COMMENTS OF THE COMPETITIVE ENTERPRISE INSTITUTE REGARDING EPA'S BIOPESTICIDES REGISTRATION ACTION DOCUMENT AND PROPOSED LABEL FOR COAT PROTEIN GENE OF PLUM POX VIRUS

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The Competitive Enterprise Institute (CEI) appreciates the opportunity to submit these comments regarding EPA's Biopesticides Registration Action Document (BRAD) and Proposed Label for Coat Protein Gene of Plum Pox Virus. CEI is a non-profit research and advocacy organization, and for over 25 years CEI scholars have been extensively involved in research on issues of food and environmental safety, innovative food production technologies, and other issues of public health and consumer protection, including crop biotechnology.

CEI commends the Environmental Protection Agency for concluding that use of the Coat Protein Gene of Plum Pox Virus (CPG-PPV) in C5 Honey Sweet Plum would not result in unreasonable adverse effects to the environment or to human health. Indeed, the use of transgenic virus resistance in other crop plants—including papaya, squash, and potato–grown within the United States has already proven to deliver clear environmental benefits and no known risks to the environment or to human health. Commercial scale release of the C5 Honey Sweet Plum can be expected to provide the same safe and environmentally beneficial solution to the long-standing and intractable problem of PPV infection of plum trees. We therefore applaud the agency's decision to exempt the C5 Honey Sweet Plum from the requirement of a tolerance for residues of the CPG-PPV.

However, there is no scientifically justifiable reason for EPA to even consider the CPG-PPV in C5 Honey Sweet Plum to be a plant-incorporated protectant (PIP), a condition that makes it subject to burdensome pre-market and post-market regulatory requirements. The novel CPG-PPV transgene's mode of action means that little or no virus coat proteins will be produced in the fruit. We recognize that the Federal Insecticide, Fungicide and Rodenticide Act defines a "pesticide" based on the manufacturer's intent, not biochemical mode of action. Nevertheless, because no virus coat proteins are intended to be produced, the C5 plum does not in any meaningful sense contain a "substance" that should be classified as a PIP. EPA has had to classify both the virus coat protein and the novel DNA as a PIP. But it is not the coat protein that is intended to confer virus resistance, and EPA has never before considered DNA alone to be a pesticidal substance.

Even if the novel protein were to be expressed and PIP status could be defended, there is also no scientific justification for EPA to require C5 plum trees or fruit to carry a label indicating the presence of a pesticide product. EPA recognizes that plant viruses, including PPV, have a long history of safe consumption by humans, so the virus coat protein would not be injurious to human health or the environment in any way. Ultimately, trees and fruits of the C5 plum are functionally no different from non-transgenic plum infected with the PPV virus, but there is a substantial risk that consumer confusion would result from mandatory PIP labeling. We therefore urge EPA to remove the C5 Honey Sweet Plum's classification as a PIP or, at the very least, to exempt trees, plantlets, cuttings, and fruit from the requirement to bear a pesticide product label.

Background

Plum pox is the most threatening viral disease of stone fruits, which include plums, peaches, nectarines, apricots, and cherries. The virus therefore poses a substantial threat to agriculture in the United States. Although plum pox poses no danger to consumers, PPV infection reduces the quality of fruits, and eventually renders infected trees incapable of producing fruit. Once the virus is present, it is nearly impossible to eradicate without burdensome quarantine requirements and the destruction of infected trees. Since it was first detected in Pennsylvania in 1999, PPV has reappeared in at least two other U.S. states and Canada. It has subsequently been listed as an invasive species by the US Department of Agriculture.

Because the risk of PPV infection is so severe, growers currently must use copious amounts of chemical insecticides to protect orchards from the aphids that spread the virus. Introduction of the C5 Honey Sweet Plum can therefore be expected to generate substantial economic benefits to growers and can help to prevent the further spread of a problematic invasive species. Perhaps most importantly, introduction of Honey Sweet Plum will yield important environmental benefits because traditional pesticides will no longer need to be used to protect the trees from insect vectors.

As the EPA recognizes, plant viruses, including PPV, have a long history of safe consumption by humans. The BRAC itself indicates that "[p]lant viruses are not pathogenic to humans," and that "[h]uman exposure to a variety of natural plant viruses and plant viral proteins is common in the diet, and exposure includes plant virus coat proteins (PVCPs)." It is not uncommon for human consumers to eat plums that have been infected with the PPV virus and which contain the DNA sequences that code for the PPV coat protein as well as the coat protein itself. This is particularly relevant because the viral coat protein levels found in naturally infected plants can be 100 to 1,000 times higher than the levels expressed in transgenic virus-resistant plants.

Although the EPA has classified the CPG-PPV in C5 Honey Sweet Plum as a plant-incorporated protectant, neither the trees nor the fruits contain any novel proteins or other compounds that are toxins or otherwise injurious to human health. Little or no PPV coat protein is expected to be produced because the Plum Pox Virus Resistance transgene initiates the plant's defense mechanism before detectable virus coat proteins can be transcribed. These DNA sequences are only effective if they are inside a living plum cell infected by PPV. They have no biological activity if they are outside a living plum cell, and they have no biological activity against any other known organism. Nor is it possible for the engineered plum trees to produce new PPV virions because the C5 plum tree contains only the DNA sequences necessary to produce PPV coat protein.

EPA has also considered the possible effects that the CPG-PPV might have on mammalian, avian, fish, and invertebrate species, as well as other cultivated or wild plants, and the agency has concluded that no adverse effects are likely to arise. Because the C5 plum does not express any novel proteins and cannot produce new copies of the PPV virus, there is no logical pathway through which any such harm could occur. And, though transgenic plants may sometimes spread novel genes to non-transgenic cultivated plants and to closely-related wild species, this is extraordinarily unlikely to occur with the C5 plum, a transgenic cultivar of *Prunus domestica*.

