USDA/APHIS Determination on a Petition 94-308-01p of Monsanto Agricultural Company Seeking Nonregulated Status of Lepidopteran- Resistant Cotton Lines 531, 757, 1076

Environmental Assessment And Finding of No Significant Impact

June 1995

The Animal and Plant Health Inspection Service (APHIS), United States Department of Agriculture (USDA) has prepared an environmental assessment prior to the determination that lepidopteran-resistant cotton lines 531, 757, and 1076 developed by Monsanto Corporation are no longer deemed regulated articles under 7 CFR 340. This environmental assessment has reached a finding of no significant impact to the environment from its determination that lepidopteran- resistant cotton lines 531, 757, and 1076 or their progeny shall no longer be regulated articles.

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Key Words: cotton; insect resistance; Bacillus thuringiensis; cryIA(c); delta-endotoxin protein; marker gene; nptII; neomycin phosphotransferase; kanamycin resistance.

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I. SUMMARY

USDA/APHIS has prepared an Environmental Assessment in response to a petition (APHIS Number 94-308-01p) from Monsanto Agricultural Company, Inc., St. Louis, Missouri (hereafter referred to as Monsanto) for the determination of their nonregulated status of their genetically engineered lines of cotton (Gossypium hirsutum L.) designated "BollgardTM cotton Line 531, 757, and 1076" (hereafter referred to as lepidopteran-resistant cotton). Monsanto requested a determination from APHIS that these genetically engineered cotton lines no longer be considered regulated articles under 7 CFR Part 340. Lepidopteran insect resistant cotton lines are defined as those cotton lines that express cryIA(c) gene coding for cryIA(c) toxin protein from the soil bacterium Bacillus thuringiensis var. kurstaki that confers insect resistance to lepidopteran insects in general, and cotton bollworm, tobacco budworm, and pink bollworm, in particular. They also express the nptII gene from Escherichia coli coding for the neomycin phosphotransferase enzyme that confers resistance to the antibiotic kanamycin.

Separate Environmental Assessments (EA) were prepared before granting the permits for field trials of these lepidopteran-resistant cotton lines. These EA addressed questions pertinent to plant pest risk issues concerning the conduct of field trials under physical and reproductive confinement, but they do not address several issues that are of relevance to the unconfined growth of genetically engineered cotton lines. With respect to these new issues, APHIS concludes the following:

1. Lepidopteran-resistant cotton lines 531, 737, and 1076 exhibit no plant pathogenic properties. Although pathogenic organisms were used in their development, these cotton plants are not infected nor can they cause disease in other plants.

2. Lepidopteran-resistant cotton lines are no more likely to become weeds than the nonengineered parental varieties. Cotton is not a serious, principal or common weed pest in the U.S., and there is no reason to believe that expression of the lepidopteran-resistane trait would cause these cotton plants to become weed pests.

3. The potential for gene introgression from genetically engineered cotton lines into wild or cultivated sexually compatible plants is very low, and such events are highly unlikely to increase the weediness potential of any resulting progeny.

4. Lepidopteran-resistant cotton lines are substantially equivalent in composition and lint quality to their nontransgenic counterparts and should have no adverse impacts on raw or processed agricultural commodities.

5. Lepidopteran-resistant cotton lines exhibit no significant potential either to harm organisms beneficial to the agricultural ecosystem or to lead to increased pest nature of other nontarget insect pests.

6. The use of genetically engineered cotton lines should present no greater risk of decreasing the ability to control cotton bollworm, tobacco budworm, and pink bollworm than any other method of insect control in cotton.

Therefore, after a review of the available evidence, APHIS believes that lepidopteran-resistant cotton lines will be just as safe as nontransgenic cotton plants that are typically grown using other methods to control cotton bollworm, tobacco budworm, and pink bollworm, and which are not subject to regulation under 7 CFR Part 340. APHIS concludes that there should be no significant impact on the human environment if these lepidopteran-resistant cotton lines were no longer considered regulated articles under regulations at 7 CFR Part 340.

