1. SCIENCE POLICIES

EPA'S PROGRESS IN DEFINING THE CRITICAL SCIENCE AND REGULATORY DECISION RULES THAT WILL GUIDE FQPA IMPLEMENTATION

The FQPA contains three critical new provisions designed to assure adequate margins of safety for infants and children in setting tolerances. The first requires EPA to impose an additional safety factor of up to 10-fold when establishing the acceptable daily intakes of pesticides (the 10-X provision). The second requires EPA to take into account all routes of exposure to a pesticide in judging the safety of any given use (often called aggregate exposure). The third requires EPA to consider as a group all pesticides that pose risks to human health through a common mechanism of toxicity, the so-called cumulative risk assessment (CRA) provision.

To implement these three innovative provisions, EPA has had to develop a series of new operating principles and science policies, a task the Agency started soon after the FQPA was signed into law, in August 1996. In a January 31, 1997 *Pesticide Regulation Notice*, EPA codified its interim decision rules. Since then, several meetings of EPA's scientific and advisory committees have reviewed many drafts of policies, and EPA has published more than two dozen technical papers supporting policy development. The process is still under way and more such work will be needed to finalize all the key policies.

Core Implementation Issues in Nine Science Policy Areas

Within a few months of passage of the FQPA, EPA had articulated and sought advice on several core implementation issues:

- Whether, how and when to use human test data as the basis for establishing Reference Doses (RfDs). Before the FQPA was enacted, RfDs based on human data had been set for about a dozen pesticides, most of them organophosphate insecticides.

- How to integrate safety factors on the books prior to the FQPA with the FQPA's 10-X provision. About 50 active ingredients had additional safety factors embedded in their Reference Doses when the FQPA passed, several of which were triggered by concerns over pre- and postnatal toxicity.

- What constitutes evidence of "heightened sensitivity" following pre- and postnatal exposures to pesticides?

- What toxicological data gaps are significant enough to warrant imposition of an added safety factor under the FQPA's 10-X provision?

- When should limited exposure data and lack of precision in exposure assessments trigger an added FQPA safety factor?

- When EPA determines that an added safety factor is required, what level should it be set at between one and ten? If an added safety factor is deemed necessary for two or more reasons, can the combined added safety factor exceed 10?

As time passed and EPA had dialogues with stakeholders and its scientific advisory bodies, the list of issues grew and evolved. **Table 1.1** summarizes what eventually settled out as nine critical areas of science-policy needs.

We have assessed EPA's progress in developing its critical science policies by reviewing the documentary history, including technical papers, Federal Register notices, records of advisory committee meetings, dockets with public comments on EPA's proposals, and the Agency's responses to those comments, for each of those nine key science policies. Our evaluation focused on timeliness—how effectively the EPA has kept to a schedule compatible with implementation deadlines in the FQPA itself—and quality of results, in terms of both EPA's responsiveness to issues raised by stakeholders or public comments, and our judgment of how well the Agency's policies address the intent of the statute. In addition, we have examined how closely EPA has followed its own policies in decisions it has made in reassessing safe exposure limits and tolerances under the FQPA.

Table 1.2 summarizes the critical issues in each of the nine key policy areas. **Table 1.3** presents our grades for EPA's progress in each policy area for timeliness, responsiveness to the statute and public comments, and consistency in adherence in the implementation process. Explanations of the basis for each grade follow.

Science Policy #1: Extra 10-X Safety Factor

The 10-X provision of the FQPA directs EPA to impose an added safety factor of up to 10-fold when evaluating pesticide toxicity and establishing acceptable levels of exposure. In **Part 2** of this report, we examine EPA's application of this provision in its decisions on the organophosphate family of insecticides. Here, we evaluate EPA's policy outlining its judgments on how the 10-X provision should be applied.

The 10-X provision is of little consequence for pesticides posing modest risk because of low toxicity or lack of exposure, because there is already an adequately wide margin of safety between maximum "safe" doses and likely actual exposures. But for higher-risk pesticides, a ten-fold reduction in allowable exposure is both more obviously necessary in order to ensure "reasonable certainty of no harm," and more likely to place pesticide uses in jeopardy because it will require risk-reduction steps.