Hybridization of *Prunus domestica* with other *Prunus* species is highly unlikely because the former has a hexaploid genome, whereas native species are mainly diploid. Nor is it likely that the transferred gene would be spread to non-transgenic *Prunus domestica* plants since, under normal circumstances, the genetic composition of plum fruits is derived from the maternal tree, and there is no genetic contribution from male, pollen-producing plants. Even intentional forced hybridization between two plants of the *Prunus domestica* species is known to be highly inefficient. And, in the rare occasions

when hybridization is successful, surviving hybrids show very low fertility and low vigor. Finally, plum trees are propagated vegetatively by grafting, so even if hybridization were to occur, transfer of the novel gene to off-spring through seed is extremely unlikely.

Treatment of C5 Honey Sweet Plum as a Plant-Incorporated Protectant

In light of these facts, it is therefore troubling that EPA even considers the CPG-PPV in C5 Honey Sweet Plum to be a plant-incorporated protectant (PIP). Unlike many other transgenic pest-resistant crops, in which novel DNA sequences confer pest protection by coding for the production of a toxin or other substance, the C5 plum produces little or no novel protein. Instead, the transgene initiates the plant's defense mechanism before detectable virus coat proteins can be produced.

The Federal Insecticide, Fungicide and Rodenticide Act defines a "pesticide" as a "substance or mixture of substances **intended** for preventing, destroying, repelling, or mitigating any pest" (emphasis added). For most PIPs, EPA classifies the novel protein conferring pest resistance as the pesticidal substance. But the C5 plum is not intended to produce novel proteins in order to confer virus resistance. Consequently, the product does not in any meaningful sense contain a "substance" that should be classified as a PIP, because it is not the virus coat protein that is intended to confer resistance to PPV. In order to get around this inconvenient fact, EPA has had to classify the transgenic DNA itself as a PIP. But classifying DNA that is unconnected to a pesticidal protein as a PIP is unprecedented and makes no rational, scientific sense.

Plant breeders routinely use non-transgenic methods to manipulate the DNA of crop varieties with the **intent** of generating innate pest resistance, often introducing new genes from wild species into cultivated plant populations. For obvious reasons, EPA does not normally consider DNA alone to be a pesticide—the chemical substances that comprise DNA are known to be safe for human consumption and have no biological activity outside living cells. There is no rational, scientific reason for treating transgenes in a different fashion. Thus, relying on a framework that counts mere DNA as a plant-incorporated protectant calls into question the classification of any C5 plum constituents as a pesticide.

Even if the novel protein were generated, EPA is fully aware that the CPG-PPV would not be injurious to human health or the environment in any way. Because the tree and fruit of the C5 plum are functionally indistinguishable from non-transgenic plum infected with the PPV virus, there is no scientific rationale for treating the former as containing a PIP—a condition that makes only the C5 plum subject to extremely burdensome pre-market and post-market regulatory requirements. Indeed, given the demonstrated likelihood that transgenic C5 plum will confer substantial environmental benefits but pose minimal or no risk to humans or the environment, it is ludicrous to consider it to be a pesticide product.

CEI is also very much concerned that EPA's classification of the virus coat protein in C5 plum as a PIP may require C5 plum trees, plantlets, cuttings or fruit to bear a label indicating that the products contain a PIP. Treating perfectly safe and environmentally beneficial products in such a way cannot be justified scientifically, particularly in light of the fact that analogous non-transgenic plants containing the identical DNA sequences coding for plum pox viral coat protein are not subject to pesticide product regulation in any form. Mandatory pesticide product labeling could, however, cause substantial damage to the market for C5 Honey Sweet Plums.

Forcing the C5 plum to bear a PIP label could needlessly stigmatize this tremendously useful product, as consumers perceive pesticides to be toxic substances. Consequently, treating the DNA or harmless protein as a pesticide is likely to result in substantial consumer confusion, and it will needlessly scare consumers. Doing so would also set an unfortunate precedent that could subsequently force future transgenic virus-resistant crop plants to be treated in the same unscientific and irrational manner. Never

before has the EPA classified novel proteins in a transgenic virus-resistant crop plant as PIPs, nor have such plants ever been subject to pesticide product labeling requirements. This prior treatment was perfectly reasonable and could be justified on both legal and scientific grounds. Classification of the virus coat protein as a PIP that must be labeled cannot. We therefore urge EPA to exempt the C5 Honey Sweet Plum, and any other DNA that does not produce a harmful substance, from all pesticide product labeling requirements.

Conclusion

Once again, the Competitive Enterprise Institute commends EPA for reaching the scientifically justifiable conclusion that use of the CPG-PPV in C5 Honey Sweet Plum would not result in unreasonable adverse effects to the environment or to human health. And we applaud the agency's decision to exempt the C5 plum from the requirement of a tolerance for residues of the virus coat protein.

However, there is no scientifically justifiable reason for EPA to consider the presence of virus coat protein or novel DNA in the C5 plum to be a plant-incorporated protectant. Such a classification is also legally suspect because it is not the coat protein that gives C5 plums their virus resistance, and EPA has never before considered DNA alone to constitute a pesticidal substance. Nor is there any scientific justification for EPA to require C5 plum trees or fruit to carry a label indicating the presence of a pesticide product.

We therefore urge EPA to remove the C5 Honey Sweet Plum's classification as a PIP or, at the very least, to exempt trees, plantlets, cuttings, and fruit from the requirement of bearing a pesticide product label. We further urge EPA to exempt from the labeling requirement any DNA or transgenic plants that do not rely on the production of a known toxin or other substance that is injurious to humans or the environment for pest resistance.

Respectfully submitted,

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