

Monsanto Petition (19-091-01p) for Determination of Nonregulated Status for Insect-Protected MON 88702 Cotton

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Acronyms and Abbreviations

a.i.	active ingredient
APHIS or USDA-APHIS	Animal and Plant Health Inspection Service (USDA)
BRS	Biotechnology Regulatory Services (USDA)
Bt	acronym for the soil bacterium <i>Bacillus thuringiensis</i>
CAA	Clean Air Act
CFR	Code of Federal Regulations
CWA	Clean Water Act
Cry	abbreviation for insecticidal “crystal” proteins derived from <i>Bacillus thuringiensis</i>
Cyt	abbreviation for insecticidal “cytolytic” proteins derived from <i>Bacillus thuringiensis</i>
EA	Environmental Assessment
EIS	Environmental Impact Statement
EPA	U.S. Environmental Protection Agency
ESA	Endangered Species Act
EO	Executive Order
FAO	Food and Agriculture Organization of the United Nations
FDA	U.S. Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FONSI	Finding of No Significant Impact
FR	<i>Federal Register</i>
GE	genetically engineered
HR	herbicide-resistant
IPPC	International Plant Protection Convention
IPM	integrated pest management
IR	insect resistant
IWM	integrated weed management
Lb	pound (unit of weight, U.S.)
MOA	mode of action
NAAQS	National Ambient Air Quality Standards
NASS	National Agricultural Statistics Service (USDA)
NEPA	National Environmental Policy Act
NHPA	National Historic Preservation Act
NMFS	National Marine Fisheries Service
NO_x	nitrogen oxides
NPDES	National Pollution Discharge Elimination System
NPS	nonpoint source pollution
NRCS	Natural Resources Conservation Service (USDA)
NWQI	National Water Quality Initiative
OECD	Organization for Economic Co-operation and Development

PIP	plant-incorporated protectant
PM	particulate matter
PPA	Plant Protection Act of 2000
PPRA	Plant Pest Risk Assessment
SDWA	Safe Drinking Water Act
SIP	State Implementation Plan (for air quality standards under the CAA)
Spp	species (plural)
TSCA	Toxic Substances Control Act
U.S.	United States
U.S.C.	United States Code
USDA	U.S. Department of Agriculture
Vip	abbreviation for insecticidal proteins produced by <i>Bacillus thuringiensis</i> during vegetative growth
WHO	World Health Organization
WPS	Worker Protection Standard (by EPA for agriculture)
WSSA	Weed Science Society of America

1 PURPOSE AND NEED

1.1 Background

Monsanto Company (referred to as Monsanto in this document) submitted a petition (19-091-01p) to the U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS) in May of 2019. It requested that genetically engineered (GE) cotton cultivar, MON 88702, and any progeny derived from it in crosses with non-regulated cotton varieties, not be considered regulated articles under Title 7 of the Code of Federal Regulations part 340 (7 CFR part 340) (Monsanto 2019). MON 88702 cotton is currently regulated by APHIS because it was developed using the plant pest *Agrobacterium tumefaciens*, a regulated article under 7 CFR part 340.2.¹

As part of evaluation of Monsanto's petition, APHIS has developed this draft Environmental Assessment (EA) to consider the potential impacts of a determination of nonregulated status for MON 88702 cotton on the human environment.² This EA has been prepared in compliance with the National Environmental Policy Act (NEPA, 42 U.S.C. § 4321 et seq.), the Council of Environmental Quality's (CEQ) NEPA-implementing regulations (40 CFR parts 1500-1508), and USDA and APHIS NEPA-implementing regulations (7 CFR part 1b, and 7 CFR part 372).

1.2 Purpose of MON 88702 cotton

Monsanto developed MON 88702 cotton for resistance to certain insect pests that can cause economic damage to cotton grown by U.S. cotton producers (Cook 2018). Insect resistance was conferred by introducing a modified insecticidal protein (mCry51Aa2) derived from *Bacillus thuringiensis* (Bt), a naturally occurring soil bacterium. The introduced mCry51Aa2 protein protects against feeding damage caused by certain pests in the insect orders Hemiptera and Thysanoptera. Infestations of thrips (Thysanoptera: *Frankliniella* spp.) during the seedling stage and tarnished plant bugs (Hemiptera: *Lygus* spp.) during the reproductive stage can significantly reduce cotton yields (Allen et al. 2018; Cook 2018; North et al. 2019). Thrips are found throughout the Cotton Belt (Cook et al. 2011), which is comprised of North and South Carolina, Georgia, Alabama, Mississippi, western Tennessee, eastern Arkansas, Louisiana, eastern Texas, and southern Oklahoma. The tarnished plant bugs (also referred to as lygus bug) occur mainly in the mid-south and southeast United States, while the western tarnished plant bug is more abundant in the western part of the U.S. Cotton Belt (Layton 2000; Akbar et al. 2019). The introduced mCry51Aa2 protein also exhibits insecticidal activity against two coleopteran insect pests: Colorado potato beetle (*Leptinotarsa decemlineata*) and corn rootworm (*Diabrotica undecimpunctata howardi*), which typically are not pests of cotton (Monsanto 2019).

Thrips can be controlled through a combination of seed treatment and foliar insecticides, however, development of resistance in some populations to both pyrethroid and organophosphate insecticides (Bielza 2008), as well as neonicotinoids, has made these pests more difficult to control (Huseth et al. 2016; Hesler et al. 2018). Historically, lygus bugs have been controlled by broad spectrum insecticides such as organophosphates, carbamates, and pyrethroids. However, development of resistance to these

¹ Disarmed *A.tumefaciens* is commonly used in the genetic modification of plants. Disarmed means the *A.tumefaciens* variant used is non-virulent.

