> "The new federal food safety law, which swept through Congress without opposition and was blessed by many industry and environmental groups, is a rare legislative compromise in which all sides can declare a measure of victory." (*Washington Post*, July 28, 1996).

[1] For details on the FQPA, its passage, President Clinton's signing statement and news accounts of the passage of the bill, see http://www.ecologic-ipm.com/fqpa.html

In his August 3rd statement at the FQPA signing ceremony, President Bill Clinton said –

> "From the day I took office I have worked hard to meet what I think is a fundamental promise that we should make to our people. People should know that the food they eat and the water they drink will not make them sick…
>
> "Today we add the cornerstone to this solid foundation [of new laws] with the Food Quality Protection Act. I like to think of it as the 'peace of mind' act, because it'll give parents the peace of mind that comes from knowing that the fruits, the vegetables, the grains that they put down in front of their children are safe. It's long overdue. The old safeguards that protected our food from pesticides were written with the best of intentions, but they weren't up to the job. And as you can see from the vast array of support here across every sector of American life, nobody liked them very much and no one thought that they really worked as they were supposed to. Bad pesticides stayed on the market too long, good alternatives were kept out." (Posted in full at http://www.ecologic-ipm.com/pandv.html)

III. The FQPA's Major New Provisions

The FQPA incorporated into federal law the major recommendations of the 1987 and 1993 NAS/NRC reports. A new and consistent standard – "reasonable certainty of no harm" – was put in place to govern the review, establishment, and adjustment of all pesticide tolerances. The EPA was directed to place greater weight on the risks faced by pregnant women and infants and children. New provisions were added to FIFRA to transform the statute's risk-benefit decision rule to a purely health-based standard for the purpose of tolerance setting. Effective on the date of passage, all new petitions for pesticide tolerances were to be reviewed and approved in accord with the new "reasonable certainty of no harm" standard.

The EPA was also directed to review the 9,721 tolerances on the books to assure they were in compliance with the FQPA's new safety standard. The agency was responsible for reviewing the riskiest one-third of pesticide tolerances within three years of passage (i.e., by summer 1999). Two-thirds of existing tolerances were to be reviewed and brought into compliance with the new statute six years after passage (summer 2002). Within 10 years, all tolerances were to be reviewed and adjusted as needed, or by August 2006.

There were four major changes made by the FQPA in how the EPA evaluates pesticide dietary risks and makes tolerance decisions:

- Assure that pesticide tolerances are safe for vulnerable populations, in particular, infants, children, and the elderly, based on a "reasonable

certainty of no harm" standard (i.e., a health-based standard, not cost-benefit balancing);
- Aggregate exposure to a pesticide from all dietary sources, drinking water, residential, and other routes must be taken into account;
- An added 10-fold safety factor shall be added in setting pesticide Reference Doses (RfDs) to account for the unique risks faced by infants and children, unless the Administrator has solid data supporting a determination that existing RfDs were fully health protective, even for infants, and that exposures were fully and accurately characterized;
- For pesticides that pose human risks through a common biological mode of action (like the organophosphate insecticides), aggregate exposures to all such pesticides must be evaluated together in determining whether a given tolerance is safe.

IV. Impacts of the FQPA's 10-X Provision

The FQPA requires EPA to impose an added 10-fold safety factor when setting acceptable levels of exposure to pesticides and when establishing tolerances. In practice, the EPA does this by dividing existing acute and chronic Reference Doses by the applicable FQPA safety factor, reducing allowable aggregate exposures up to ten-fold. The resulting estimates of acceptable daily exposure are called acute and chronic "Population Adjusted Doses" (aPADS, cPADs) and are usually reported in milligrams of pesticide per kilogram of bodyweight.

An FQPA safety factor less than 10-fold can be adopted if the Administrator has solid data supporting three judgments:
- A pesticide is no more toxic to young animals than adults, and
- A pesticide's Reference Dose is fully protective of infants and children, and
- The agency has ample data to accurately estimate exposures and risks from all pathways.

In many cases the EPA lowered the FQPA safety factor to three or zero. Safety factors other than zero, three, and ten were periodically considered, but never applied. EPA pledged to base its 10-X decisions on the "weight of the evidence."

