Statement of the American Phytopathological Society
Submitted to
Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel
of the Environmental Protection Agency

At a hearing to evaluate issues associated with the review of proposed rules to exempt certain plant-incorporated protectants based on virus coat protein genes.

December 5, 2005
[OPP-2005-0249]

Thank you for the opportunity to submit comments on behalf of the American Phytopathological Society (APS), a scientific society that represents approximately 5,000 members who work with plant pathogens and the diseases they cause and devise ways of managing losses caused by them. The APS supports the use of biotechnology as a means of improving plant health, food safety, and sustainable growth in plant productivity.

In 2001, the APS issued a Position Statement on Biotechnology that included the following points that are relevant to the issues under review today:

> "Insertion of viral sequences into the plant genome causes the plant to resist virus infection through a process akin to immunization, providing an effective new genetic approach for managing plant viruses";
>
> "Future environmental benefits of biotechnology for improved management of plant diseases are enormous, particularly the potential to reduce the dependency on commercial and non-commercial growers on synthetic pesticides, and enhance approaches that minimize adverse effects on the environment"; and
>
> "The concerns that are being raised of environmental and food safety risks of biotechnology through *gene exchange* and *evolution of new pathogens*, or from a putative increased or unexpected allergenicity, are legitimate risks that will be addressed as have similar potential risks with any new plant or plant product. Assessment and management of these and other risks of new technologies in a formal process is appropriate, and must be conducted in a science-based manner and also include economic, human and animal health, and ecological consequences."

The APS also takes the position that the assessment of risks of plants modified through biotechnology must be viewed in perspective to other modification methods, and that the consequences of not using biotechnology must be considered as well.

The APS historically has supported EPA's proposal to exempt plant viral coat proteins incorporated as protectants (PVCP-PIPs) for the management of plant virus diseases, and

participated in the October 2004 FIFRA-Scientific Advisory Panel (SAP) meeting. With regard to the issues discussed at that meeting, the APS:

- concurs that gene flow from plants containing PVCP-PIPs to wild or weedy relatives can occur. Gene transfer alone, however, should not be considered an environmental hazard. Mitigation of gene flow could be accomplished by spatial and temporal separation of the species.
- recognizes that the potential exists for any viral transgene to recombine with viruses infecting the transgenic plant, and that recombination to form new viruses or virus strains will occur in certain circumstances. However, new virus emergence *per se* does not pose environmental hazards.
- supports the exemption from tolerance of plant viral coat proteins, as there is no known toxicity or allergenicity to humans.

The APS continues to support the exemption of PVCP-PIPs for the control of plant virus diseases. The APS supports the conduct of risk assessment and management in a science-based manner. Risks must be viewed in perspective, in context, and relative to the risks of using other genetic modification and virus management methods.

Most importantly, the APS strongly urges EPA in their proposed rules to consider the **benefits** resulting from deploying these resistant plants, as we conclude benefits far outweigh the risks. Benefits include improved yield and quality of virus-resistant, and the reduction in pesticides used in attempts to control arthropod and other vectors.

The issues now raised by EPA for discussion by the SAP in their review of the proposed rules include the potential human health effects from exposure to residues of PVCP-PIPs, the potential for non-target impacts, and the potential environmental consequences associated with gene flow and recombination.

EPA has recognized PVCP-PIPs that generally pose low risk, have defined a series of potential and perceived risks, and have defined criteria to identify those cases that could or could not be exempt. Non-exempt PVCP-PIPs would require, in the proposed rules, considerable data from the developer to be approved for use. The APS is concerned that it will not be cost-effective for developers to provide these data, and would thus not utilize what many consider to be the best approach to virus disease management.

The questions posed to the panel for discussion, and on which comments are requested, are complex. Time does not permit as in depth a review as the subject warrants, particularly with the late release of the documentation for the meeting. We trust, however, that the APS members and other experts on the panel will provide considerably more documented information and evaluation.

The APS makes the following specific comments in response the issues identified in the Meeting Document.

<u>Gene Flow Issues</u>

The APS notes that gene flow issues are considered by USDA APHIS in their review of transgenic plants for release into the environment. Even though the issues raised by the USDA are relevant primarily to non-agricultural areas, no mention is made in the documentation for the SAP that initial authority lies in another agency and that

considerable information is thus reviewed by APHIS. Similarly, weediness and invasive species are also covered by other agencies as well.