II. BACKGROUND

A. Development Of Lepidopteran-Resistant Cotton Lines.

Monsanto has submitted a "Petition for Determination of Non-regulated Status" to the USDA, APHIS for three lepidopteran-insect resistant cotton (BollgardTM) lines 531, 757, and 1076 are defined as those cotton lines that express cryIA(c) gene coding for cryIA(c) toxin protein from the soil bacterium Bacillus thuringiensis var. kurstaki that confers insect resistance to lepidopteran-insects in general, and cotton bollworm, tobacco budworm, and pink bollworm, in particular. Upon ingestion of this protein by susceptible insects, feeding is inhibited, eventually resulting in death. The protein coding region of the gene was modified for optimal expression in plants. To express the gene, this region is fused to the promoter derived from the 35S gene of cauliflower mosaic virus (CaMV) with a duplicated enhancer region and to the nontranslated region of the soybean alpha subunit of the beta-conglycinin gene which provides the mRNA polyadenylation signals (7S 3' terminator sequence). The lines also express the nptII gene from Escherichia coli coding for the neomycin phosphotransferase enzyme, which confers resistance to the antibiotic kanamycin. These two genes were introduced into cotton lines via an Agrobacterium- mediated transformation protocol. This is a well-characterized procedure that has been used widely for over a decade for introducing various genes of interest directly into plant genomes.

These lepidopteran-resistant cotton lines have been field tested since 1991 in the major cotton growing regions of the United States under 10 APHIS permits numbers 90-347-01, 91-144-01, 91-347-02, 93-011-02,

93-011-05, 93-056-05, 94-025-01, 94-026-03, 94-027-03, and 94-054-02 in 14 states and 125 sites. Lepidopteran-resistant cotton lines have been evaluated extensively in laboratory and field experiments to confirm that these exhibit the desired agronomic characteristics and do not present a plant pest risk. Although the field tests have been conducted in agricultural settings, the permit conditions for the tests have stipulated physical and reproductive confinement from other plants.

B. APHIS Regulatory Authority.

APHIS regulations at 7 CFR Part 340, which were promulgated according to the authority granted by the Federal Plant Pest Act, (7 U.S.C. 150aa-150jj) as amended, and the Plant Quarantine Act, (7 U.S.C. 151- 164a, 166-167) as amended, regulate the introduction (importation, interstate movement, or release into the environment) of certain genetically engineered organisms and products. An organism is no longer subject to the regulatory requirements of 7 CFR Part 340 when it is demonstrated not to present a plant pest risk. A genetically engineered organism is considered a regulated article if the donor organism, recipient organism, vector or vector agent used in engineering the organism belongs to one of the taxa listed in the regulation and is also a plant pest, or if there is reason to believe that it is a plant pest. Lepidopteran-resistant cotton lines described in the Monsanto petition have been considered regulated articles because noncoding DNA regulatory sequences and portions of the plasmid vector are derived from plant pathogens.

Section 340.6 of the regulations, entitled "Petition Process for Determination of Nonregulated Status", provides that a person may petition the Agency to evaluate submitted data and determine that a particular regulated article does not present a plant pest risk and should no longer be regulated. If APHIS determines that the regulated article is unlikely to pose a greater plant pest risk than the unmodified organism, the Agency can grant the petition in whole or in part. As a consequence, APHIS permits would no longer be required for field testing, importation, or interstate movement of that article or its progeny.