Consumers Union (CU) released a report in 2001 analyzing the impacts of the FQPA five years after its passage (Consumers Union 2001). It assessed the EPA's 10-X decisions on organophosphate (OP) insecticides, the agency's major focus in the first five years of the FQPA implementation process.

Out of 49 OPs subject to FQPA review, five were not registered in the U.S. and were not evaluated. Because of the acute nature of OP cholinesterase inhibition, EPA chose to establish both acute and chronic PADs. By the end of

2000, acute PADS were established for 38 OPs, and chronic PADs for 44, for a total of 82 10-X decisions on the OPs.

CU reports that EPA retained a full 10-X added FQPA safety factor in only 13 of the 82 10-X decisions on OPs, or just 16 percent. In another 16 percent of these decisions, EPA retained a 3-X added FQPA safety factor. Combining cases with a 3-X and 10-X FQPA safety factor, an extra safety factor designed to ensure "reasonable certainty of no harm" to children was retained by EPA in one-third of its decisions on OP Population Adjusted Doses. In two-thirds of its OP PAD decisions, the agency set the FQPA safety factor at zero, decisions that remain controversial and in the eyes of many, incompatible with a core provision of the FQPA.

The most commonly cited reason for retaining the full 10-X was the absence of an adequately designed developmental neurotoxicity (DNT) study (10 of 13 cases). Evidence of neurotoxicity and/or evidence of heightened sensitivity of offspring or prenatal/developmental toxicity were the next most frequent reasons EPA cited for retaining an extra safety factor.

V. Impacts of the FQPA on Dietary Exposures and Risk

The EPA faced a daunting task in implementing the FQPA. A number of new science policies had to be developed to translate the law's new provisions into risk assessment procedures and decision-making rules. Much new data had to be compiled and integrated in ways to support aggregate and cumulative risk assessments.

There were 9,721 pesticide tolerances in place when the FQPA passed and 1,780 involved economically important food uses (based on applications to 1 percent or more of national crop acreage[2]). Of these, 381 were covered by pesticide residue data collected by USDA's "Pesticide Data Program" (PDP). According to dietary risk analyses carried out by Consumers Union, 125 of these 381 pesticide-food combinations accounted for 99 percent of dietary risk based on PDP residues, and of these, 63 were organophosphate (OP) insecticides. This is why the EPA has focused so much attention on the OPs in the FQPA implementation process.

The EPA regulates dietary risks under the FQPA at the 99.9th percentile level of exposure, based on a probabilistic distribution of dietary exposures. Monte Carlo simulation methods are used to generate hundreds of thousands to millions of "eating day episodes" for a person of known weight. A simulated estimate of pesticide exposure per kilogram of bodyweight is made based on the actual foods reported as eaten by the individual in the USDA's food consumption survey. Each food is also linked to a distinct record in the PDP residue data file

[2] Based on pesticide use data from annual surveys of the USDA's National Agricultural Statistics Survey.

for the same food. The computer randomly selects a residue value, such that the most common levels are chosen more frequently, and higher residue levels are picked only as frequently as they appear in PDP sampling.

A person's daily exposure to a given pesticide is estimated by summing exposures across all foods. The results are expressed in milligrams of pesticide ingested per kilogram of bodyweight and are arrayed from the highest exposure to the lowest.

Under FQPA science policies, all tolerances covering food uses of a pesticide are regarded as acceptable if the child at the 99.9th percentile level of the exposure distribution curve ingests less of the pesticide than "allowed." The amount of OP exposure allowed by the FQPA's "reasonable certainty of no harm" standard is based on the pesticide's acute Population Adjusted Dose (aPAD). Risk reduction measures are typically invoked in cases where EPA judges that exposures at the 99.9th level exceed the applicable aPAD.

Typically, the age group that is exposed to the greatest amount of pesticides per kilogram of body weight is one to two year old children, or children through age 13. This is why EPA has focused so heavily on children's exposures and risks throughout the FQPA implementation process, and why the impacts of the FQPA should be judged relative to changes in risks to children.