From the beginning of the implementation process, EPA stated that it would, as a default position, initially impose the full 10-X in establishing allowable exposures. EPA states in

its May 1999, document, "The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process:"

> "The FQPA Safety Factor provision, however, was not simply a codification of existing [safety factor] practice. It was both a codification and expansion. Prior to the enactment of the FQPA, OPP already considered both the observed adverse effects shown in studies and the completeness of the toxicology database in determining the appropriate composite uncertainty factor to be applied in calculating the RfD. It was only on rare occasions, however, that OPP found that an additional factor was needed…. Congress, by specifically including a reference to potential pre- and postnatal toxicity…has effectively expanded OPP's pre-FQPA practice….An additional expansion of pre-FQPA practice was effected by Congressional reference to the completeness of the exposure database." (page 13)

The Act allows EPA to reduce the additional safety factor or to remove it entirely if the Agency has sound data on exposure and ample toxicological data demonstrating that a given pesticide, as currently used, does not impose heightened pre- or postnatal risks. EPA has pledged that its decisions to reduce or remove the 10-X would be based on the "weight of the evidence."

Congress enacted the 10-X provision in part to shift the burden of proof traditionally borne by EPA at least partly to pesticide registrants and users. Before the FQPA, EPA could take regulatory actions on pesticides only when it had "sufficient and verifiable data" showing that risks exceed benefits under real-world conditions. Under the laws governing pesticide regulation, registrants have multiple opportunities to interject new information, challenge EPA risk calculations, and raise doubts about the scientific basis for EPA's actions. Prior to 1996, such challenges typically led to agreements between the EPA and registrants to develop better information, often through new toxicity tests or collection of exposure data. In the meantime, the pesticide stayed on the market. Even with EPA's "Special Review" expedited procedures, such risk concerns sometimes were not resolved for a decade or more.

For years, public-health and environmental advocates tried to shift the burden of proof, to require registrants to provide more convincing evidence of a pesticide's safety, before a product is introduced or allowed to remain on the market. This effort largely succeeded for new active ingredients and initial registration decisions, but not for already-registered products, which once on the market were traditionally "innocent until proven guilty."

Many strategies were considered over the years to shift some measure of the burden of proof to pesticide manufacturers. As the FQPA took shape, Congress agreed some steps were needed in this direction. The 10-X provision emerged as the consensus solution. When EPA lacks solid information on toxicity to young animals and/or reliable exposure data, the FQPA requires EPA to impose an added safety factor of up to 10-X, without waiting for additional data. Such steps would be more likely to restrict pesticide uses, while registrants develop new data to resolve concerns. EPA's decisions would be more

protective of public health in the interim and there would be incentives for companies to develop needed data as quickly as possible.

We regard the 10-X provision as the most important of several major policy innovations in the FQPA, and the EPA's performance in implementing this part of the law is central to our overall evaluation. The Agency's performance here is mixed.

For timeliness in developing its 10-X policy, EPA earns a **B**. Just weeks after the FQPA became law, the Agency advanced a Spartan but clear explanation of how it would apply the 10-X provision. At a series of meetings of its Food Safety Advisory Committee in the fall of 1996, EPA focused on 10-X issues and received general support for its policy direction. The Agency's Scientific Advisory Panel (SAP) also reviewed the interim 10-X decision logic at its October 1996 meeting and generally supported the EPA's approach, while asking for more details and concrete examples.

By early 1997, EPA had identified key scientific and policy issues in dispute and sought comments widely, from both its stakeholder advisory committees and scientific experts. This process took time, indeed more than was really needed. Multiple reviews did little to sharpen understanding of issues or strengthen the scientific case for one option versus another. Instead, the advisory process, particularly the Tolerance Reassessment Advisory Committee, provided a forum for interested parties to re-open debates about whether the 10-X provision was justified (a debate Congress had already resolved with its unanimous vote), rather than focusing on how to implement it. Eventually, by early 1999, EPA was finalizing detailed explanations of the process, criteria, decision-rules, and defenses of the ultimate judgments the Agency made, in applying the 10-X provision.