C. EPA And FDA Regulatory Authority

These lepidopteran-resistant cotton lines are also subject to regulation by other agencies. The EPA is responsible for the regulation of pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136 et seq.). FIFRA requires that all pesticides, including insecticides, be registered prior to distribution or sale, unless exempt by EPA regulation. Accordingly, Monsanto has submitted to EPA an application to register this plant- pesticide, ie. the B.t.k. control protein as produced by the cryIA(c) gene and its controlling sequences in these lepidopteran-resistant cotton lines. On February 15, 1994, EPA announced receipt of this application (EPA File Symbol 524-UTI) in the Federal Register (59 FR 49663). This is one of the applications for registration of a transgenic plant pesticide under section 3(c) of FIFRA, as amended, in which a plant has been genetically altered to produce a pesticide. The EPA has not yet announced its final decision on this registration application; however, the Office of Pesticides Program has made available in the public docket a preliminary scientific position document regarding this registration application in preparation for a FIFRA Scientific Advisory Panel meeting, as announced in the Federal Register, January 25, 1995, Docket No. 95-2009, p. 4910. Before a product may be registered as a pesticide under FIFRA, it must be shown that when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment. FIFRA also authorizes EPA to issue Experimental Use Permits (EUP) and otherwise regulate the use of unregistered pesticides under FIFRA section 3(a). EUPs are generally issued (as authorized under FIFRA section 5 and 40 CFR part 172) for large-scale testing of pesticides on more than 10 cumulative acres of land. Contained within the scope of the regulation, however, is the presumption that small-scale testing, i.e., on not more than 10 cumulative acres of land, does not require an EUP provided that the crops are destroyed or an appropriate tolerance is in place (40 CFR 172.3(a)).

Under the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 U.S.C. 301 et seq.), pesticides added to (or contained in) raw agricultural commodities generally are considered to be unsafe unless a tolerance or exemption from tolerance has been established. Residue tolerances for pesticides are established by EPA under the FFDCA; and the FDA enforces the tolerances set by the EPA. Monsanto has submitted to the EPA a pesticide petition (PP 3F4273) proposing to amend 40 CFR part 180 to establish a tolerance exemption for residues of the plant pesticide active ingredient B.t.k. the insect control protein as expressed in plant cells. On December 8, 1993, EPA announced receipt of this petition [58 FR 64583-64584]. EPA announced its decision on this petition in which the agency approved a limited registration to produce large quantities of seeds (March 30, 1995). The EPA has announced a final rule establishing an exemption from the requirement of a tolerance for residues of nptII and the genetic material necessary for its production when used as a plant pesticide inert ingredient (59 FR 49351-49353, Docket No. 94-23762) as it is considered in the lepidopteran-insect resistant cotton lines.

Safety concerns for human and animal consumption of products with kanamycin resistance are also specifically addressed by the FDA in 21 CFR Parts 173 and 573. The FDA policy statement concerning regulation of products derived from new plant varieties was published in the Federal Register on May 29, 1992, and appears at 57 FR 22984-23005. The Monsanto Company has satisfactorily completed their food safety and nutritional assessment as recommended under this FDA policy statement. III. PURPOSE AND NEED

Monsanto, submitted this petition to USDA, APHIS requesting that APHIS make a determination that lepidopteran-resistant cotton lines shall no longer be considered regulated articles under 7 CFR Part 340. APHIS has prepared this EA to make a determination on the status of lepidopteran-resistant cotton lines as regulated articles under APHIS regulations.

This EA was prepared in compliance with the National Environmental Policy Act (NEPA) of 1969 (40 CFR 1500-1508) and the pursuant implementing regulations published by the Council on Environmental Quality (42 USC 4331 et seq.; 40 CFR 1500-1508; 7 CFR Part 1b; 60 FR 6000-6005).

Consistent with the "Coordinated Framework for Regulation of Biotechnology" (51 FR 23302-23350, June 26, 1986), when appropriate, APHIS and the EPA have coordinating their review of these lepidopteran-resistant cotton lines to avoid duplication and assure that all relevant issues are addressed. Therefore, reference is made to EPA review documents which address certain environmental issues.

IV. ALTERNATIVES

A. No Action.

Under the Federal "no action" alternative, APHIS would not come to a determination that lepidopteran-resistant cotton lines are not regulated articles under the regulations at 7 CFR Part 340. Permits or acknowledgement of notifications from APHIS would still be required for introductions of lepidopteran-resistant cotton lines. APHIS might choose this alternative if there were insufficient evidence to demonstrate the lack of plant pest risk from unrestricted cultivation of lepidopteran-resistant cotton lines.

B. Determination That Lepidopteran-Resistant Cotton Lines Are No Longer Regulated Articles APHIS Under Federal Plant Pest Act and Federal Quarantine Act.