EPA's Cumulative Risk Assessment of the OPs

In response to requests from interested parties, the EPA released detailed results of its June 2002 cumulative risk assessment (CRA) of the OPs, allowing assessment of the distribution of risks across foods, pesticides, and food-pesticide combinations. Some key insights emerge from the OP-CRA results –

- Eight of 30 OP insecticides accounted for 97 percent of total estimated OP-related risk;
- A single insecticide (dimethoate and its metabolite omethoate) accounted for 47 percent of total risk, largely from residues in just two foods, grapes and apples;
- Grapes, apples and pears accounted for over three-quarters of total risk; and
- Fresh fruits and vegetables accounted for the vast majority of exposure and risk.

The June 2002 OP-CRA confirmed Consumer Union's earlier finding -- a relatively small number of OP insecticide uses account for the majority of risks faced by infants and children. Grapes, in particular, emerged as a major risk-driver.

Impacts of EPA Actions on Dietary Risks

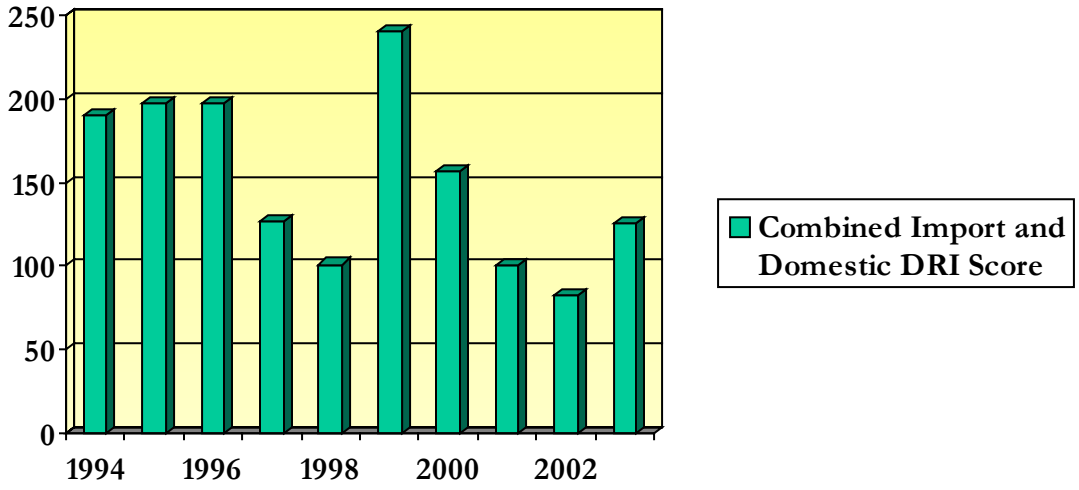
The vast majority of pesticide uses do not result in detectable residues in food. The EPA's cumulative risk assessment of the OPs, as well as CU's assessment of all foods, show that well less than 100 uses account for well over 90 percent of dietary risk. Likewise, Benbrook's EPA-OIG analysis of residues in all PDP foods from 1994 through 2003 shows that a few dozen risk drivers account for most of aggregate dietary risk (Benbrook 2005).

In the EPA-OIG analysis, aggregate DRI scores over time for 16 foods were calculated for domestically grown food, imports, and all samples combined. The foods were selected from all PDP-tested foods as a function of the number of years each food had been tested from 1994 through 2003; foods tested in three or fewer years were excluded.

The most reliable indicator of trends in aggregate DRI scores is the average DRI score per food tested in a given year. This is because of significant variation in the number of the 16 foods tested by PDP in a given year. For example, in 1997 and 1998 only three of the 16 foods were tested, whereas 10 of the 16 were tested in domestic samples in 1994, 2000, 2001, and 2002.

Average domestic DRI scores per food tested fell from 225 in 1994 to 65 in 2003, while the average of DRI scores per food for imports rose from 98 to 244. Across all samples, average DRI scores per food fell from 191 to 126. Trends in domestic, imported and combined average DRI scores are shown in Figure 1.

FIGURE 1. Average DRI Levels per Food Tested, 1994-2003



Growing Importance of Imports

In most of the United States, consumers rely on imported fresh fruits and vegetables for three to five months each year. Residue data collected by the USDA's PDP identifies the geographic origin of each sample, making it possible to assess risk levels in imported grapes, apples, or tomatoes, compared to domestically grown produce.