² Human environment includes the natural and physical environment and the relationship of people with that environment. When economic or social and natural or physical environmental effects are interrelated, the NEPA analysis may address these potential impacts as well (40 CFR §1508.14).

insecticides has been steadily increasing in lygus populations since the mid-1990s (Snodgrass 1996; Parys et al. 2015). Resistance to pyrethroids among lygus was first observed in 1993 in the Mississippi Delta (Snodgrass 1996). Resistance to pyrethroids and organophosphates is now widespread in many areas of the mid-south (Gore et al. 2012). Some lygus populations also exhibit cross-resistance to organophosphate and carbamate insecticides.

Increased resistance to pyrethroids and organophosphates resulted in an increased use of neonicotinoid insecticides for lygus insect control in cotton during pre-flowering and flowering stages. However, neonicotinoid usage may be associated with declines in honey bee (*Aphis mellifera* Linnaeus) and other insect pollinator populations (Woodcock et al. 2017). Pollinators are important to both wild plants and agriculture, and their conservation is the subject of public and private sector efforts (for example see <https://www.pollinator.org>). Pollinator population decline and the potential causes are of great concern (Stewart et al. 2014; Luttrell et al. 2015), prompting a ban of neonicotinoid use in several countries (Woodcock et al. 2017; North et al. 2019). In the United States, EPA announced in May of 2019 that the registrations for 12 of the total of 59 neonicotinoid-based insecticide products (e.g., those containing the active ingredients clothianidin, imidacloprid, thiamethoxam) would be canceled (US-EPA 2019a).

To provide an additional option for control of thrips and *Lygus* spp., Monsanto developed insect-resistant (IR) MON 88702 cotton; it is a variety of upland cotton (*Gossypium hirsutum*) (Monsanto 2019). Monsanto has indicated that that MON 88702 cotton will not be grown commercially for production of fiber and other commodities derived from cotton. Rather is intended for use in seed production and breeding of hybrid GE IR *G. hirsutum* varieties. GE IR cotton is sometimes referred to as Bt cotton.³ Both “IR” and “Bt” are used interchangeably in this EA.

1.3 Coordinated Framework for the Regulation of Biotechnology

On June 26, 1986, the White House Office of Science and Technology Policy issued the Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework), which outlined federal regulatory policy for ensuring the safety of biotechnology products. The primary federal agencies responsible for oversight of biotechnology products are the U.S. Department of Agriculture (USDA), the U.S. Environmental Protection Agency (EPA), and the U.S. Food and Drug Administration (FDA). On January 4, 2017, USDA, EPA, and FDA released a 2017 update to the Coordinated Framework (USDA-APHIS 2018a) and accompanying National Strategy for Modernizing the Regulatory System for Biotechnology Products (ETIPCC 2016).

The USDA-APHIS is responsible for protecting animal and plant health. The USDA-APHIS regulates products of biotechnology that may pose a risk to agricultural plants and agriculturally important natural resources under the authorities provided by the plant pest provisions of the Plant Protection Act (PPA), as amended (7 U.S.C. 7701–7772), and implementing regulations at 7 CFR part 340 (USDA-APHIS 2018a).

The purpose of EPA oversight is to protect human and environmental health. The EPA regulates pesticides, including pesticides that are produced by plants through genetic engineering, such as the mCry51Aa2 protein in MON 88702 cotton. GE plant-produced pesticides are termed plant incorporated

³ Insect resistant crops (Bt crops) contain a gene from a soil bacterium, *Bacillus thuringiensis* (Bt), which produces a protein or proteins that is/are toxic to specific insects.

protectants (PIPs) and are regulated by EPA under the authority of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et seq.*). The EPA also sets tolerances (maximum residue levels) for pesticide residues that may remain on or in food and animal feed, or establishes an exemption from the requirement for a tolerance, under the authority of the Federal Food, Drug, and Cosmetic Act (FFDCA; 21 U.S.C. 301 *et seq.*). The USDA and FDA enforce tolerances to ensure the safety of the nation's food supply (US-EPA 2019c; USDA-AMS 2019). EPA also regulates certain GE microorganisms (agricultural uses other than pesticides) under the Toxic Substances Control Act (15 U.S.C. 53 *et seq.*).

The purpose of FDA oversight is to ensure human and animal foods and drugs are safe and sanitary. The FDA regulates a wide variety of products, including human and animal foods, cosmetics, human and veterinary drugs, and human biological products under the authority of the FFDCA and the Food Safety Modernization Act (FSMA). The FDA created the Plant Biotechnology Consultation Program in 1992 to cooperatively work with GE plant developers to help them ensure foods made from their new GE plant varieties are safe and lawful (US-FDA 1992, 2006). In this program, FDA evaluates the safety of food from the new GE crop before it enters the market. Although the consultation program is voluntary, GE plant developers routinely participate in it before bringing a new GE plant to market. The FDA completed its first plant biotechnology consultation in 1994. Thus far, FDA has evaluated more than 150 GE plant varieties through this program.

A more detailed description of the roles and responsibilities of USDA, EPA, and FDA under the Coordinated Framework can be found on USDA's website (USDA-APHIS 2018a).

1.4 Purpose and Need for USDA-APHIS Action

APHIS regulations at 7 CFR part 340 govern the introduction (importation, interstate movement, and environmental release) of GE organisms that may pose a plant pest risk. A GE 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 7 CFR § 340.2, such as *A. tumefaciens*, which was used in development of MON 88702 cotton. The regulations allow any person to submit a petition to APHIS requesting that a GE organism should not be regulated because it is unlikely to present a plant pest risk.⁴ As required by 7 CFR § 340.6, APHIS must respond to such petitioners with a regulatory status decision. A GE organism is no longer subject to the requirements of 7 CFR part 340 or the plant pest provisions of the PPA if APHIS determines, through conduct of a Plant Pest Risk Assessment (PPRA), that it is unlikely to pose a plant pest risk.

