Comments on Petition for Determination of Nonregulated Status of Cotton Genetically Engineered for Insect Resistance
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Sustainability is a global challenge in agriculture as we meet the needs of a growing population for food and fiber. That challenge is no smaller for the cotton industry, where even apparel manufacturers wish to source cotton from sustainable systems. Bt as a source of an entire class of proteins arguably has been a breakthrough technology for overcoming some of cotton’s largest pest problems such as the pink bollworm (*Pectinophora gossypiella*) and the tobacco budworm (*Heliothis virescens*). Of course, Bt was of little consequence until plants were engineered with genes expressing their proteins. Since then, the pink bollworm has been eradicated from the United States and northern Mexico, largely on the back of this very effective and safe technology.

Bt and the plants bearing their modified genes produce proteins with a high degree of selectivity owing to their specificity largely to the class of insects. Bt proteins are exceptionally well known toxicologically and have an excellent record for vertebrate safety, with no ill effects for birds, fish, mammals and most wildlife. There are also high degrees of safety for invertebrates outside of Class Insecta, protecting soil and other systems where these organisms provide vital ecosystem services.

The engineering of an agricultural plant with such a well-characterized set of proteins, which has a spotless record of widespread vertebrate and invertebrate safety, is tantamount to the goals of host plant resistance and traditional breeding methods that have existed for centuries. Breeding agricultural plants and animals that can resist infestation and pest damage is a cornerstone practice of integrated pest management (IPM; see Figure 1). IPM, in turn, is the worldwide standard for pest management that protects economic, environmental, human health and social interests. IPM, a durable concept with its origins in science now 60 years ago (Stern et al. 1959; Naranjo & Ellsworth 2009), has helped to save growers billions of dollars, protected environments from unnecessary pesticide applications, and safeguarded society from unwanted risks posed by pests and pest management practices (see Figure 2 for Arizona cotton example).
The standards for development of a genetically engineered (GE) crop in the U.S. are stringent, with regulation by both USDA and EPA. These standards require a large set of complex and diverse sources of scientific evidence of biological, cultural and ecological safety, which exceed what is required for the registration, for example, of a traditional pesticide that is potentially sprayed on millions of acres. These high standards assure society and the scientific community, in particular, that known risks are mitigated and unforeseen and unintended risks are anticipated, insofar as is possible. Consumer and marketplace acceptance is a much more complex dynamic that is not easily predicted by the hard science that supports the development of these technologies. As such, comments to this docket include perhaps well intended, but unsupported claims of undue risks to human health and the environment. No matter anyone’s personal opinion of the industries engaged in its development, there is no evidence that MON 88702 or the Cry protein it produces, mCry51Aa2, pose any risk to human health or the environment. According to APHIS standards, this genetically engineered (GE) cotton has no capacity to serve as a “plant pest” and indeed marks another major advance in biotechnology.

That said, the assemblage of invertebrate fauna will likely change, as one would expect when a new resistant cultivar is introduced to a region. Broad-acre crops with novel proteins of high selectivity and safety to the vast majority of invertebrate organisms present will change the agroecosystem. There will be broad-scale reduction in insecticide inputs, including some that are broadly toxic and have negative impacts on invertebrates, aquatic systems, wildlife and human health and safety. Ecological effects are guaranteed. However, the net benefits to the ecosystem services supplied by invertebrates will be substantially increased by this new GE cotton, contributing to lower target pest densities and fewer insecticidal inputs. The resulting lower ecotoxicological footprint of cotton will therefore create new opportunities over millions of acres where it is grown in the U.S. to support biological control, pollination services, and nutrient recycling.

The track record for safe and sensible deployment of Bt Cry proteins in Arizona cotton is outstanding and borne out by the extensive sets of data available to us. The cotton IPM system of Arizona has historically focused on three key pests that drive the vast majority of insecticide use there. The pink bollworm has been eradicated officially since 2018. However, growers stopped spraying broadly toxic insecticides for the pink bollworm since 2008, when Cry1a- and Cry2-based Bt cottons were planted over the majority of acres. The insecticides effectively eliminated from the cotton production system in Arizona include broadly toxic organophosphates like methyl parathion and chlorpyrifos.