EPA also earns a **B** for responsiveness to public comments on its 10-X proposals. The Agency has generally done a good job in responding to questions and criticisms of its use of toxicological data. Its policy clarifies what constitutes "reliable" toxicological data and "heightened sensitivity."

The decision to require submission of developmental neurotoxicity (DNT) studies on all organophosphate and carbamate insecticides was sound and appropriate. But we disagree with the Agency's decision to impose at most a 3-X safety factor for pesticides lacking DNT data. We don't believe that DNT effects are sufficiently well understood currently to be certain that an extra 3-X safety margin is adequate to cover the range of possible differences in sensitivity to neurotoxicity in adult animals versus immature animals.

EPA has determined that it can impose up to an added 10-X safety factor for evidence of pre- or postnatal toxicity, and up to another 10-X safety factor for exposure data gaps. We agree with this approach and hope EPA will someday use this authority. However, as we explain below, EPA has chosen not to impose additional safety factors to compensate for lack of exposure data.

While EPA's science policy decisions on use of the 10-X provision have generally been sound, the Agency has too often fallen short of adhering to its own policies. As we show

in detail in **Part 2** of this report, EPA has reviewed its definitions of "safe exposure" for the organophosphate (OP) insecticides. In its 10-X policy, EPA defines DNT as a critical effect for OPs, and very few of them have been tested adequately for DNT. EPA has required manufacturers to submit DNT data for all members of this family of neurotoxic insecticides. However, although it lacks DNT data for most OPs, EPA has applied an added FQPA safety factor (10-X or 3-X) in setting safe exposure doses for just 13 of 44 OPs. It has cited lack of DNT data as a justification for the added safety factor in 10 of those cases. But for more than 20 other OPs that also lack DNT data, EPA has imposed no additional FQPA safety factor at all. We think lack of DNT data justifies an added safety factor for every OP inadequately tested for this effect. EPA's failure to apply the 10-X provision consistently in this manner seems both an abandonment of the FQPA's commitment to make public-health the top priority when data are lacking, and at odds with portions of the Agency's own 10-X policy.

A second shortcoming in EPA's 10-X policy lies in the way the Agency has chosen to address uncertainties on dietary exposure. EPA apparently decided early on not to take Congress seriously when it identified exposure data gaps as one reason to impose an added safety factor, and has budged very little from that stance in response to public comments and expert advice. When it lacks good exposure data, EPA has chosen to rely on "conservative models" and estimates of exposure that reflect "worst-case" scenarios, instead of applying an added safety factor. By doing so, the Agency retained the burden of defending its exposure estimates and default assumptions (which interested parties have often attacked as unreasonable). EPA has also failed to take full advantage of the key FQPA provision, which could provide a powerful incentive to develop better data on actual exposures to pesticide residues.

A recent review by the General Accounting Office concluded that EPA had produced a reasonably clear set of provisions governing 10-X decisions and had in fact followed them consistently. We largely agree on the toxicological side of the equation, but not in how the Agency has dealt with data gaps. Overall, for this inconsistent performance in following its stated policies, we grade EPA just a **C** for its responsiveness to the statute and adherence in implementation decisions in this policy area.

Science Policy #2: Key Choices in Dietary Exposure Assessment

EPA has struggled for almost four years with the many highly technical and interrelated science policy decisions embedded in dietary exposure assessment. One area of intense debate has involved whether and how to use "Monte Carlo" probabilistic modeling as a tool for projecting likely exposures from existing food consumption and residue data. In the end, after lengthy consultations with its expert and stakeholder advisory bodies and exhaustive debate, the Agency outlined a scientifically sound and reasonable approach for using dietary exposure models.

There has been more consensus on some aspects. For example, EPA's early judgment to rely heavily on the USDA's Pesticide Data Program (PDP) as its main source of residue

data garnered wide support. Almost from its start in 1991, the PDP has been focused on children's foods and has measured residues in foods "as eaten," avoiding problems often encountered with older residue data. In certain other respects, however, reliance on the PDP data raised new problems that EPA needed to address (see SP Area **#4**, below).

