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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Evaluation of Public Interest Documentation for the Conditional Registration of Fluoxastrobin Fungicide

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THRU: Arnet Jones, Chief
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PEER REVIEW PANEL: May 26, 2004

Summary. Bayer has proposed registration of a new fungicide active ingredient, fluoxastrobin, in the public interest. Fluoxastrobin is a member of the group of quinol "outer" or "oxidizing" binding site inhibitor (QoI) fungicides. Fluoxastrobin is a strobilurin fungicide, a subgroup of QoI chemicals, which includes such important fungicides as azoxystrobin, pyraclostrobin, and trifloxystrobin. Although fluoxastrobin is a member of the strobilurin group that includes already marketed active ingredients, BEAD believes that growers would benefit from a new active ingredient that can be an effective disease management tool, for both curative and preventative purposes. In many cases, the efficacy of this chemical will be comparable to others currently on the market, however, diverse qualities of strobilurin fungicides suggest that there can be a valuable place for this strobilurin active ingredient for some important diseases of peanuts, potatoes, various vegetables, and turf.

Agency Public Interest Finding Policy. The registration of a new pesticide ingredient is presumed to be in the public interest if one or more of the following criteria are applicable: 1) the pesticide is a replacement for another pesticide that is of concern to the Agency; 2) the pesticide has a use for which a Section 18 emergency exemption has been granted because of the lack of a suitable alternative; and 3) the pesticide is to be used against a pest of public health significance.

For the presumption of public interest, if any of the above criteria do not apply then one of the following three criteria must be met: 1) there is a need for the new pesticide that is not being met

by currently registered pesticides; 2) the new pesticide is less risky than currently registered pesticides; 3) the benefits from the new pesticide are greater than those from currently registered pesticides or non-chemical control measures. This review focuses on item 1 (needs) and item 3 (benefits).

General Information. Fluoxastrobin is a member of the group of quinol "outer" or "oxidizing" binding site inhibitor (QoI) fungicides. These fungicides act at the quinol outer binding site of the cytochrome bc1 complex of mitochondria by inhibiting electron transfer and respiration. Within this group of chemicals, fluoxastrobin is a strobilurin fungicide, synthetic derivatives of metabolites that are found in wood decaying fungi such as *Strobiluris tenacellus*. Since the strobilurin fungicide azoxystrobin was first registered in the U. S. in 1997, there have been numerous other strobilurin fungicides (e.g., pyraclostrobin, picoxystrobin, trifloxystrobin) registered on well over 50 use sites. In a short time, these chemicals have become among the most used fungicides in agriculture throughout the world (Bartlett et al, 2002). Because of their single-site mode of action, the QoI fungicides (which also include non-strobilurin fungicides such as famoxadone and fenamidone) have been put in Group 11 resistance category, which designates members as possessing cross-resistance properties (resistance found to one member of the group is likely also to have resistance to all other members). Since 1999, there have been reports of resistance by several pathogens to QoI fungicides (e.g., Kim et al, 2003). The North American Fungicide Resistance Action Committee (NAFRAC; http://www.frac.info/frac_regional.htm) recommendations now include limitations on seasonal application of QoI fungicides. NAFRAC also recommends mixing or alternating QoI fungicides with fungicides of different modes of action as a means to delay development of resistance to QoI fungicides.

Projected Use. The initial label for fluoxastrobin is projected to allow a maximum seasonal use rate of 0.72 lb active ingredient (ai) per acre for peanuts, potato and tuber vegetables, leafy vegetables, and fruiting vegetables. For turf the maximum seasonal rate would be 2.2 lb ai per acre, and for seed treatments (potato pieces, peanut, turf seed) 0.72 lb ai per acre.

Numerous fungal pathogens are targeted by fluoxastrobin and include those responsible for some of the most important diseases of the proposed sites (see Appendix A). For the most part, these are pests that are also targets of strobilurin fungicides that have already been registered. Bayer's data suggest that fluoxastrobin has comparable activity to azoxystrobin for many sites.

Section 18 History. No Section 18 requests have been made for fluoxastrobin.

Registrant's Claims for Public Interest Finding While fungicides in the same chemical group may be of similar structure to allow cross resistance, differences can be significant enough to affect important characteristics such as systemic activity within plants (Bartlett et al., 2002). These differences can influence the choice for the most appropriate fungicide for a particular crop and disease. For example, picoxystrobin is rapidly absorbed into plant tissue and is valued for early-season use in cereal crops (Bartlett et al., 2002). Some strobilurin fungicides simply move into the leaf and remain at this site ("locally systemic"). The locally systemic fungicide trifloxystrobin, for example, is considered a translaminar fungicide since it remains isolated

below the leaf surface. Bayer claims fluoxastrobin, like azoxystrobin and picoxystrobin, is a strobilurin that moves upward throughout the plant within the xylem, and is therefore a "xylem-mobile systemic" fungicide. Bayer claims fluoxastrobin's "...metabolism in the plant is relatively slow compared to other strobilurins such as azoxystrobin".