The EPA's cumulative risk assessment of the OPs identified dimethoate and its metabolite omethoate in grapes as by far the major OP risk driver, accounting for 44 percent of total OP risk. When all positive dimethoate grape samples in the PDP database are ranked from highest to lowest, 94 of the top 100 residue values were found in imported grapes. Likewise, 2002 PDP testing showed found that 94 of the top 100 chlorpyrifos residue values were in imported peaches and the highest 13 samples were all from Chile.

The major and growing contribution of imported fruits and vegetables in dietary risk is evident as well in the results of the analysis carried out by Benbrook for the EPA's Office of Inspector General. (The purpose of that study and its methodology are described in Benbrook's paper, this session). Dimethoate Dietary Risk Index (DRI) scores in domestic grapes in 1996, 2000, and 2001 were respectively 0.1, 0.03, and 0.3. DRI values for dimethoate in imported grapes were 35.1, 42.9, and 21.6 in the same years.

The large increase in DRI scores per food tested for imports is worrisome for several reasons. Imports account for about one-third of domestic consumption of fruits and vegetables. The consumption of imported produce in the U.S. typically occurs during the late fall and winter months. These results point to rather large reductions in pesticide risk during the peak of U.S. fruit and vegetable production, from April through late fall, when imports are very modest, but also a large increase in risks in the winter when several imported foods, especially grapes, peaches, pears, and tomatoes, enter the market.

The shift in OP exposures from domestically grown to imported produce reflects the differential impact of the FQPA. The vast majority of FQPA-driven risk reduction actions have entailed changes in pesticide use patterns, such as lower application rates, fewer applications, longer pre-harvest intervals, and other restrictions designed to lower farm worker risks. These changes in pesticide use patterns are brought about through label amendments that impact pesticide use only in the U.S. In nearly all cases where the EPA has added new label restrictions, it has left tolerances unchanged.

Label changes only impact U.S. pesticide use; tolerance changes impact farmers here and abroad, since they apply to all food imported to the U.S. For this reason, U.S. farmers have adopted lower-risk use patterns, while growers

outside the U.S. have been able to continue using older, higher-risk pesticides in ways no longer permitted in the U.S.

The only way for the FQPA -- and EPA actions -- to impact pesticide dietary exposures in foods imported in the U.S. is through lowering or revoking tolerances. Unfortunately, EPA has lowered or revoked very few tolerances covering contemporary food uses of pesticides as a result of the FQPA.[3]

Focus on Risk Drivers

Perspective can also be gained on the impact of EPA actions on pesticide dietary risk by focusing on regulatory actions targeting the riskiest pesticide-food combinations. EPA, in its cumulative OP risk assessment, CU in its FQPA work, and Benbrook in his EPA-OIG analysis have produced very similar lists of "risk driver" pesticide-food combinations. Benbrook's OIG analysis is the most recent and will be drawn on in this section. Any pesticide-food combination with a DRI value equal to or greater than 30 was considered a "risk driver."

In food grown domestically, 28 pesticide-crop combinations had DRI values greater than or equal to 30 in at least one year prior to 2000. The highest score was 799 for residues of methyl parathion in peaches in 1996.

Table 1 (Appendix A) covers these 28 domestically grown food-pesticide combinations, plus one use of methyl parathion impacted by EPA regulations (processed green beans) and methamidophos in cucumbers (DRI score of 29.8). For each pesticide food combination, a pre-FQPA DRI score is reported, along with the most recently available, post-FQPA score. The changes in these scores can in several cases be attributed to EPA actions. Any reduction in DRI score for a food-pesticide combination for which the tolerance was revoked or voluntarily canceled,[4] or reduced, is credited to "EPA action." Domestic food-pesticide combinations in the table are ranked by the percentage decrease in pre-FQPA risk levels, from the largest decrease to the least (or largest increase).

The impact of EPA actions in the course of implementing the FQPA on this set of 30 risk drivers is an important measure of the FQPA's effectiveness. EPA actions reduced the dietary risks associated with 10 of these 30 risk drivers. Risks stemming from seven of the 30 food-pesticide combinations increased from the pre-FQPA period to the most recent year the foods were tested by the PDP.