EPA also had to decide where to draw the line that defines "excessive" exposures, based on the FQPA's "reasonable certainty of no harm" standard. In assessing short-term or acute risks, EPA chose to assure that the individual at the 99.9th percentile of exposure to a pesticide is not exposed over his or her personal "safe" dose (based on body weight and the EPA's definition of a safe dose). We support this decision as clearly protective of public health, but not excessively so. While exposures above the dose EPA defines as "safe" do not, based on the best available data, fall in the "reasonable certainty of no harm" range, exposures just marginally above the "safe" dose also clearly do not mean a "reasonable certainty of harm."

For timeliness in developing this policy, we give the Agency a **C+**. The process has taken almost four years, but the complexity of the issues warranted a deliberate approach. EPA earns an **A** for adherence to the statute and responsiveness to public comments in establishing its dietary exposure and 99.9th-percentile policies. To date the Agency has stuck reasonably close to the policy in decisions on individual chemicals, earning a **B+** for adherence in implementation. Since decisions so far have concentrated on the OPs and other pesticides for which acute dietary exposure is the central risk concern, it is not yet clear how EPA will address risks of chronic exposure, such as cancer risk.

Science Policy #3: Threshold of Regulation and Limits of Detection

Complex issues arise in determining how to deal with the limits of analytical chemistry for detecting residues. EPA correctly recognizes that just because no residues have been detected, it does not necessarily mean none are present. To ensure that any "nondetects" are properly considered in risk assessment and risk mitigation, EPA has decided to set a default value of half the limit of detection (LOD) for commodities known to have been treated with pesticides, but on which no detectable residues are found.

We believe this is a reasonable assumption, which strikes a fair balance between other options (such as presuming zero, or presuming just less than the LOD). Obviously, as residue detection science improves, and tests can detect lower residue levels, this default assumption will more closely model actual residues found on any particular commodity. For its responsiveness to the statute and to public comments, we give EPA a **B+**. For adherence in implementing this policy, EPA earns an **A**, and for timeliness, a **B-**.

Science Policy #4: Dietary Residue Estimation

In conducting risk assessments for particular uses of particular pesticides, EPA needs to know how much residue of the pesticide is in particular foods consumed by particular

populations. Sometimes, EPA has reliable residue test data; often, data are incomplete or absent, and certain key questions (such as highest residues likely to be encountered on a reasonably frequent basis) can't be adequately answered, and EPA must make estimates, based on existing information and reasonable assumptions.

One such problem is related to the composite nature of PDP samples. The PDP aims to measure representative average residue levels in foods, and tests composite samples made up of several pounds of food. While this is a sound way to estimate average (chronic) exposures, it tends to obscure variation in residues among individual servings, especially of fresh fruits and vegetables. In 1997, at the urging of its advisory bodies, EPA decided to regulate certain acutely toxic pesticides, including the OPs, on the basis of short-term (24 hour) exposures. This decision heightened the need to calculate exposures based on what children actually eat in a given day, rather than on "average" data. Outside experts and public comments warned EPA that composite data could significantly underestimate dietary exposure among children exposed to higher-than-average residues.

EPA scientists developed a sophisticated statistical algorithm to "de-composite" PDP residue levels from a single number to 10 or more values (the number reflecting how many individual apples or potatoes are included in the average composite sample). The algorithm produces a much bigger residue data set for acute dietary exposure estimation and improves the statistical reliability of the resulting estimates.

As part of this effort, EPA also asked the PDP staff to do some special single-serving surveys for apples, pears, potatoes and peaches. The results of these resource-intensive surveys have allowed EPA to compare the residue levels found in composite samples with the actual residue levels found in each individual fruit that made up the composites. EPA has tested and refined the performance of its algorithm compared to real world data. This process has made the valuable PDP data that much more useful and largely removed one source of downward bias in acute dietary exposure estimates.