Under this alternative, lepidopteran-resistant cotton lines would no longer be regulated articles under the regulations at 7 CFR Part 340. Permits from APHIS would no longer be required for introductions of lepidopteran-resistant cotton lines. One basis for this determination could be a "Finding of No Significant Impact" under the National Environmental Policy Act of 1969 (42 USC 4331 et seq.; 40 CFR 1500- 1509; 7 CFR Part 1b; 60 FR 6000-6005). V. AFFECTED ENVIRONMENT AND POTENTIAL ENVIRONMENTAL IMPACTS

This EA addresses potential environmental impacts from a determination that lepidopteran-resistant cotton lines should no longer be considered regulated articles under APHIS regulations at 7 CFR Part 340. Previous EA prepared by APHIS for permits to field test lepidopteran-resistant cotton lines have addressed various attributes of lepidopteran-resistant cotton lines. This EA discusses the genetic modification, and the potential environmental impacts that might be associated with the unconfined cultivation of lepidopteran-resistant cotton lines.

Additional technical information is included in the determination document appended to this EA and the EA prepared for contained field tests under APHIS permits, 90-347-01, 91-144-01, 91-347-02, 93-011-02, 93-011-05, 93-056-05, 94-025-01, 94-026-03, 94-027-03, and 94-054-02. The field tests took place at 125 sites in the following 14 states: Alabama, Arizona, Arkansas, California, Florida, Georgia, Hawaii, Louisiana, Mississippi, Missouri, North Carolina, South carolina, Tennessee, and Texas. The EA for all these tests contain detailed discussions of the biology of cotton, the genetic components used in the construction of lepidopteran-resistant cotton lines, and the analyses that lead APHIS to conclude that lepidopteran-resistant cotton lines have no potential to pose plant pest risks.

This EA is concerned with potential environmental impacts from the unrestricted introduction of lepidopteran-insect resistant cotton.

A. Potential For Lepidopteran-Resistant Cotton Lines To Exhibit Increased Weediness Relative To Traditionally Bred Cotton Varieties

Almost all definitions of weediness stress as core attributes the undesirable nature of weeds from the point of view of humans; from this core, individual definitions differ in approach and emphasis (Baker, 1965; de Wet and Harlan, 1975; Muenscher, 1980). In further analysis of weediness, Baker (1965) listed 12 common weed attributes, almost all pertaining to sexual and asexual reproduction, which can be used as an imperfect guide to the likelihood that a plant will behave as a weed. Keeler (1989) and Tiedje et al. (1989) have adapted and analyzed Baker's list to develop admittedly imperfect guides to the weediness potential of transgenic plants; both authors emphasize the importance of looking at the parent plant and the nature of the specific genetic changes.

The parent plant in this petition, G. hirsutum, does not show any appreciable weedy characteristics. The genus also seems to be devoid of any such characteristics; although some New World cottons show tendencies to "weediness" (Fryxell, 1979; Haselwood et al., 1983), the genus shows no particular weedy aggressive tendencies. The standard texts and list of weeds give no indication that cotton is clearly regarded as a weed anywhere (Holm et al., 1979; Muenscher, 1980; Reed, 1970; Weed Science Society of America, 1989). Any reports that cottons behave as a weed are rare and anecdotal, and vague as to the nature of the problem.

The single trait introduced into cotton (lepidopteran-resistance) is unlikely to increase weediness of this cotton. Weediness is a multigenic trait. Assuming that domesticated cotton has the potential to become a weed, any increase in the weediness of the transgenic cotton plant would have to result from the transgenic plant having a competitive advantage over the parental, nontransgenic cotton line (Tiedje et al., 1989; Office of Technology Assessment, 1988). Because lepidopteran-resistant cotton is expected to be cultivated like any other cotton in a managed agricultural ecosystem, the likelihood that sufficient selective pressure would be present for the lepidopteran- resistant cotton to become a weed is low.