EPA revoked the tolerances covering 8 of these 30 risk-driver food uses, leading to a 100 percent decrease in risk for each use (after full implementation

[3] EPA has revoked several hundred tolerances covering food uses of old, obsolete pesticides that are no longer manufactured or used.

[4] Most voluntary cancellations are sought by registrants in lieu of imminent steps by EPA toward cancellation, and hence can be considered a result of EPA action.

of the actions and time for food to clear market channels). Six involved the highly toxic OP methyl or ethyl parathion.

Regulatory actions taken against methyl and ethyl parathion on six crops, and chlorpyrifos on three crops, accounted for 98 percent of the total risk reduction associated with EPA actions on these top 30 risk-driver food-pesticide combinations.

The same analysis was carried out on imported foods with DRI scores equal to or over 30. The results are similar. Parathion plus chlorpyrifos actions accounted for nearly all of the 1,390 DRI point reduction achieved in imported foods (99 percent).

VI. Impacts of the FQPA on Children's Pesticide Exposures and Risks

The EPA used the new authorities of the FQPA to act decisively to reduce residential uses of OP insecticides. By the end of 2000, all high-risk OP residential use patterns had been removed from the market, either by agency action or the imminent threat of action.

EPA's actions on residential OP uses have already improved children's health. Research by a team led Dr. Robin Wyatt has focused on the impacts of OP residential exposures during pregnancy and after birth among minority women in public housing projects in New York City. They found that chlorpyrifos exposures significantly reduced birth weight and length, as shown in Table 2.

Table 2. Differences in birth weight (g) and birth lengths (cm) by cord plasma OP exposure groups: Group 1 lowest exposure, Group 4 highest.

Birth Weights	CHLORPYRIFOS	CHLORPYRIFOS & DIAZINON
Group 1 vs group 2	39.2	-78.5
Group 1 vs group 3	-50.9	-33.1
Group 1 vs group 4	-150.1	-186.3
Birth Lengths		
Group 1 vs group 2	0.17	-0.06
Group 1 vs group 3	-0.21	-0.005
Group 1 vs group 4	-0.75	0.8

Source: Whyatt et. al., Prenatal insecticide exposures and birth weight and length among an urban minority cohort. *EHP*, 2004 July;12:10.

They used regression analysis to assess whether there was a difference in the association between chlorpyrifos exposures and birth outcomes before and after the EPA's actions in the summer of 2000 that ended residential uses of chlorpyrifos. Prior to 2001, chlorpyrifos clearly impacted birth outcomes, but after the EPA actions taken in June 2000, levels of exposure declined and there was no longer a statistically significant association between insecticide exposures and birth outcomes, as shown in Table 3 (Whyatt et al., 2004; Whyatt et al., 2005). This study provides the most encouraging evidence we know of linking an action driven by the FQPA to a significant reduction in prenatal and infant exposures and risk.

Table 3. Regression analyses of birth weight and length and organophosphate levels in umbilical cord plasma samples for infants born before and after 1 January 2001.

Born Before Jan 1 2001	**BIRTH WEIGHT (g)**	**BIRTH LENGTH (cm)**
Chlorpyrifos	-67.3	-0.43
Sum Chlorpyrifos & diazinon	-72.5	-0.46
Born After Jan 1 2001		
Chlorpyrifos	30.7	0.07
Sum Chlorpyrifos & diazinon	0.6	-0.07

Source: Whyatt et. Al., Prenatal Insecticide Exposures and Birth Weight and Length among an Urban Minority Cohort. *EHP*, 2004 July;12:10.

While the EPA's decisive actions on residential uses of OP insecticides were justified and welcomed, EPA has probably overestimated the portion of infant and child exposures to OPs associated with residential uses. The agency has taken strong actions against all residential uses of OPs, and only nine of some 60 food uses of OP insecticides with significant potential to contribute to children's risks.

Biomonitoring data lends further support to the conclusion that day-to-day dietary exposures to the OPs are more important than residential exposures in terms of explaining population-wide exposure patterns. Humans metabolize OPs quickly; metabolites found on a given day of monitoring likely reflect exposures in the preceding few days.