The PDP has generated extensive pesticide residue data on only 40 foods out of hundreds eaten daily (25 or so fresh fruits and vegetables, and 15 or so processed foods). There are also, however, many foods not tested by PDP that are also important in the diets of some infants and children, particularly fresh fruits and vegetables sometimes consumed in large quantities, especially when in season. While the PDP may eventually test such foods, at this point they represent gaps in EPA's exposure data. We hope EPA and USDA will expand the scope of PDP testing to include another 10 to 20 key children's foods over the next few years.

Until such data can be obtained, dietary exposure science policies spell out how EPA develops exposure estimates for these additional foods. Just as in the case of a food tested by PDP, food consumption estimates for non-PDP foods are derived from the large food consumption databases compiled by USDA; residue data are developed from surveys by the Food and Drug Administration (FDA), from market basket tests, field trial data, and sometimes from other sources.

We think the procedures EPA has developed are sound and the Agency has made good use of available data. For these actions EPA earns a **B+** for its responsiveness to public comments and to the statute, and an **A** for consistency in application, but just a **C** for timeliness. The slow pace in finalizing dietary exposure assessment procedures set back all other aspects of implementation.

Science Policy #5: Drinking Water Exposure

To date EPA has broken little new ground in the methodologies it proposes to use or the databases available to estimate drinking water exposures. It has also not completed risk assessments under the FQPA for any pesticide for which drinking water exposure is a major contributor to overall risk. The science policies set forth in this area codify past Agency procedures. Some refinements have been made in models used to estimate water-based exposures from, for example, farm ponds or drinking water from a municipal water district that uses various kinds of filtration systems. But any attempts to develop further policies needed to address FQPA mandates have been too tentative to evaluate.

For several widely used herbicides applied to millions of acres in the Midwest (such as atrazine and the other triazines), drinking water exposure accounts for virtually all human exposure. Residues are seldom if ever found in foods. If the FQPA will require actions to reduce risks from these herbicides, it will be because of drinking water exposure. We cannot predict how EPA will finalize and apply its science policies in this area, or what actions EPA might take to reduce drinking water exposures and risks. The only grade we can give the Agency in this area is an "**Incomplete."** By the Clinton EPA's schedule, at least, key decisions on the triazine herbicides are expected by the end of 2001.

Science Policy #6: Residential Exposure

Some of the same pesticide chemicals used in agriculture that contribute to dietary risk are also used in pesticide products formulated and sold to consumers or professional pest control companies, for use in and around the home, in schools, in the workplace, and in other public places. While residential, lawn and garden, school and workplace exposures are an issue for a small subset of pesticides, such exposures can account for a large share of a pesticide's aggregate risks, and for extremely high single-dose exposures, especially for children.

Unfortunately, EPA's science policies in this area have broken little new ground; to date, the Agency has for the most part merely spelled out its current approach. In a few cases, when reviewing specific chemicals like chlorpyrifos and diazinon, EPA has negotiated withdrawal of many home use products from the market—often with a fairly long phase-out period. But the Agency has allowed pesticide registrants to move at a snail's pace in fulfilling new residential exposure data requirements, a process that began early in the 1990s and has not markedly accelerated nor broadened since passage of the FQPA.

Still, EPA's actions on chlorpyrifos and diazinon set a strong precedent and raised the bar for new registrations. The Agency invested much time and effort in evaluating extensive data submitted by the manufacturer to defend residential uses of chlorpyrifos. It built a compelling case to end virtually all home uses, and the registrants ultimately accepted the Agency's view that such steps were necessary (albeit for different stated reasons). The maker of diazinon recently decided to voluntarily cancel all home uses, based on the risk assessment EPA had prepared to support proposed product cancellations, more to avoid the costs of contesting EPA's proposed actions than because it necessarily agreed with the EPA assessment. While the science policy process has done little to address key data gaps on residential exposure, EPA has effectively emphasized reducing such exposures in these two decisions. Its actions have demonstrated that an elaborate new science policy is not needed to address relatively clear-cut and straightforward risks. For these reasons EPA earns a **B** here for timeliness, responsiveness, and consistency in implementation.