1.5 Public Involvement

APHIS seeks public comment on draft EAs through notices published in the *Federal Register*. On March 6, 2012, APHIS announced in the *Federal Register* updated procedures for the way it solicits public comments on petitions for determinations of nonregulated status.⁵ Details on policy and procedures for

⁴ Petitioners must present a full statement explaining the factual grounds why the organism should not be regulated under 7 CFR part 340. The petitioner is required to include copies of scientific literature, copies of unpublished studies, when available, and data from tests performed upon which to base a determination. The petition must include all information set forth in paragraph (c) of 7 CFR 340.6.

⁵ USDA-APHIS Biotechnology Regulatory Services; Changes Regarding the Solicitation of Public Comment for Petitions for Determinations of Nonregulated Status for Genetically Engineered Organisms. FR Vol. 77, No. 44, Tuesday, March 6, 2012, p.13258: Available at: <http://www.gpo.gov/fdsys/pkg/FR-2012-03-06/pdf/2012-5364.pdf>

public participation in the petition review and NEPA process are available in the *Federal Register* notice and on the APHIS website (USDA-APHIS 2018b).

1.5.1 Public Involvement for Petition 19-091-01p

On September 26, 2019, APHIS announced in the *Federal Register* that it was making Monsanto's petition available for public review and comment to help identify potential environmental and interrelated economic impacts that APHIS should consider in evaluation of the petition. APHIS accepted written comments on the petition for a period of 60 days (until midnight November 25, 2019). At the end of the comment period, APHIS had received a total of 35 comments on the petition. Fifteen comments from the agricultural, academic, and private sector were in support of Monsanto's petition. Fourteen comments from individuals were opposed to approval of Monsanto's petition. Six comments provided input on analyses to be considered in the EA, or comments on insect resistant crops in general. A full record of each comment received is available online at www.regulations.gov (Docket ID APHIS-2019-0050).⁶

1.6 Scope of Analysis

APHIS developed a list of topics for consideration in this draft EA based on issues identified in public comments on the petition, prior EAs for regulated cotton varieties, public comments submitted for other EAs and EISs evaluating petitions for nonregulated status, the scientific literature on agricultural biotechnology, and issues identified by APHIS specific to wild and cultivated *G. spp.* The following topics were identified as relevant to the scope of analysis (40 CFR § 1508.25):

Agricultural Production

- Acreage and Areas of Cotton Production
- Agronomic Practices and Inputs

Physical Environment

- Soils
- Water Resources
- Air Quality

Biological Resources

- Soil Biota
- Animal and Plant Communities
- Gene Flow and Weediness
- Biodiversity

Human Health Considerations

- Consumer Health and Worker Safety

Animal Health and Welfare

Socioeconomics

⁶ Public comments can be reviewed at: <https://www.regulations.gov/docket?D=APHIS-2019-0050>

- Domestic Economic Environment
- International Trade

In addition, potential cumulative impacts relative to the issues considered, potential impacts on threatened and endangered species (T&E), and adherence of the proposed action to Executive Orders, and environmental laws and regulations to which the action may be subject, were also evaluated.

2 ALTERNATIVES

NEPA implementing regulations (40 C.F.R. § 1502.14) require agencies to evaluate all alternatives that appear reasonable and appropriate to the purpose and need for a federal action (in this case, a regulatory status decision by APHIS). Two alternatives are evaluated in this EA: (1) No Action, denial of the petitioner's requested action, which would result in the continued regulation of MON 88702 cotton and (2) Preferred Alternative, a determination of nonregulated status for MON 88702 cotton, i.e., approval of the action requested by the petitioner.

2.1 No Action Alternative: Continuation as a Regulated Article

CEQ regulations at 40 CFR § 1502.14 require that one of the alternatives that must be considered by APHIS is a "No Action Alternative." APHIS does not have the option of not responding to a petition, which could be considered "no action," because the regulations at 7 CFR § 340.6 require APHIS to respond to all petitioners with a regulatory status decision. Thus, for APHIS, No Action in this context means no change in regulatory status. Under the No Action Alternative, APHIS would deny the petitioner's request for nonregulated status and MON 88702 cotton would remain a regulated article under 7 CFR part 340. Permits issued or notifications acknowledged by APHIS would be required for the introduction of MON 88702 cotton. Because APHIS concluded in its draft PPRA that MON 88702 cotton is unlikely to pose plant pest risk (USDA-APHIS 2019), this alternative would not be an appropriate response to the petition for nonregulated status as it would not satisfactorily meet the purpose and need for providing a science-based regulatory status decision to the petitioner, as required by 7 CFR § 340.6.

2.2 Preferred Alternative: Determination of Nonregulated Status for MON 88702 Cotton

Under this alternative, APHIS would approve the regulatory action requested in the petition. MON 88702 cotton and progeny derived from it in crosses with non-regulated cotton would no longer be subject to regulation under 7 CFR part 340 because it was determined that, based on the scientific evidence before the Agency, MON 88702 cotton is unlikely to pose a plant pest risk (USDA-APHIS 2019). Permits issued or notifications acknowledged by APHIS would no longer be required for introductions of MON 88702 cotton. This alternative would best meet the purpose and need to respond appropriately to the petition for nonregulated status pursuant to the requirements of 7 CFR § 340.6, and the Agency's statutory authority under the PPA.