OP metabolite levels found in NHANES and other testing are relatively stable throughout the year and across regions (Adgate et al., 2001; Centers for Disease Control and Prevention 2001). If residential uses were the major source

of exposure, spikes in exposure levels would be expected in the spring and summer when pesticides are used more frequently in and around the home, and in southern and humid regions compared to northern, colder regions. No such spikes are evident in NHANES data or registrant submitted data on OPs such as chlorpyrifos.

The FQPA has brought about a modest to moderate reduction in pesticide dietary risks. Organophosphate insecticide urinary metabolite biomonitoring data collected by the Centers for Disease control, through periodic NHANES surveys, supports this conclusion. NHANES surveys were carried out in 1988-1994, 1999-2000, and 2001-2002; the first survey was before the FQPA, the later two well after passage, and after the only major actions taken to date by EPA targeting high-risk OPs (methyl parathion and chlorpyrifos).

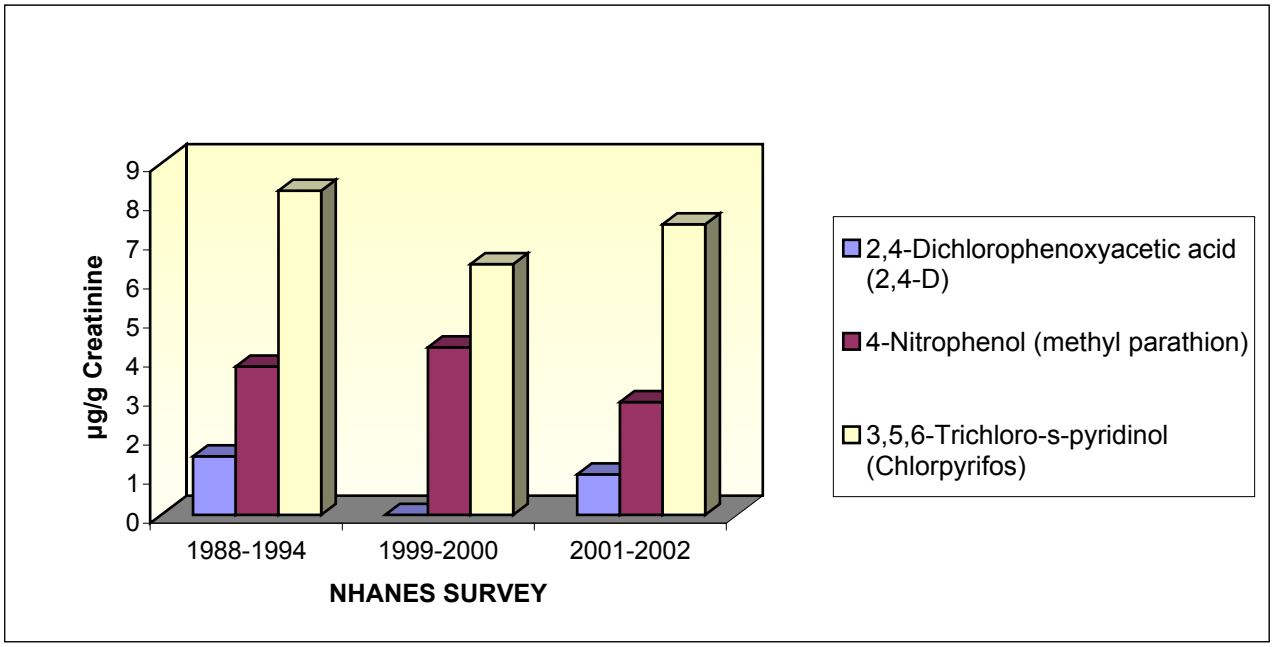
Figure 2 shows trends in three metabolites corresponding to the herbicide 2,4-D, and the OPs methyl parathion[5] and chlorpyrifos (Centers for Disease Control and Prevention 2001; Hill et al., 1995). While modest declines are evident, these data are worrisome. All food uses of methyl parathion resulting in residues, according to PDP testing, were cancelled in 1999 and residues should have been out of the food supply by 2001. Likewise, major actions were taken in 2000 to end chlorpyrifos residential uses and reduce chlorpyrifos in the diet, yet the levels actually went up from 1999-2000 to 2001-2002 and have changed little since the 1988 sampling.