Environmental consequences and risk scenarios presented by EPA for review are related to increased weediness or invasiveness associated with acquisition of PVCPs by gene flow. The data on effects of viruses on naturalization and fitness of either crop species are very limited. Only recently have plant ecologists recognized that viruses may impact establishment and invasiveness. These few results should be viewed more as individual cases, not typical of all host-virus combinations. Plant pathologists, however, have long recognized that viruses are commonly found in weedy and naturalized plants, as they serve as reservoirs of virus for spread to crop plants.

EPA asks for data supporting or refuting the rationale that plants to which PVCPs transfer would not be expected to become weedy or invasive. The question should be reversed as it is nearly impossible to obtain data to prove a negative. Further, criteria making a plant weedy or invasive are quite difficult to predict.

EPA states they expect to evaluate the Federal Noxious Weed List and lists from other groups for information, but that inclusion on these lists will not be determinative. It is not clear what criteria would EPA use, and how conflicts with others would be dealt with.

Viral Interaction Issues

EPA is proposing to limit PVCP exclusion to those viral pathotypes naturally infecting plants in the United States, its possessions, or territories. This limitation, we presume, is to preclude introduction of sequences from non-native pathogens, including those on the USDA-APHIS quarantine list. This is reasonable from the standpoint of decreased risk of introducing new pathogens, but not from the standpoint of disease. This limitation results in greater regulatory requirements if the PVCP technology is used for mitigation of emerging or threatening virus diseases, such as plum pox, new geminiviruses, etc. Further, APHIS should address this issue or at least be in consultation with EPA.

The APS agrees that viruses that naturally infect the plant are unlikely to acquire the CP sequence through recombination and produce a viable virus with significantly different properties than either parent virus.

PVCP-Protein Production Issues

EPA appears to propose a case-by-case review of any PVCPs that have undergone minimal modifications from a natural viral CP, whether to make it more effective in imparting virus resistance to plants, or to reduce recombination frequency or ecological risk of new pathotypes. Criteria to not exempt these minor changes should be considered carefully, as we do not think they should be relegated entirely to case-by-case review. Natural viral CP itself is far from uniform in sequence between isolates of a viral species, nor even within the same infected plant. Viral coat proteins are structurally well-defined by virtue of the constraints of packaging into virus particles, but can have several levels of functional equivalence in diverse sequences.

Post-Transcriptional Gene Silencing (PTGS) Issues

EPA has now recognized that viral resistance can be imparted by viral sequences that either are not CP or do not produce CP (RNA-mediated resistance), and states the

proposed rules will apply to all viral nucleic acids used for the intent of protecting plants from virus. The APS concurs that the FIFRA-PIP rules should acknowledge this form of genetic modification. The evaluation of risk is affected in that the only new component is nucleic acid. Therefore EPA has little justification to regulate untranslatable constructs. The likelihood of RNA making protein at some time is extremely remote, given the current understanding of molecular biology and protein synthesis. There is no evidence that PTGS involves viral proteins, except in its suppression by known viral sequences. Since these sequences enhance, not suppress, virus symptoms, they would not be used to develop resistant plants.

In response to EPAs request, we expect that RNA-mediated resistance would have no effect on gene flow, and would reduce the potential for recombination.

Food Safety Issues

Comment is requested on the potential for novel human exposure to a PVC-protein if it from a virus not naturally infecting the food crop. This is highly unlikely because if the virus did not infect the food crop, a developer would never use this CP to protect the plant.

Viral coat proteins have never been associated with toxicity or allergenicity. Considerable serological data exist on location of epitopes on individual CP or on viral capsids formed of CP. Surface antigens may be a more powerful tool to analyze allergenicity that looking at primary sequence data. The extensive knowledge of viral CP structure could be used to address questions raised. One major difference in a natural virus infection and CP-expressing plant is the state of aggregation or assembly of the CP - whether it exists free or in small aggregates known to be precursors for virus particle assembly.

Chimeric constructs have been shown to give resistance to multiple viruses, but have these been CP-mediated or RNA mediated? If the latter, than the questions regarding increased toxicity or allergenicity to chimeric proteins is mute.

Other Issues

The APS concurs with the assessment by EPA of the six selectable markers, and support the conclusion that they pose a low probability of environmental risk and should be exempt.

Thank you for the opportunity to provide these comments on behalf of the APS.

Stella Melugin Coakley
APS Public Policy Board Chair

American Phytopathological Society
3340 Pilot Knob Road
St. Paul, MN 55121-2097
+1.651.454.7250 (main)
+1.651.454.0766 (fax)
mailto:aps@scisoc.org (email)
http://www.apsnet.org