Science Policy #7: Aggregate Exposure

The FQPA requires EPA to consider all sources of exposure to a given pesticide when regulating any individual use of that chemical. For example, when setting safe limits for a residue on a food, EPA must consider residues of the same pesticide on all other foods, and must also examine exposure by other routes. The most common non-food routes of exposure to pesticides are contaminated drinking water and residential uses of the same agricultural pesticides that leave residues in foods.

Occupational exposure is a key source of pesticide doses for farmers, farm workers, and their children, as well as for professional pest control operators and others who handle and apply pesticides. The FQPA does not specifically require EPA to take occupational exposures into account, and EPA has to date not tried to include it in its assessments. We think EPA should identify any populations (such as farm children) at risk of heightened exposure because of their families' occupation. Such identifiable sub-populations also deserve to be brought within the FQPA's "reasonable certainty of no harm" standard.

EPA's models for estimating dietary exposure (See **Science Policies #'s 2 and 4**, above) address aggregate exposure across multiple foods. The Agency's policies for addressing drinking water and residential exposures were described under **Science Policies #'s 5** and **6**, respectively. A fundamental question, not yet fully resolved, is how best to aggregate exposures that occur on widely different scales of quantity and time—repeated low doses encountered daily in foods, and shorter-lasting but occasionally very large "spikes" of exposure from drinking water or residential treatments. EPA has (correctly, we think) established "safe" exposure limits for both acute exposure (spikes) and chronic exposure (most dietary residues); see **Part 2** for details. Ensuring that the "reasonable certainty of no harm" standard is met for a given pesticide is in effect ensuring that neither the acute nor the chronic safe dose is exceeded, regardless of the route(s) of exposure involved.

To date, in its decisions on a few individual chemicals, EPA has dealt with residential exposures and dietary exposures essentially as separate problems, but has addressed both

in the same review process, which we think meets the intent of the law. As noted above, EPA has not yet addressed drinking water exposure to any significant degree. EPA earns a **B+** for its responsiveness to the statute, and a **B** for responsiveness to public comments on this policy area. The slow pace that has left some core issues unresolved so far earns a **C** for timeliness, and the lack of actions affecting drinking water exposure to date make the grade for adherence to the policies an **"Incomplete."**

Science Policy #8: Cumulative Risk Assessment

Next to the "10-X" provision, perhaps the most important innovation in the FQPA is its requirement that EPA consider the cumulative effects of all pesticides with a common mechanism of toxicity as one problem. EPA can no longer regulate such pesticides "one at a time," setting limits for each one is if it were the only residue children are exposed to; it must consider the combined effects of the multiple residues children (and everyone else) encounter, in foods and by other exposure routes.

This requirement has far-reaching effects. Until EPA can determine what cumulative dose of all pesticides combined meets the "reasonable certainty of no harm" standard, it cannot convincingly define the acceptable exposure limits for individual pesticides in a class that shares a mechanism of toxic action. In practice, working out how to do these cumulative risk assessments (CRAs) has been a substantial scientific and policy-making challenge. EPA could not afford to postpone all reviews of individual chemicals until it had figured out its CRA approach; the Agency has therefore completed its reviews of toxicity data and redefined the "safe doses" under the FQPA standard, for several dozen of the most toxic insecticides (see **Part 2**). It seems clear, though, that once it completes its CRA work, EPA will need to re-examine the limits it has set one-chemical-at-a-time, and probably will need to adjust many of those individual limits downward to ensure that cumulative risk does not exceed the FQPA safety standard.

EPA has worked hard for the last year or two, trying to develop its CRA policy, with an initial focus on the organophosphate insecticides (OPs). Seven meetings of the Scientific Advisory Panel have been devoted at least in part to discussion of CRA science policies, and the Agency recently produced its first "case study," a CRA for a group of 24 OPs. While we generally support EPA's efforts, as far as they go, the current approach needs substantial improvement (see our presentation at the December 7-8 2000 SAP meeting, at http://www.ecologic-ipm.com/findings_CU.html#comments.) The work on this Science Policy area is also far from complete; it will require a great deal of additional work and is likely to undergo significant changes as EPA's FQPA implementation evolves.