2.3 Alternatives Considered but Dismissed from Detailed Analysis in this EA

APHIS has evaluated several other alternatives for consideration in this and other EAs for petitions for nonregulated status. APHIS has considered alternatives that would entail approving a petition request in part (7 CFR § 340.6(d)(3)(i)), mandatory isolation or geographic restriction of GE and non-GE cropping systems, and requirements for testing for the presence of GE crop plant material in non-GE crops and commodities. Based on the draft PPRA for MON 88702 cotton, APHIS concluded that MON 88702 cotton is unlikely to pose a plant pest risk (USDA-APHIS 2019). Therefore, the imposition of testing, release, and/or isolation requirements on MON 88702 cotton would be inconsistent with the Agency's statutory authority under the plant pest provisions of the PPA, implementing regulations at 7 CFR part 340, and the federal regulatory policies of the Coordinated Framework. Since APHIS does not have

federal authority to implement these actions, it would be unreasonable for the Agency to evaluate alternatives related to them, so they were not considered for detailed analysis in this EA.

2.4 Summary of the No Action and Preferred Alternative Analyses

Table 2-1 includes a summary of the potential environmental impacts associated with the No Action Alternative and Preferred Alternative that are evaluated in this draft EA. Details about the affected environment and an analysis of potential environmental impacts are included in Chapters 3 and 4, respectively.

Table 2-1. Summary of Potential Impacts of the Alternatives Considered		
Attribute/Measure	No Action Alternative: Continue to Regulate MON 88702 Cotton as a Plant Pest	Preferred Alternative: Approve the Petition for Nonregulated Status for MON 88702 Cotton
Meets Purpose and Need, and Objectives	No	Yes
Unlikely to Pose a Plant Pest Risk	Satisfied through use of regulated field trials.	Satisfied by the plant pest risk assessment (USDA-APHIS 2019).
Agricultural Production		
Acreage and Areas of Cotton Production	Denial of the petition would have no effect on the areas or acreage utilized for cotton production. Fluctuations in production areas and acreage would be relative to weed, insect pest, and disease pressures, and market demand for cotton commodities. Regulated field trials would be conducted on lands allocated for this purpose.	MON 88702 cotton will be used for seed production and breeding of stacked-trait insect resistant (IR) cotton varieties. Cultivation of MON 88702 cotton and stacked-trait progeny would be on lands used for agricultural field experiments, crop production, crop seed production, and new variety plant development. These lands are regularly used for agricultural purposes.
Agronomic Practices and Inputs	Agronomic practices and inputs used in cotton crop production, to include regulated field trials, would remain unchanged.	The agronomic practices and inputs used for MON 88702 cotton hybrid production would be the same as for other varieties of GE IR cotton. Relative to non-IR cotton varieties, MON 88702 cotton could require less insecticide use; an average of 1.2 fewer insecticide applications per crop cycle.
GE Cotton Production	Denial of the petition would have no effect on the use of existing varieties of GE IR cotton. GE varieties of cotton containing either herbicide resistance (HR), IR, or a combination of traits comprised about 98% of all cotton planted in the United States in 2019.	Approval of the petition would provide for production of stacked-trait GE cotton varieties that are resistant to economically important Lepidoptera, Hemiptera, and Thysanoptera insect pests.
Physical Environment		
Soil Quality	Agronomic practices and inputs associated with cotton crop production potentially impacting	The agronomic practices and inputs used for MON 88702 cotton production that can potentially impact soil quality would be the

Table 2-1. Summary of Potential Impacts of the Alternatives Considered

Attribute/Measure	No Action Alternative: Continue to Regulate MON 88702 Cotton as a Plant Pest	Preferred Alternative: Approve the Petition for Nonregulated Status for MON 88702 Cotton
	soils, to include regulated field trials, would continue consistent with current trends.	same as those currently used, apart from reductions in insecticide use with MON 88702 cotton hybrids, as compared to non-IR varieties.
Water Resources	Denial of the petition, which would preclude commercial production of MON 88702 cotton, would have no effect on water resources in the United States. Regulated field trials are limited on a spatial-temporal scale, and present negligible risks to water resources.	Because the agronomic practices and inputs utilized for MON 88702 cotton production would be the same as those currently used, and MON 88702 cotton would not entail any increase in acreage or alter the areas of cotton production, sources of potential impacts on water resources, (i.e., NPS pollutants in agricultural run-off), would not be expected to substantially differ from those of the No Action Alternative. However, runoff from MON 88702 cotton/progeny production fields may include lesser quantities of insecticide residues than what is associated with the No Action Alternative, so potential risks to surface waters and groundwater may be reduced.
Air Quality	Emission sources, (i.e., tillage and machinery combusting fossil fuels), and the level of emissions associated with cotton crop production, to include regulated field trials, would be unaffected by denial of the petition.	Because the agronomic practices and inputs used for MON 88702 cotton would remain unchanged, no changes to emission sources are expected. As a GE IR crop there could be reductions in insecticide use compared to current cotton production practices, which would reduce use of fossil fuels in the machinery used for application, and thereby the quantity of related emissions. There would also be commensurate reductions in insecticide drift and volatilization associated with MON 88702 cotton/stacked-trait progeny crops.
Biological Resources		
Soil Biota	Potential impacts of cotton crop production, to include field trials, on soil biota would be unaffected by denial of the petition.	The agronomic practices and inputs used for MON 88702 cotton production that can impact soil biota would be no different from those currently used. The insecticidal mCry51Aa2 protein, derived from naturally occurring soil bacterium <i>B. thuringiensis</i> , is unlikely to present a significant risk to populations of soil biota and their ecological interactions (US-EPA 2018b).
Animal Communities	Regulated field trials of MON 88702 cotton would present negligible risk to animal communities.	There are no hazards to vertebrate taxa associated with exposure to mCry51Aa2 protein (Koch et al. 2015; US-EPA 2018b, e). Adverse effects on non-target insects (e.g., ladybird beetles, rove beetles, parasitic