No other variation seen in lepidopteran-resistant cotton lines is indicative of increased weediness. Monsanto data from greenhouse studies show a variation in germination rates among transgenic seed lines but no evidence of specific changes in the rate from parent to transgenic plant compared to nontransgenic cottons was found. In addition, Monsanto field reports show no obvious increase in volunteers from seed, regrowth from stubble, or increase in seed dormancy. Lint characteristics showed no changes from that of nontransgenic cotton. Monsanto's report on lint characteristics showed practically no changes from those of nontransgenic cotton.

Monsanto did observe some decrease in boll size in line 531, the overall yield of line 531 cotton was superior to that of nontransgenic cotton. Even if such a decrease is reproducible on a larger scale, APHIS believes that no competitive advantage affecting weediness would be conferred on the transgenic plants by this change. APHIS believes that a relationship between seed size and increase in weediness potential should only apply in small-seeded crops, in which seed dispersal is affected by factors like wind, and not in large-seeded crops like cotton.

With respect to potential effects of the cultivation of the lepidopteran-resistant cotton outside the United States, APHIS notes that there is already considerable cultivation of nontransgenic cotton around most centers of cotton diversity. The major threat to many relatives of cotton appears to be habitat destruction (Fryxell, 1979). Several other factors are relevant. (1) Crop plants and seeds exported from the United States, whether transgenic or non-transgenic varieties, are still subject to the phytosanitary restrictions of the importing nation. (2) APHIS has no jurisdiction over agricultural practices in foreign nations and our action does not constitute approval for field testing or commercialization of this cotton in any other nation. (3) Foreign laws restricting or regulating field testing or commerce with transgenic cotton are unaffected by our action. (4) APHIS has no jurisdiction over approval for the use of lepidopteran- resistant cotton plants in foreign nations.

Scenarios in which an impact of lepidopteran-resistant cotton on wild cotton varieties is envisioned depend, at a minimum, on a biologically unlikely scenario coupled with a failure of regulatory oversight in a foreign nation. Knowledge about the ecology of wild cottons and the insects with which they interact is incomplete. APHIS believes that the lack of increased weediness observed for the transgenic cotton lines strongly suggests that any potential gene transfer to wild cotton would not likely result in increased weediness on their part.

B. Potential Impacts Associated With Potential Gene Introgression From Lepidopteran-resistant Cotton Lines To Sexually Compatible Plants (With Wild and Cultivated Relatives)

None of the relatives of cotton found in the United States (G. barbadense, G. thurberi, and G. tomentosum) shows any weedy tendencies. Successful sexual transmission of genetic material via pollen is possible only to certain cotton relatives. In the United States, the compatible species are G. hirsutum (wild or under cultivation), G. barbadense (cultivated Pima cotton), and G. tomentosum.

Lepidopteran-resistant cotton is chromosomally compatible with wild G. hirsutum. However, according to Dr. Paul Fryxell of Texas A & M University (personal communication), a leading authority on the systematics and distribution of these species, wild cottons are found only in southern Florida (virtually exclusively in the Florida Keys), whereas cultivated cottons are found in northernmost portions of the State. Other wild G. hirsutum is to be found along the Mexican coast, largely along the Yucatan, and populations do not extend as far north as the Texas border. G. hirsutum has also been grown in several United States Territories and Possessions, and may even to a greater or lesser degree be spontaneous or naturalized in places such as the Northern Mariana Islands, Puerto Rico, and the Virgin Islands. However, there are no peculiarities of cotton in these areas that would require unique review. Most wild G. hirsutum populations are geographically isolated from cultivated cotton, and do no cross with native or cultivated cotton species (Alan C. York, North Carolina State University, personal communication). Even if the non- agricultural land containing any wild cotton populations were near sites of commercial cotton production, there would be no significant impacts, APHIS believes, because: (1) any potential effects of the trait are not expected to alter the weediness of the wild cotton; and (2) wild cotton populations have not been actively protected, but have in fact been, in some locations such as Florida, subject in the past to Federal eradication campaigns, because they can serve as potential hosts for the boll weevil, Anthonomus grandis Boh.