While developing CRA methodology may be the most complex challenge imposed on EPA by the FQPA, and we sympathize with the Agency on the difficulty of the task, the pace of work on this vital policy has been far too slow, earning EPA a **C** for timeliness. The Agency deserves a **B** for responsiveness to the statute. Public comment and response processes are still under way, and the issue of whether EPA's decisions have adhered to its policy has not arisen yet. Grades for these components are "**Incomplete**."

Science Policy #9: Common Mechanism of Toxicity

In order to define classes that require cumulative risk assessments, EPA needed to spell out its definition of a "common mechanism of toxicity" (CMT). Several major pesticide families, including the OPs, carbamates and synthetic pyrethroids among insecticides, the triazine and acetanilide herbicides, the EBDCs and several other groups of fungicides, share toxic mechanisms in each case. So far, EPA has focused primarily on the OPs.

Pesticide makers and users have an interest in keeping the definition of such "common mechanisms" as narrow as possible, to limit the size of regulated classes and allow any given member of a class a slightly larger share of the acceptable risk. We think EPA has needlessly complicated policy in this area, and made more work for itself, by defining a common toxic mechanism too narrowly. In defining a common mechanism for the OPs, the Agency determined that for each chemical with a CMT there must be evidence of the same, very specific toxic endpoint, in the same species and sex of test animals, such as cholinesterase inhibition in brain cells of male rats. We believe this narrow definition will make it difficult to carry out meaningful cumulative risk assessments, whereas use of a broader criterion—such as any evidence of cholinesterase inhibition in an appropriate organ system of an appropriate test species—would better suit the need.

EPA also allowed debate over how to define CMT drag on for over three years, slowing development of related policies such as **Science Policy #8**, on CRA. A consensus has long existed that all OPs (plus the carbamates) inhibit cholinesterase and thus share a common mechanism of toxicity; in fact, recognition of this fact led to the CMT provision the FQPA. For that reason, EPA gets a **D** for timeliness on this policy; we can't see any real excuse why it should have taken so long or been so difficult. The Agency chose not to heed much of the advice it got from its expert panels and public comments, so we've given it a **C** for responsiveness to comments. And the policy is still far from finished; EPA has thus far ducked the issue of whether OPs and carbamates share a CMT, and has not addressed several other classes of pesticides with a known CMT. For responsiveness to the statute and consistency in adherence, we give EPA an "**Incomplete**."

Summary Assessment on "Core Implementation Issues"

In the opening section of this Part of our report, we highlighted several core issues EPA raised at the beginning of the FQPA implementation process. Some of those issues cut across several of the nine "key areas" subsequently identified for development of science policies, and a few fall outside of the nine "key areas." To supplement our assessment of the nine key science policies, we here briefly summarize EPA's answers to the initial set of "core implementation issues." Responses are drawn from more than two dozen major science policy papers EPA has produced.

Whether, how and when to use human test data as the basis for establishing Reference Doses.

This issue, which is not covered by any of the nine policies reviewed above, should have been the easiest to answer quickly and decisively. Given the clear ethical unacceptability of generating or using toxicological data on the effects of pesticides on pregnant women and babies, and the scientific inappropriateness of using data from exposures of healthy adults to assess risks of, say, effects on the developing nervous system, EPA could have resolved this issue immediately, simply by excluding the use of human data in setting Reference Doses. Instead, EPA allowed debate on this question to drag on for more than two years, using time at scientific and policy advisory committees that could have been better devoted to other, more equivocal issues.

In the end, EPA did determine that it will not request, nor generally use, human data in setting RfDs, but it left the door open for future reconsideration. We believe EPA should have stated much more forcefully and much sooner the sound scientific and ethical basis for concluding that human data contribute little if anything to the specific assessments of pesticide toxicity of greatest concern to the Agency and the public.

How to integrate existing safety factors with the FQPA's 10-X provision.

In developing both its 10-X policy and its CRA methodology, EPA has thoughtfully addressed and integrated the respective roles of the standard, pre-FQPA safety factor (typically 100-fold); additional safety factors used by EPA pre-FQPA, for weak databases or signs of exceptional toxicity; and the FQPA's additional 10-X provision. The Agency has used a clear, open process and achieved worthy final policy positions.