Although activity against certain pathogens can vary, so can adverse effects. For example, azoxystrobin is toxic to some MacIntosh apple cultivars, while trifloxystrobin is toxic to Concord grapes (Hartman, 2000). Bayer did not list any toxic problems for fluoxastrobin.

Bayer's request for a public interest finding is primarily based on their claim that fluoxastrobin will make available a fungicide that "...is more systemic than currently registered strobilurins", and therefore, its product will have a value not currently met by other strobilurins. No data to that effect were provided. While fluoxastrobin does not provide a new mode of action, BEAD believes that fluoxastrobin can provide an additional tool to growers when a particular pest problem arises. However, resistance issues are the same for fluoxastrobin as for other chemicals of Group 11, which includes all strobilurin and QoI fungicides. Therefore the use of any QoI fungicide restricts the number of application of any other within that group.

Conclusions and Recommendations. One major issue for the finding of a public interest for fluoxastrobin registration is its value to disease management when several other strobilurin fungicides are already available. While fungicides with new modes of action are highly desirable they are not easily developed. New products with modes of action already available have value to growers, since subtle differences in chemical structure can have large impacts on effective disease management and yield. Although fluoxastrobin is a member of the strobilurin group that includes already marketed active ingredients, BEAD believes that growers would benefit from a new active ingredient that can be an effective disease management tool, for both curative and preventative purposes. In many cases, the efficacy of this chemical will be comparable to others currently on the market, however, diverse qualities of strobilurin fungicides suggest that there can be a valuable place for this strobilurin active ingredient for some important diseases. In addition, new chemicals, especially with similar attributes, increase competition, and should lower prices. Thus, growers will receive benefits through lower production costs, which presumably, would be passed to the consumer.

References.

Bartlett, D. W., Clough, J. M., Godwin, J. R., Hall, A. A., Hamer, M., and Parr-Dobrzanski, B. 2002. The strobilurin fungicides. Pest Management Science 58:649-662.

Hartman, J. 2000. Disease control with strobilurin fungicides. University of Kentucky extension. http://www.uky.edu/Agriculture/kpn/kpn_00/pn000515.htm

Kim, Y., Dixon, E. W., Vincelli, P., Farman, M. L. 2003. Field resistance to strobilurin (QoI) fungicides in *Pyricularia grisea* cause by mutations in the mitochondrial cytochrome b gene. Phytopathology 93:891-900.

Appendix A.

Proposed Targets for Fluoxastrobin (Bayer HEC 480 SC Fungicide)

Peanut:

Early leaf spot (*Cercospora arachidicola*)
Late leaf spot (*C. personatum*)
Leaf rust (*Puccinia arachidis*)
Stem rot, White mold, Southern blight (*Sclerotium rolfsii*)
Rhizoctonia limb rot (*Rhizoctonia solani*)

Potato and tubers (including: arracacha, arrowroot, Chinese artichoke, Jerusalem artichoke, canna, cassava, chayote (root), chufa, dasheen, ginger, leren, sweet potato, tanier, turmeric, yam):

Early blight (*Alternaria solani*)
(suppression) Late blight (*Phytophthora infestans*)

Leafy vegetables (cardoon, celery, Chinese celery, celtuce, Florence fennel, rhubarb, Swiss chard):

Early blight (*C. apii*)
Late blight (*Septoria apliicola*)
Rhizoctonia root rot (*Rhizoctonia solani*)

Fruiting vegetables (eggplant, groundcherry, pepino, pepper, tomatillo, tomato)

Early blight (*Alternaria solani*)
Southern blight (*Sclerotium rolfsii*)
Target spot (*Corynespora cassiicola*)
(suppression) Late blight (*Phytophthora infestans*)

Seed Treatment (potato seed pieces, peanut, turf):

(suppression) *Rhizoctonia solani*

Turf

Brown patch (*Rhizoctonia solani*)
Southern blight (*Sclerotium rolfsii*)
Target spot (*Corynespora cassiicola*)
Summer patch (*Magnaporthe poae*)
(suppression) Snow mold (*Typhula incarnata*, *Microdochium nivale*)