The remaining two key pests in the Arizona cotton system are the invasive whitefly, Bemisia argentifolii, and the indigenous plant bug, Lygus hesperus. Highly selective and safe insecticides for whitefly control have been in development for the past three decades and now include 7 different modes of action that are fully selective and 1 additional mode of action that is partially selective. The opportunities for safe and effective control of whiteflies without harm to the suite of invertebrates that support the Arizona cotton system are many.

Prior to 2006, control of Lygus was dependent on broadly toxic insecticide inputs including the organophosphate acephate, the organochlorine endosulfan, and the carbamate oxamyl.
Endosulfan has since been banned in the US and many other countries around the world because of the ecotoxicological hazards it presented. Oxamyl is on the highly hazardous pesticide list worldwide and usage should be curtailed wherever possible. Acephate was the number one cotton insecticide used in Arizona for many years running prior to 2006. Since 2006 and then since 2012, respectively, two fully safe and selective insecticides were developed for efficient Lygus control, flonicamid and sulfoxaflor. These two insecticides have all but eliminated further uses of acephate or oxamyl in Arizona cotton.

Reliance on a narrow set of insecticidal tools carries with it greater chances for the development of resistance, reducing the benefits of their use and greatly increasing costs of control for farmers. Alternatively, access to a broader suite of controls as promoted by IPM enables a sustainable path forward even in the face of existing resistances. For example, whiteflies are controlled through the use of 1 or more of 8 modes of action currently. Active resistances are known in some whitefly populations to at least 3 of these modes of action (e.g., acetamiprid, pyriproxyfen). Yet, producers are able to manage these resistances through wise product selection and rotation among effective modes of action. This approach makes even the products compromised by resistances available and effective for longer periods of time. These use patterns are made even more sustainable because of their enabling selective attributes that conserve natural enemy populations in cotton fields. These natural enemies provide “free” pest control by continuing suppression of key pests like whiteflies and Lygus bugs and prevent all other secondary pests from breaking out to economic levels in Arizona cotton. Their action likely helps prevent resistance to any one compound becoming problematic for growers.

Unlike whiteflies, Lygus chemical control depends on just two modes of action. While these are highly effective products with high degrees of safety to the beneficials in the system, over-reliance on just one or two modes of action carries with it much larger risks for resistance. The addition of a GE cotton that is developed to resist Lygus populations and lower their damage provides a much needed third mode of action and an entirely new alternative to traditional Lygus chemical control. Just like a three-legged stool, the addition of this technology will only serve to strengthen the sustainability of the Lygus management system, providing durability to all measures for a longer period of time.

The Arizona system has come to rely extensively on the conserved fauna naturally present in cottonfields, namely arthropod predators with generalized habits of feeding on key and secondary pests throughout the season. Conservation biological control is central to the function of the cotton insect IPM system. Loss of control of Lygus with the existing two modes of action (flonicamid or sulfoxaflor) would lead to greater reliance on broadly toxic insecticides like acephate. This, in turn, would erode the function of biological control of whiteflies and other pests, forcing growers to spray more frequently. This so-called “pesticide treadmill” can be overcome through the wise use of IPM. Bt-based GE cottons are key enabling technologies for cotton IPM (Anderson et al. 2018).

Over half a billion dollars has been saved by the cotton growers of Arizona since the initial introduction of Bt cottons there in 1996. These savings come in the form of fewer insecticides used and yield loss prevented by Bt and other technologies. The estimated share of savings in arthropod pest management due to biological control since 1996 is 42%. This is hard
Evidence that Bt cottons have served as one of the key enabling technologies for cotton IPM in Arizona. Historians will look back to this period in time as a watershed change in approach to insect management and the capacity of IPM to provide sustainability into the future.