What constitutes evidence of "heightened sensitivity" following prenatal and postnatal exposures to pesticides?

EPA has developed detailed and generally appropriate guidance to determine evidence of heightened sensitivity from the Agency's standard battery of toxicology studies. The endpoints the Agency has chosen are sound, as far as they go, and the threshold defining a "heightened" effect is set at about the right level. But EPA has done a less satisfactory job of developing and using new data requirements to strengthen the overall toxicology database. In particular, not enough has been done to require tests with the sensitivity to identify subtle developmental effects. Nor has much progress has been made yet toward developing a pesticide-specific battery of tests on endocrine disruption, or on translating the results of such tests into new risk assessment methods.

What toxicological data gaps are significant enough to warrant imposition of an added safety factor under the FQPA's 10-X provision?

EPA has been tentative and equivocal in imposing the FQPA's 10-X provision in the face of toxicological data gaps. It decided to apply no greater than a 3-X added safety factor in setting organophosphate RfDs in the absence of developmental neurotoxicity studies,

despite ample evidence that studies of this type are most likely to lead to the lowest "No Observable Adverse Effect Level." This timid policy seems to go against the intent of the law to require added safety margins in the face of critical data gaps.

EPA has also been excessively reluctant to impose added safety factors in cases of known endocrine disrupters, even though EPA scientists have done much of the critical research demonstrating pesticide perturbations of normal endocrine functions, with impacts on reproduction, development and the immune system.

The intent of the 10-X provision is clear: to reward pesticide manufacturers who do needed research on hazards like endocrine and developmental effects, and to penalize those whose weak data leave major uncertainties on these questions. By failing to use this authority more fully or assertively, EPA is missing a key opportunity to advance the science it needs to assure full protection of public health.

> *When should limited exposure data, and lack of precision in exposure assessments trigger an added FQPA safety factor?*

In our judgment, the answer should be "often." In practice, EPA has rarely done so, preferring instead to estimate exposure using conservative assumptions when either good residue data or verified exposure models are lacking. Instead of applying at least a 3-X routinely for exposure data gaps, the Agency has stubbornly insisted on continued use of outdated, unsophisticated models that sometimes lead to nonsensical results. Such results have been featured prominently in attacks on the Agency for its "unscientific" methods. Again, this policy decision undermines the intent of the FQPA to provide incentives to fill data gaps and resolve uncertainties.

> *When EPA determines an added safety factor is required, what level should it be set at between one and ten? If an added safety factor is deemed necessary for two or more reasons, can the combined added safety factor exceed 10?*

EPA has set FQPA safety factors at just two levels: 3-X and 10-X. By thus limiting its choices, the Agency has avoided creating an unduly complex range of what might appear to be arbitrary choices, but has also lost degrees of freedom in matching the size of the added FQPA safety factor to unique issues raised by a particular pesticide's toxicological profile and exposure patterns.

EPA has determined that added safety factors can exceed 10-X if warranted for two or more reasons, but has not yet applied greater than a 10-X FQPA added safety factor in any specific decisions.

Overall, the EPA has bypassed many opportunities to take full advantage of the FQPA's key new provisions. In addition, during the lengthy debates that have helped to define and refine its science policies, the Agency has too often allowed participants to roam too

far afield, reopening the debate over the provisions themselves, rather than focusing on how to implement them.

Given how quickly the FQPA took final shape in Congress in 1996, the Agency did face the practical need to educate various constituencies on what the provisions meant and why they were included in the final bill. As the science policies took shape, the Agency certainly did reach out widely and often for both policy and scientific advice. Each round of review and comment led to a new, sharper draft.

The process has generally been transparent, exhaustive, and for many, exhausting. While all policy papers are termed "living documents" subject to further refinement, most are in close to their final form. On the whole, the Agency has made significant progress toward crafting a robust and well-grounded series of science policies and deserves an overall **C+** for its efforts in this area. But much work still remains to be done to finalize many of the policies, and once they are completed, implementation is another hurdle. Nevertheless, in the past four years EPA has taken many positive steps that should, in the end, help ensure that the FQPA delivers on its basic promises.