These data suggest that there are significant sources of exposure to these OPs other than those EPA identified as contributing most heavily to aggregate exposure. These might be additional crop uses in the U.S., or uses abroad, leading to exposures via imported foods.

Given the mandate of the FQPA, the EPA will almost certainly need to further reduce OP dietary exposures. Thus far, the FQPA has sharply reduced less than a dozen high-risk OP uses in the U.S., and restricted a few dozen more, but has left most uses untouched abroad. In the absence of tolerance revocations and reductions, the FQPA may simply further shift risks from U.S. grown produce to food imported from abroad.

[5] 4-nitrophenol residues could reflect the use of other pesticides including nitrofen and EPN. Residue data in food suggests that methyl and ethyl parathion is the primary pesticide source of 4-nitrophenol in people's urine, although other sources cannot be ruled out.

FIGURE 2. 95th percentile of urine concentrations (µg/g creatinine corrected) for the U.S. population aged 20-59 years, three NHANES surveys



Changing patterns of residues in domestic versus imported foods, and analyses of the distribution of OP dietary risks show a dramatic shift of risk from fresh fruits and vegetables grown in the U.S. to those imported from abroad. This shift has distinct economic and trade ramifications.

The costs of pest management systems in the U.S. have risen, as farmers have dropped high-risk, but relatively cheap OPs and adopted newer, lower-risk but more expensive pesticides and Integrated Pest Management systems. Some, and perhaps most growers abroad are still using many older, high-risk and low-cost OPs and carbamates in ways no longer allowed in the U.S. A number of studies have shown that fruit and vegetable pest management costs in the U.S. often exceed costs in Mexico, Central, and South America by several hundred dollars per acre. Farmers may be receiving lower prices and losing market share as a result of these FQPA-driven differences in pest management costs, and U.S. consumers may become more reliant on higher-risk imported foods.

In the three foods impacted by actions on chlorpyrifos and the six crops impacted by revocation of parathion tolerances, U.S. farmers have typically replaced these high-risk OPs with reduced risk insecticides and biopesticides. In particular, imidacloprid (Admire) and other nicotinyl insecticides, spinosad, improved formulations of *Bacillus thuriengiensis* (*Bt*), and several new-generation insect growth regulators (IGRs) have replaced the higher-risk OPs impacted by

EPA regulatory actions. Whether this remains the case deserves close monitoring by EPA, and will eventually become evident in PDP test results.

The lack of a significant number of OP tolerance revocations and reductions, however, increases the chances that new risk drivers will periodically emerge in children's foods, especially in imported foods. This risk is especially great during winter months when a significant share of fresh produce is imported.

The EPA has imposed significant regulatory restrictions on only two major risk driver pesticides, both organophosphate insecticides. Other risk drivers persist in children's foods that have yet to be impacted significantly by EPA actions. Pesticides at or near the top of this list include methamidophos, dimethoate, azinphos methyl, endosulfan, methomyl, carbaryl, and dicofol.

The EPA has nearly completed a cumulative risk assessment (CRA) on just one family of chemistry – the OPs. A CRA of the carbamates is well along, but no regulatory actions have been taken as a result of the carbamate CRA. Several other families of chemistry await CRAs, including the triazine and acetanilide herbicides, the EBDC fungicides, and the synthetic pyrethroid insecticides.

The agency will have to decide whether to conduct a cumulative risk assessment of the OPs and carbamates together, given that both families of chemistry work through a common mode of action.

A last point deserves emphasis. The EPA carried out the CRA of the OPs focusing on cholinesterase inhibition because it had relatively good data on this endpoint for most OPs, and it is indeed a common mechanism shared by these insecticides. Cholinesterase inhibition, while an important and reliable indicator of neurotoxicity, is not the biological impact of gravest concern associated with OP exposures.