Gossypium thurberi, the wild relative found in Arizona, is not compatible with pollen from G. hirsutum, so that genetically engineered insect resistant cotton can have no effect on this species. Movement to G. hirsutum and G. barbadense is possible if suitable insect pollinators are present, and if there is a short distance from transgenic plants to recipient plants. Any physical barriers, intermediate pollinator-attractive plants, and other temporal or biological impediments would reduce the potential for pollen movement.

Movement of genetic material from cultivated cottons varieties that have been engineered for lepidopteran resistance to G. tomentosum is more speculative (see determination for discussion). The wild species is chromosomally compatible with G. hirsutum, but there is uncertainty about the possibility for pollination. The flowers of G. tomentosum seem to be pollinated by moths, not bees, and they are reportedly receptive at night, not in the day. Both these factors greatly lessen the possibility of cross-pollination. There have been reports based on morphological suggestions (Stephens, 1964; Fryxell, 1979) that G. tomentosum may be losing its genetic identity from hybridization with cultivated cottons by unknown means. However, the most recent data, from DeJoode and Wendel (1992), indicate that despite the morphological suggestion of such hybrid populations, biochemical (allozyme) studies show no evidence of any such changes. Major factors influencing the survival of G. tomentosum are construction and urbanization, i.e., habitat destruction (Fryxell, 1979). APHIS believes that it is these factors, rather than gene movement from cultivated cottons, that are of real significance to this species. Cotton lines bred by traditional means, which should be no more or less likely to interbreed with G. tomentosum than genetically engineered insect resistant cotton, are not considered to pose a threat to the wild cotton and are not subject to particular State or Federal regulation on this basis. Neither the weediness nor the survival of G. tomentosum will be affected by the cultivation of genetically engineered insect resistant cotton because: the transgenic variety poses no increased weediness itself; the two species are unlikely to successfully cross in nature; and the added traits will confer no selective advantage in the wild species habitat.

In contrast to the situation with G. tomentosum, gene movement from G. hirsutum to G. barbadense is widespread in advanced cultivated stocks. However, it is conspicuously low or absent in material derived from natural crosses such as that from Central America or the Caribbean where G. hirsutum and G. tomentosum grow together. The absence of natural introgression may be caused by any one of several isolating mechanisms of pollination, fertilization, ecology, gene incompatibility, or chromosome incompatibility (Percy and Wendel, 1990). Movement of gene material from genetically engineered insect resistant cotton to cultivated or occasional non-cultivated G. barbadense would therefore not likely occur at a high level. Any movement of genetic material from genetically engineered insect resistant cotton cottons into G. barbadense is likely to be the result of intentional breeding practice rather than accidental crossing.

Even if such movement did occur, it would not offer the progeny any clear selective advantage over the parents use.

C. Potential Impact On Nontarget Organisms Including Beneficial Organisms Such As Bees And Earthworms

Consistent with its statutory authority and requirements under NEPA, APHIS evaluated the potential for the lepidopteran-resistant cotton plants and plant products and the Btk insect control protein to have damaging or toxic effects directly or indirectly on nontarget organisms, particularly those that are recognized as beneficial to agriculture and to those which are recognized as threatened or endangered in the United States. APHIS also considered potential impacts on other "nontarget" pests, since such impacts could have an impact on the potential for changes in agricultural practices.

CryIA(c), expressed in lepidopteran-resistant cotton lines, shows a strict host-range specificity for lepidopteran insects and has no deleterious effects on nontarget organisms. Invertebrates such as earthworms, and all vertebrate organisms, including non-target birds, mammals and humans, are not expected to be affected by the Btk insect control protein because they would not be expected to contain the receptor protein found in the midgut of target insects. Results from high dose feeding studies on bobwhite quail, rats, non-lepidopteran insects, birds, mammals and mice demonstrated no adverse effects. Ecological effect studies submitted to the EPA in support of the earlier registration of foliar microbial Btk pesticides indicated no unreasonable adverse effects on nontarget insects, birds, and mammals (EPA, 1988).