Table 2-1. Summary of Potential Impacts of the Alternatives Considered

Attribute/Measure	No Action Alternative: Continue to Regulate MON 88702 Cotton as a Plant Pest	Preferred Alternative: Approve the Petition for Nonregulated Status for MON 88702 Cotton
		wasps, bees) as a result of exposure to mCry51Aa2 are not expected.
Plant Communities	Regulated field trials of MON 88702 cotton would present negligible risks to plant communities.	Because the agronomic practices and inputs that will be used for MON 88702 cotton production are the same as those for other GE and non-GE cotton varieties (apart from reduced insecticide use), the potential impacts on vegetation next to cotton fields would not substantially differ from the No Action Alternative.
Gene Flow and Weediness	Under the No Action Alternative MON 88702 cotton could be grown under APHIS regulatory authority. Any potential for gene flow from MON 88702 cotton permitted testing sites would be evaluated on a case-by-case basis relevant to the site-specific containment conditions imposed to prevent gene flow.	MON 88702 cotton, if grown for commercial purposes, would be cultivated as are current cotton varieties and present the same potential risk for gene flow, specifically the propensity and frequency of gene flow associated with current cotton varieties. Accordingly, a determination of nonregulated status for MON 88702 cotton and its progeny would not be expected to present more or less risk for gene flow to wild relative species as do current cotton varieties. Available evidence indicates that there is a low potential for introgression of transgenic material from MON 88702 cotton into wild or feral relative species (USDA-APHIS 2019).
Biodiversity	Denial of the petition, and further regulated field trials of MON 88702 cotton, would present negligible risks to biodiversity in an around MON 88702 cotton crops.	The production of MON 88702 cotton would be expected to affect biodiversity in and around MON 88702 cotton hybrid crops similar to other IR cotton cropping systems, with minor transient differences in the targeted insect populations affected (thrips, lygus bugs [tarnished plant bugs], bollworms, tobacco budworm, and armyworm), and predator-prey relationships. Indirect effects of GE IR crops on agricultural ecosystems due to multi-trophic exposure, loss of prey, or reduction of prey quality, are generally negligible compared with the direct effects of the significant environmental manipulations associated with current standard agricultural practices (Storer et al. 2008).
Human and Animal Health		
Human Health and Worker Safety	Denial of the petition would have no direct or indirect effects on human health or welfare. MON	Approval of the petition would not be expected to present any risks to public health. Monsanto consulted with FDA on

Table 2-1. Summary of Potential Impacts of the Alternatives Considered

Attribute/Measure	No Action Alternative: Continue to Regulate MON 88702 Cotton as a Plant Pest	Preferred Alternative: Approve the Petition for Nonregulated Status for MON 88702 Cotton
	88702 cotton would remain a regulated article and would not be available for food, feed, or fiber uses.	MON 88702 cotton (BNF 000160) in September 2018. The FDA found that MON 88702 cotton does not raise any safety or regulatory issues with respect to its uses in human or animal food (US-FDA 2019). The EPA concluded that there are no unreasonable adverse effects and there is a reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to the mCry51Aa2 protein and the genetic material necessary for its production in MON 88702 cotton (US-EPA 2018b). The EPA issued an exemption from the requirement of a tolerance for residues of Cry51Aa2.834_16 protein in or on cotton (US-EPA 2018e).
Animal Health and Welfare	Denial of the petition would have no effect on the quality or availability of animal feed or on animal health and welfare.	Stacked-trait IR varieties produced using MON 88702 cotton would provide for animal feed products (e.g., oil, meal, whole seed). As discussed for human health, Monsanto consulted with FDA, which found that MON 88702 cotton does not raise any safety or regulatory issues with respect to its uses for animal food (US-FDA 2019).
Socioeconomic		
Domestic Economy and International Trade	Cotton commodities markets would be unaffected by denial of the petition.	Approval of the petition and eventual production of MON 88702 cotton progeny would have no effect on cotton commodities markets, or trade of cotton commodities.
Cumulative Impacts		
Agriculture, Physical and Biological Resources, Public Health, Socioeconomic	There are no cumulative impacts on any aspect of the human environment evaluated that would derived from denial of the petition.	MON 88702 cotton/progeny production would entail the use of pesticides and fertilizers, and to some extent tillage, which will contribute to potential cumulative impacts on water, soil, and air quality, the same as current cotton production methods. If MON 88702 cotton stacked-trait IR varieties are adopted by growers, this could potentially contribute in a cumulative manner to a reduction in insecticide runoff from agricultural sites. As with all uses of Bt Cry based insecticides, insect resistant management will be an inherent aspect of production of MON 88702 cotton and its progeny.
Coordinated Framework		

Table 2-1. Summary of Potential Impacts of the Alternatives Considered		
Attribute/Measure	No Action Alternative: Continue to Regulate MON 88702 Cotton as a Plant Pest	Preferred Alternative: Approve the Petition for Nonregulated Status for MON 88702 Cotton
U.S. Regulatory Agencies	Denial of the petition would have no effect on FDA and EPA oversight of MON 88702 cotton. Introductions of MON 88702 cotton would be regulated by USDA.	Monsanto has consulted with FDA as to the food/feed safety of MON 88702 cotton, and obtained appropriate registrations and established tolerances for mCry51Aa2 from EPA.
Regulatory and Policy Compliance		
ESA, CWA, CAA, SDWA, NHPA, EOs	Compliant	Compliant

3 AFFECTED ENVIRONMENT

This chapter provides an overview of those aspects of the human environment potentially affected by the APHIS decision to either approve or deny the petition. Those aspects considered are U.S. cotton production, the physical environment, biological resources, public health, animal health and welfare, and socioeconomics. Because the introduced genes are involved in protecting MON 88702 cotton from insect pests, the primary focus of this EA is on: (1) insect and insect resistance management, (2) effects of exposure to the introduced IR trait gene and gene product on human health, livestock, and wildlife, and (3) gene flow and the potential weediness of MON 88702 cotton.