Our laboratory has been actively evaluating MON88702 for many years now. Efficacy against Lygus spp. and Frankliniella spp. is well established in the registrant’s submission and in our local trials. Lygus control by MON88702 is not absolute, unlike what was found for the Cry1Ac-based Bt cottons initially deployed for the control of pink bollworms. However, we estimate that grower use of this new GE cotton will lead to substantial reductions in the need to spray for Lygus. In general, growers spray for all arthropod pests about 2.2 times per season, around 1–1.5 of those targeting Lygus bugs. **We expect this new technology to eliminate the need for 1 of those Lygus sprays.** Control by this GE cotton is therefore akin to an incomplete resistance common in conventionally bred, constitutive resistances in resistant cultivars. Some sprays against Lygus may still be necessary, but growers will greatly reduce their reliance on the two chemical modes of action available, leading to more sustainable use patterns for all technologies over time. Growers that may have sprayed twice may see the need to spray only once for Lygus with this new cotton. Others who only spray once for Lygus may be able to eliminate Lygus sprays altogether. **The likely savings to growers is very high. One Lygus spray costs $25.24 per acre. Growers would likely save over $3.7 million per year in Arizona alone.**

The focus of the registrant’s submission to this docket is on the safety of this protein and the cotton engineered to produce it. **There is a high degree of confidence that this protein and the GE cotton are safe to human health and to vertebrate systems in general.** As a toxin in an invertebrate system (Lygus and thrips), there is a sensible rationale to examine the array of effects possible in invertebrate systems, which this registrant has done extensively. **Our IPM system in Arizona depends both on the efficacy of developed technologies as well as their selectivity and safety to non-target organisms, including especially those responsible for biological control services in our fields** (see Vandervoet et al. 2018).

Our laboratory has been and continues to be involved in the development of non-target organism (NTO) data associated with the use of this new GE cotton in contrast to conventional cotton that is untreated with insecticides as well as to conventional cotton sprayed with the array of insecticides that would otherwise be needed to protect against Lygus bugs. Our work includes research independent of the registrant’s, which is supported by federal competitive grant dollars through the USDA-Biotechnology Risk Assessment Program (Huseth, Kennedy, Ellsworth & Naranjo). This study examines potential non-target effects, but is dedicated to measurement of the trade-offs of ecological changes as related to the key ecosystem services of biological control. We are especially interested in the ecosystem services provided by *Orius* spp. and one of the targets of this technology, *Frankliniella occidentalis*. **While this work is ongoing and will continue, more and larger format work can be completed once MON88702 is granted non-regulated status.** In the meantime, however, the registrant has provided ample and extensive data on the safety of MON88702 towards NTOs including key invertebrates. And, there is no indication in their submitted data or our own ongoing independent work that would suggest that MON88702 poses any risk as a plant pest in our system or any undue or unexpected risk to invertebrates of the cotton system.
We urge the USDA to grant the registrant’s request for unregulated status. The evidence for safety is compelling and more than complete to meet the requirements of the Plant Protection Act. The registrant exceeded any requirements by completing Tier 1 through Tier 4 testing for a potentially sensitive non-target species (i.e., Orius spp) and many other studies of surrogate non-target invertebrates. Indeed, the granting of non-regulated status of this cotton will enable important research that can be conducted at even larger scales of relevance. This approval will permit us to better prepare and advise adopting and non-adopting growers about what to expect and how to incorporate this valuable technology into their IPM strategies. The addition of this key technology will support other key chemical and non-chemical (especially biological control) practices needed to sustainably produce cotton for the future, while protecting human health, the environment and society.