Most toxicologists are far more concerned about the developmental impacts of the OPs, yet the agency lacks the data and methods to conduct a cumulative risk assessment based on neurological, immune, or reproductive developmental impacts. When such assessments are completed, it is likely that additional restrictions on OP use and exposures will be necessary to meet the FQPA's "reasonable certainty of no harm."

APPENDIX A

Table 10. Impact of EPA Actions on Risk Driver Pesticide-Food Combinations (Domestic), Ranked by Percentage Change in Dietary Risk Index Levels from the Pre-FQPA Period

Commodity	Pesticide	DRI Score	Year	Change in DRI Score	Pre-FQPA Tolerance	Current Tolerance
Grapes	Parathion methyl	0.0 329.1	2001 1994	-100%	1	revoked
Spinach, Processed	Parathion ethyl	0.0 88.2	1999 1998	-100%	1	revoked
Green Beans, Processed	Parathion methyl	0.0 22.6	2004 1996	-100%	1	Revoked
Peaches	Parathion methyl	0.0 799.4	2004 1996	-100%	1	revoked
Pears	Parathion methyl	0.0 78.1	2003 1997	-100%	1	revoked
Apples	Parathion methyl	0.0 52.0	2004 1996	-100%	1	revoked
Tomatoes	Chlorpyrifos	0.0 36.8	2004 1997	-100%	0.5	revoked
Wheat Flour	Chlorpyrifos methyl	0.0 149.2	2004 1996	-100%	6	voluntary cancellation
Apples	Chlorpyrifos	3.6 207.3	2002 1996	-98%	1.5	0.01
Strawberries	Vinclozolin	4.4 65.7	2000 1998	-93%	10	10
Grapes	Dicofol p,p'	10.1 82.7	2000 1996	-88%	5	5
Strawberries	Dicofol p,p'	13.4 67.3	2000 1998	-80%	5	5
Tomatoes	Methamidophos	34.9 143.4	2003 1996	-76%	1	1
Cucumbers	Dieldrin	33.6 111.3	2003 1999	-70%	0.1	0.1
Sweet bell peppers	Chlorpyrifos	20.7 65.0	2003 1999	-68%	1	1
Pears	Azinphos methyl	19.6 58.6	2003 1997	-67%	2.0	1.5
Winter Squash	Dieldrin	77.8 179.3	1999 1997	-57%	0.1	0.1
Cucumbers	Methamidophos	13.4 29.8	2003 1999	-55%	1	1
Sweet Bell Peppers	Methamidophos	60.9 119.1	2003 1999	-49%	1	1
Green Beans	Endosulfans or endosulfan sulfate	20.0 37.6	2001 1995	-47%	2	2
Strawberries, Processed	Dicofol p,p'	22.8 36.1	2000 1998	-37%	5	5
Winter Squash, Processed	Dieldrin	228.5 354.4	1999 1997	-36%	0.1	0.1

Table 10 (continued). Impact of EPA Actions on Risk Driver Pesticide-Food Combinations (Domestic), Ranked by Percentage Change in Dietary Risk Index Levels from the Pre-FQPA Period

Commodity	Pesticide	DRI Score	Year	Change in DRI Score	Pre-FQPA Tolerance	Current Tolerance
Green Beans	**Dimethoae**	**20.6** **30.1**	**2001** **1994**	**-31%**	**2**	**2**
Green Beans	Acephate	55.5 51.0	2001 1994	9%	3	3
Green Beans, Processed	Methamidophos	98.7 89.1 205.1	1998 1996 2001	11%	3 3 1	acephate tolerance (all residues associated with acephate) acephate tolerance (all residues associated with acephate)
Green Beans	Methamidophos	166.3	1995	23%	3	acephate tolerance (all residues associated with acephate)
Celery	Acephate	36.5 29.2	2002 1994	25%	10	10
Strawberries, Processed	Vinclozolin	31.6 17.9	2000 1998	76%	10	10
Potatoes	Chlorpropham	61.1 28.5	2002 1995	114%	50	50
Peaches	Dicofol p,p'	33.8 0.8	2001 1996	4131%	10	10

Impact EPA Actions	1649.0	%
Parathions	1369.4	0.83
Chlorpyrifos	240.5	0.15
Para+chlor	1610.0	0.98

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