3.1 U.S. Cotton Production

3.1.1 Areas and Acreage of Cotton Production

Cotton is the world's most widely grown crop for textile fiber, accounting for over 40% of global fiber production (Meyer et al. 2007). Other valuable commodities derived from cotton include an edible oil refined from seeds, chaff (hulls and linters), and high-protein cake and flour used for livestock feed (OECD 2008).

Cotton grows wild as a warm season perennial, but for crop production, it is grown mostly as an annual. Commercial production of cotton requires full sun, warm temperatures, and irrigation or moderate rainfall equivalent to 24-47 inches (60-120 centimeters) during a growing season (Evetts et al. 2011). Its geographic U.S. distribution is more limited than that of other major crops (e.g., corn and soybeans) because its growth to maturity requires a longer growing season (a minimum of 180 frost-free days per year) (Rude 1984; Smith and Cothren 1999; OECD 2008).

There are two species of cotton grown in the United States: upland and Pima. MON 88702 cotton is a variety of upland cotton (*Gossypium. hirsutum*), which is the one most commonly grown species in the United States, comprising about 98% of the U.S. cotton crop (Figure 3-1). Upland cotton is also known as short-staple cotton, based on the length of the cotton fibers. In 2018 and 2019, upland cotton was planted on approximately 13.8 million acres and 13.5 million acres, respectively in the United States (USDA-NASS 2019a). The five major upland cotton-producing states in 2018 were: Texas (5.6 million acres), Georgia (1.2 million acres), Mississippi (0.44 million acres), Arkansas (0.38 million) and Alabama (0.34 million acres). Pima cotton (*G. barbadense*), which is also known as extra-long staple (ELS), or Egyptian cotton, is primarily cultivated in California, with less acreage in Texas, Arizona and New Mexico for a total of approximately 250,000 and 230,000 acres planted in 2018 and 2019 respectively.

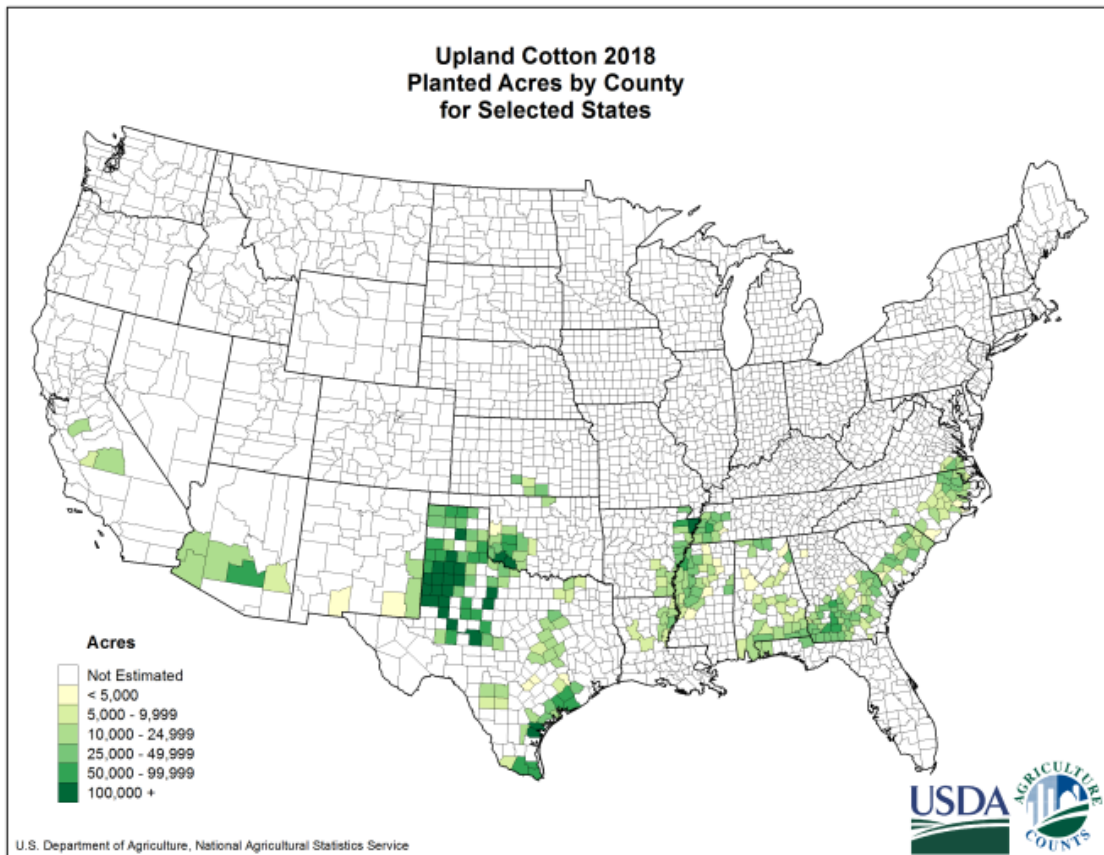


Figure 3-1. Upland Cotton Planted Acres in the United States in 2018

Source: (USDA-NASS 2019b)

3.1.1.1 GE Varieties of Cotton

GE cotton varieties that were previously regulated by APHIS, and were determined not to be subject to 7 CFR part 340 based on plant pest risk assessments and supporting data submitted by the applicants are listed in Table 3-1.