There is no reason to believe that deleterious effects or significant impacts on nontarget organisms, including beneficial organisms, would result from the cultivation of lepidopteran-resistantinsect resistant cotton. The novel proteins that will be expressed in lepidopteran resistant cotton are not known to have any toxic properties on any nontarget organisms. The lack of known toxicity for these proteins and the low levels of expression in plant tissue suggest no potential for deleterious effects on beneficial organisms such as bees and earthworms. APHIS has not identified any other potential mechanisms for deleterious effects on beneficial organisms. In addition, there is no reason to believe that the presence of lepidopteran-resistant cotton would have any effect on any other threatened or endangered species in the United States. There is no evidence of any endangered or threatened species of lepidopteran insects feeding on cotton, and as such, no effects of the CryIA(c) protein on them are predicted. There is no reason to believe that deleterious effects or significant impacts on nontarget organisms, including beneficial organisms, would result from the NPTII protein conferring kanamycin resistance used as a selectable marker during development of transgenic cotton lines.

D. Potential Impacts On Agricultural Practices Associated With The Cultivation Of Lepidopteran-resistant Cotton Plants And The Development of Insect Resistance To The Btk Insect Control Protein

APHIS considered the potential impacts associated with the cultivation of lepidopteran-resistant cotton plants on current agricultural practices used to control lepidopteran insects in general, and cotton bollworm, tobacco budworm, and pink bollworm, in particular. Pages 100-105 of the Monsanto petition discuss the impact of the lepidopteran-resistant cotton lines on cotton pest management. Monsanto strategy for maximizing the utility of these plants and delaying the development of insects resistant to the CryIA(c) insect control protein is outlined in the Determination. Their strategy was also submitted to the EPA in support of the registration of the CryIIIA and CryIA(c) proteins expressed in plants as a plant- pesticide. Since this evaluation has been made available by the EPA for the Scientific Advisory Panel meeting (Matten, EPA, 1994), the details will not be presented by APHIS. The development of effective resistance management strategies is an ongoing process, and APHIS will offer comments and suggestions, as appropriate, to the EPA and Monsanto to assist in this process. The EPA has stated that they are committed to working with Monsanto to develop product labels and informational brochures that include instructions on the proper use of the lepidopteran-resistant cotton lines consistent with resistance management. For a full discussion of current agricultural practices used to control lepidopteran insect pests of cotton and the impact of lepidopteran-resistantinsect resistant cotton lines, see both the Response to Comments and Section IV.F. of the Determination.

Both larvae and adult lepidopteran insects cause severe damage to cotton crops, and cultivation of cotton consumes the largest amount of chemical insecticides of any crop cultivated worldwide. Cultural control methods, biological and conventional insecticides, and biological control agents currently used or being developed for control of insect pests in cotton are discussed in more detail in the Determination. There is no doubt that cultivation of the lepidopteran-resistant cotton plants could reduce the use of chemical pesticides, some of which are becoming obsolete because of insect resistance (see petition pages 14-16).

There are currently no commercially available cotton cultivars that are resistant to lepidopteran insects. If commercialized, the transgenic insect resistant cotton plants could offer an important alternative to chemical insecticides, particularly to those for which resistance has already developed. They will also offer a more flexible, effective alternative for season-long control of lepidopteran insects compared to the use of some foliar microbial products. By the same token, widespread and inappropriate use of either lepidopteran-resistant cotton or foliar microbial products can and will most likely accelerate the appearance of lepidopteran populations resistant to the Btk insect control protein. Calculating the rate at which resistance will develop using either approach is difficult to predict because it depends on several factors: (1) the resistance management strategies and their acceptance and effective implementation by growers; (2) the genetics of lepidopteran resistance to this insecticide; and (3) the population and behavioral biology of the lepidopteran insect pests (Roush, 1994; Tabashnik, 1994a and b; Gould et al., 1994). The lack of field-selected resistant lepidopteran insect populations precludes the direct testing of the validity of models to predict the rate with which lepidopteran insects will develop resistance using different management strategies.