Figure 1. Conceptual diagram of integrated pest management of cotton in Arizona. Depicted are 3 key layers of sampling/detection, effective chemical use, and avoidance. At the foundation of ‘avoidance’, there are 3 additional layers of crop management, exploitation of pest biology, and areawide impact that consist of multiple tactics critical to supporting IPM. Cornerstone to this rendition is the tactic of ‘tolerant / resistant varieties’. Host plant resistance such as developed in MON88702 will better support Lygus IPM, reduced risks of resistance to the two effective and selective Lygus insecticides, flonicamid and sulfoxaflor, and better support natural enemy conservation through reduction in need of any broadly toxic Lygus insecticides.
Figure 2. Statewide average insecticide use (number of sprays per acre) for Arizona cotton, 1990–2018. Cry1Ac-based Bt cottons were introduced in 1996 and were among the first enabling technologies for broad-scale reduction in broad-spectrum insecticide inputs and conservation biological control. Pink bollworm eradication was declared by the U.S. in 2018, fully 10 years after the last grower-initiated spray was made for that pest. The success of this historic program was, in part, due to the wide-scale deployment of Cry1a- and Cry2- based Bt cottons. Lygus has been the number one yield-limiting pest of cotton since 1997, requiring broad-spectrum insecticide inputs for its control until 2006, when the first selective chemical control became available (flonicamid). Lygus chemical control advanced again in 2012 with the addition of sulfoxaflor, another selective Lygus control with full safety to non-target predators and other beneficial arthropods. Growers have averaged just over 2 sprays to control all arthropod pests since 2015, about 1.3 of which are targeting Lygus bugs. MON88702 has the capacity lower the number of sprays needed to control Lygus bugs, perhaps by about one spray per season. If successful and widely adopted, growers could see the need to spray drop to almost half the level currently used, saving the industry more than $3.7M per year.

Who We Are

The Arizona Pest Management Center is host to the University of Arizona’s expert IPM scientists including Ph.D. entomologists, weed scientists and plant pathologists with expertise in the strategic tactical use of pesticides within IPM programs that protect economic, environmental and human health interests of stakeholders and the society at large.
Dr. Peter Ellsworth is Director of the Arizona Pest Management Center (APMC), State IPM Coordinator for Arizona and Professor of Entomology / Extension IPM Specialist with expertise in developing IPM systems in cotton and other crops and measuring implementation and impact of IPM and pest management practices. Dr. Alfred Fournier is Associate Director of the APMC / Associate Specialist in Entomology, with expertise in evaluating adoption and impact of integrated pest management and associated technologies. He serves as a Regional Integrated Pest Management Network Coordinator for the Western IPM Center, representing stakeholders in the desert Southwest states. He coordinates the development of tools and data used in IPM research, education and evaluation, including APMC Pesticide Use Database.

These comments are the independent assessment of the authors and the Arizona Pest Management Center as part of our role to contribute federal comments on issues of pest management importance and do not imply endorsement by the University of Arizona or USDA of any products, services, or organizations mentioned, shown, or indirectly implied in this document.

Our Data and Expert Information
Through cooperative agreements with Arizona Department of Agriculture, the Arizona Pest Management Center obtains use of, improves upon, and conducts studies with ADA’s Form L-1080 data. Growers, pest control advisors and applicators complete and submit these forms to the state when required by statute as a record of pesticide use. These data contain information on 100% of custom-applied (i.e., for hire) pesticides in the state of Arizona. Grower self-applied pesticide applications may be under-represented in these data. In addition, the Arizona Pest Management Center is host to scientists in the discipline of IPM including experts in the usage of this compound in our agricultural systems. We actively solicit input from stakeholders in Arizona including those in the regulated user community, particularly to better understand use patterns, use benefits, and availability and efficacy of alternatives. The comments within are based on the extensive data contained in the Arizona Pest Management Center Pesticide Use Database, collected summary input from stakeholders and the expertise of APMC member faculty.

Through the Crop Pest Losses and Impact Assessment program, partially funded through the Western IPM Center, the Arizona Pest Management Center conducts annual surveys with state-licensed pest control advisors (PCAs), who are the primary pest management decision makers, in consultation with growers. The surveys, conducted at face-to-face meetings, provide detailed information on crop yield losses to specific insect pests, weeds and diseases, control costs, and pesticide use for the key crops, cotton and lettuce. Cotton data have been collected since 1991 and lettuce data since 2005. Data are collected for all of Arizona and neighboring production regions of California, with typical responses representing up to 65% of acres planted in Arizona. These data provide detailed information on shifting pest trends, chemical use and costs, and often compliment and augment information from the APMC Pesticide Use Database, particularly for pesticide uses for which the state does not mandate reporting.
**Relevant Literature**


https://cals.arizona.edu/crops/cotton/files/wfBIT.pdf