Adoption of GE IR cotton by U.S. farmers has significantly increased since the introduction of these varieties in the late 1990s. This is mostly attributable to the effectiveness of GE IR cotton to protect against insect pests, which has resulted in increased crop yields and corresponding net returns (Fernandez-Cornejo et al. 2014a). Bt cotton varieties were developed to control tobacco budworm (*Helicoverpa virescens*, cotton bollworm (*H. zea*), pink bollworm (*Pectinophora gossypiella*) and other lepidopteran pests. Farmers commonly use less insecticide when they plant Bt cotton, which saves time and reduces production costs (discussed further in Section 3.1.2–Agronomic Practices and Inputs). As of 2019, GE varieties of cotton containing either an herbicide resistance (HR), IR, or both traits comprised about 98% of all cotton planted in the United States (Figure 3-2). GE IR cotton varieties currently comprise about 89% of cotton acreage.

Table 3-1. Varieties of Nonregulated Genetically Engineered Cotton				
Petition	Applicant	Phenotype/Event	Event	Effective Date
17-292-01p	Texas A&M	Low Gossypol	TAM-66274-5	10/16/2018
17-138-01p	Bayer	Glyphosate and Isoxaflutole Resistance	GHB811	7/23/2018
13-262-01p	Dow AgroSci	2,4-D and Glufosinate Resistance	DAS-8191Ø-7	7/23/2015
12-185-01p	Monsanto	Dicamba and Glufosinate Resistance	MON-887Ø1-3	1/20/2015
12-033-01p*	Bayer	Glufosinate & Lepidopteran Resistance	T303-3	8/17/2012
08-340-01p	Bayer	Glufosinate & Lepidopteran Resistance	T304-40 x GHB119	10/12/2011
07-108-01p	Syngenta	Lepidopteran Resistance	COT67B	9/29/2011
06-332-01p	Bayer CropSci	Glyphosate Resistance	GHB614	5/22/2009
04-086-01p	Monsanto	Glyphosate Resistance	MON 88913	12/20/2004
03-155-01p	Syngenta	Lepidopteran Resistance	COT102	7/6/2005
03-036-02p	Dow AgroSci	Lepidopteran Resistance	3006-210-23	7/15/2004
02-042-01p	Aventis	Glufosinate Resistance	LLCotton25	3/10/2003
00-342-01p	Monsanto	Lepidopteran Resistance	15985	11/5/2002
97-013-01p	Calgene	Bromoxynil & Lepidopteran Resistance	31807, 31808	4/30/1997
95-256-01p	Du Pont	Sulfonylurea Resistance	19-51A	1/25/1996
95-045-01p	Monsanto	Glyphosate Resistance	1445, 1698	7/11/1995
94-308-01p	Monsanto	Lepidopteran Resistance	531, 757, 1076	6/22/1995
93-196-01p	Calgene	Bromoxynil Resistance	BXN	2/15/1994

*(Extension of 08-340-01p)

Source: (USDA-APHIS 2020)

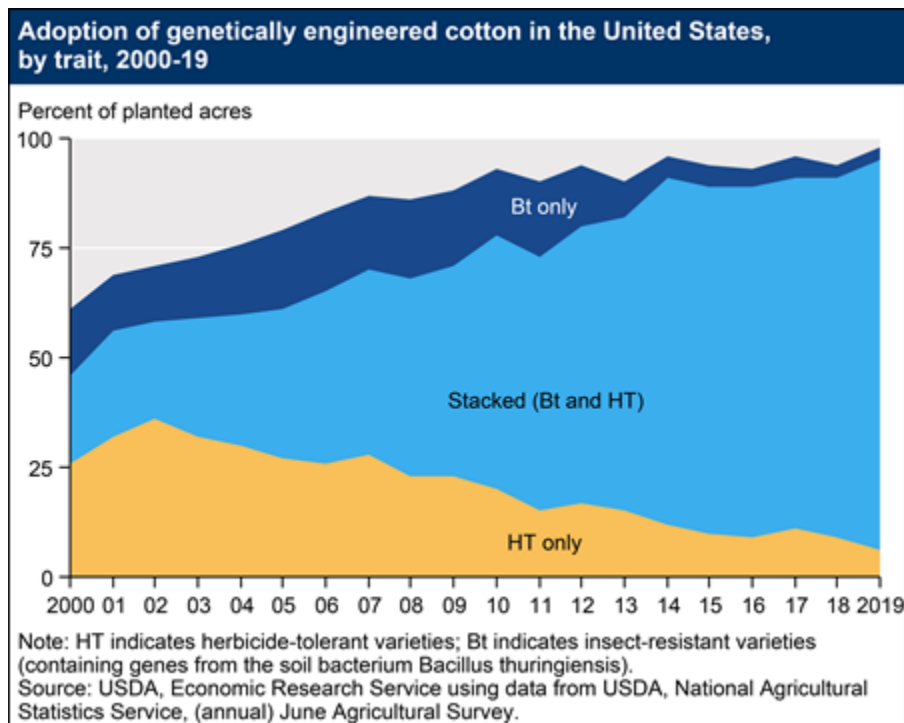


Figure 3-2. GE Cotton Varieties in the United States, 2018

Source: (USDA-ERS 2019a)

Table 3-2. Upland GE Cotton Varieties Containing Insect Resistance and/or Herbicide Resistance Traits as a Percent of Total Upland Cotton Planted in the United States in 2017 and 2018				
State	HR Only		IR Only	
	2018	2019	2018	2019
	<i>% Total Area</i>		<i>% Total Area</i>	
Alabama (2)	1	2	6	5
Arkansas	9	7	14	10
California	6	10	18	38
Georgia	1	1	3	1
Louisiana	3	3	4	4
Mississippi	2	1	6	4
Missouri (2)	6	2	20	17
North Carolina	1	2	3	6
Tennessee (2)	1	1	4	3
Texas	3	3	10	7
Other States (1)	2	2	10	6
U.S.	3	3	9	6
State	HR/IR Stacked Trait		All GE	
	2018	2019	2018	2019
	<i>% Total Area</i>		<i>% Total Area</i>	
Alabama (2)	92	92	99	99
Arkansas	76	82	99	99
California	57	41	81	89
Georgia	96	97	100	99
Louisiana	92	92	99	99
Mississippi	91	94	99	99
Missouri (2)	73	78	99	97
North Carolina	89	89	93	97
Tennessee (2)	91	95	96	99
Texas	77	88	90	98
Other States (1)	86	90	98	98
U.S.	82	89	94	98