The implementation of an active resistance management plan that is scientifically sound and acceptable to growers should delay the onset of resistance and provide alternative strategies and methods for managing or containing resistant populations if and when they occur. For example, it may be possible to control resistant lepidopteran insect populations by the use of alternative cultural control practices and alternate insecticides, particularly those to which lepidopteran insects have not yet been exposed. If resistant populations persist, insecticides based on the CryIA(c) protein would no longer be effective for controlling lepidopteran pests on cotton or on other crops for which these insecticides are registered.

APHIS has concluded that there is unlikely to be any significant adverse impact on agricultural practices associated with the appropriate use of lepidopteran-resistant cotton plants. This analysis is based on a consideration of (1) the geographical locations where the lepidopteran-resistant cotton plants will be grown, (2) the major production areas for cotton plants that are subject to lepidopteran pests pressure, (3) the usage of insecticides on these crops, and 4) the availability of alternative lepidopteran pest control measures. Resistance development in insect pest populations is a risk associated with the deployment of insecticides. But in this respect, cultivation of lepidopteran-resistant cotton plants should have no greater impacts on the control of lepidopteran pests in cotton plants and other crops than the widely practiced method of applying insecticides to control lepidopteran insect pests on cotton cultivars. Monsanto has stated that it is in their best interest to delay resistance. The EPA has stated that they will work with Monsanto to develop product labels and informational brochures that are consistent with resistance management, and this should help define the appropriate use of these cotton plants. Should resistant lepidopteran insect populations evolve, it may be possible to limit the persistence and spread of resistant populations. But as with conventional insecticides, where resistance develops, growers will lose the capability to use particular Btk insecticides to control lepidoptera on cotton. Although Btk formulations may also be a registered for use on corn, okra, soybeans and tomatoes, occurance of CryIA(c)-resistant lepidopteran insects in cotton fields should have minimal impacts on Btk uses on these crops. The only potential for any impact would occur whem the crops are cultivated very near, or in rotation with, the lepidopteran-resistant cotton. Since these insecticides are currently used infrequently in the major areas of production for these crops, and other options exist for the control of lepidopteran pests, the impact should be minimal.

VI. CONCLUSIONS

APHIS has evaluated information from the scientific literature and data submitted by Monsanto regarding characterized lepidopteran- resistant cotton lines. After careful analysis, APHIS has identified no significant impact to the environment from issuance of a determination that lepidopteran-resistant cotton lines should no longer be regulated articles under APHIS regulations at 7 CFR Part 340.

APHIS has considered the foreseeable consequences of issuing a determination that these lepidopteran-resistant cotton lines are no longer regulated articles, and has reached the following conclusions:

1. Lepidopteran-resistant cotton lines 531, 737, and 1076 exhibit no plant pathogenic properties. Although pathogenic organisms were used in their development, these cotton plants are not infected nor can they incite disease in other plants.

2. Lepidopteran-resistant cotton lines are no more likely to become weeds than insect-resistant cotton plants developed by traditional breeding techniques. Cotton is not a serious, principal or common weed pest in the U.S., and there is no reason to believe that ecpression of the insect resistant trait would cause these cotton plants to become weed pests.

3. The potential for gene introgression from lepidopteran-resistant cotton lines into wild or cultivated sexually compatible plants is very low, and such events are highly unlikely to increase the weediness potential of any resulting progeny.

4. Lepidopteran-resistant cotton lines are substantially equivalent in composition and lint quality to their nontransgenic counterparts and should have no adverse impacts on raw or processed agricultural commodities.

5. Lepidopteran-resistant cotton lines exhibit no significant potential either to harm organisms beneficial to the agricultural ecosystem or to lead to increased pest nature of other nontarget insect pests.

6. The responsible use of lepidopteran-resistant cotton lines should present no greater risk of decreasing the ability to control cotton bollworm, tobacco budworm, and pink bollworm than any other method of insect control in cotton.

Therefore, after review of the available evidence, APHIS concludes that lepidopteran-resistant cotton lines will be just as safe to grow as any other nontransgenic cotton varieties that are not subject to regulation under 7 CFR Part 340. APHIS concludes that there should be no significant impact on the human environment if lepidopteran- resistant cotton lines were no longer considered regulated articles under its regulations (7 CFR Part 340). VII. LITERATURE CITED

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