1. Includes other States in the cotton estimating program
2. Estimates published individually beginning in 2005.
Note: Values may not equal sum of components due to rounding.
Source: (USDA-ERS 2019a)

3.1.2 Agronomic Practices and Inputs

Cotton growers use a variety of agronomic practices and inputs designed to achieve optimal product quality, yield/acre, and net returns. Except for organically grown cotton, these include the occasional or regular application of manure and synthetic fertilizers; pesticides; tillage; crop rotation; and cover crops. To meet organic standards, farming systems are required to exclude certain practices, such as planting GE varieties and applying synthetic pesticides and fertilizers. Some of these practices (e.g., tillage; application of fertilizers, pesticides) may have effects on the environment such as the reduction of air, soil, and water quality. Pesticide and fertilizer use can also present risks to wildlife and human health. Even when applied according to good management practices, repeated use of these practices may have

cumulative effects on the environment. How these practices may impact the physical environment, biological resources, and human health are discussed in the subsequent sections of this chapter.

Apart from the herbicide-, insect-, or disease-resistant trait(s), there are little differences in the agronomic practices and inputs used for GE and non-GE crops. GE HR crops influence the types of herbicides used. GE IR varieties generally reduce the overall application rate of insecticides, and disease resistant crops reduce the use rates of fungicides and similar chemicals targeting plant pathogens or reduce insecticides used to control some insects that transmit pathogens. The agronomic practices, and current uses of the inputs such as fertilizers and pesticides that will be used with MON 88702cotton, are reviewed below.

3.1.2.1 Agronomic Practices

Growers use several practices for the management of pests (i.e. insects, diseases and weeds). These are summarized in Table 3-3. Scouting for weeds (used on 92% of cotton acreage) was the most widely reported monitoring practice in 2017. Crop rotation was practiced on 64% of planted acres. The most widely used preventative practice was cleaning equipment and implements after field work (64%). Maintaining ground cover, mulching, or using other physical barriers were the most commonly reported suppression practices (38%). Because tillage can present environmental risks, this practice in relation to cotton and GE crops is discussed in more detail below.

Table 3-3. Top Practices in Pest Management, 2017 Crop Year	
	% of Cotton Acres
Monitoring: Scouted for weeds	92
Avoidance: Rotated crops during last three years	64
Prevention: Cleaning equipment and implements after field work	64
Suppression: Maintained ground cover, mulched, or used other physical barriers	38

Source: (USDA-NASS 2018a)

3.1.2.2 Tillage

Tillage is used to prepare seedbeds and control weeds, soil-borne pests and diseases. Tillage types are commonly classified as conventional, reduced, and conservation tillage (to include no-till). They are characterized in part by the amount of plant residue left on the field after harvest and the degree of soil disturbance each causes. Conventional tillage involves intensive plowing leaving less than 15% crop residue in the field. Reduced tillage leaves 15-30% crop residue and conservation tillage involves leaving at least 30% crop residue (Claassen et al. 2018; OSU 2019).

The tillage practice chosen can have substantial impacts on soil quality, soil erosion, and water and air quality (discussed in Section 3.2–Physical Environment). Tillage operations can also be costly and time-consuming to implement. Over the long-term, conventional tillage reduces soil quality, and results in soil erosion and runoff that can adversely affect surface waters (Wallander 2015). Conservation tillage systems are the least intensive and, as the name implies, are designed to improve or maintain soil quality and conserve topsoil. Conservation tillage provides a variety of agronomic and economic benefits, such as reductions in fuel use and cultivation costs, preservation of soil organic matter and moisture, and

reductions in soil erosion and water pollution (Claassen et al. 2018). No-till systems leave all crop residue on the field unless those residues are removed for other reasons such as biomass production. However, conservation tillage practices, especially no till, can also cause production problems such as increased soil compaction, weed shifts to types more difficult to control (e.g., perennial weeds), buildup of plant pathogens and/or pests in crop residue, and slower early crop growth from cooler soil temperatures caused by the insulating effect of residue (Roth 2015). A systematic use of crop rotations can improve the success of conservation tillage by eliminating some of these stresses from continuous no-till corn (Roth 2015).

Decisions about selecting the amount, timing, and type of tillage involve consideration of a wide range of interrelated factors such as the variety and extent of weeds and crop pests present, soil erosional capacity, fuel and other input costs, anticipated weather patterns, and potential air and water quality issues (Roth 2015).

The use of conservation tillage systems has increased steadily since the 1980s (Figure 3-3). An increase in conservation tillage occurred in the 1980s after post-emergent herbicides became available (Fernandez-Cornejo et al. 2012), which can be applied over crops throughout the growing season (not just before planting, as had previously been the case). Another factor has been the implementation of new soil conservation programs that began in the mid-1980s, which have encouraged/incentivized conservation tillage practices to help conserve soils (USDA-NRCS 2006). Continued increases in conservation tillage since the late 1990s have also been attributable in part to the use of GE herbicide resistant (HR) crops that promote more efficient weed management by reducing the need for mechanical weed control (Towery and Werblow 2010; USDA-ERS 2012).

Trends in conservation tillage adoption

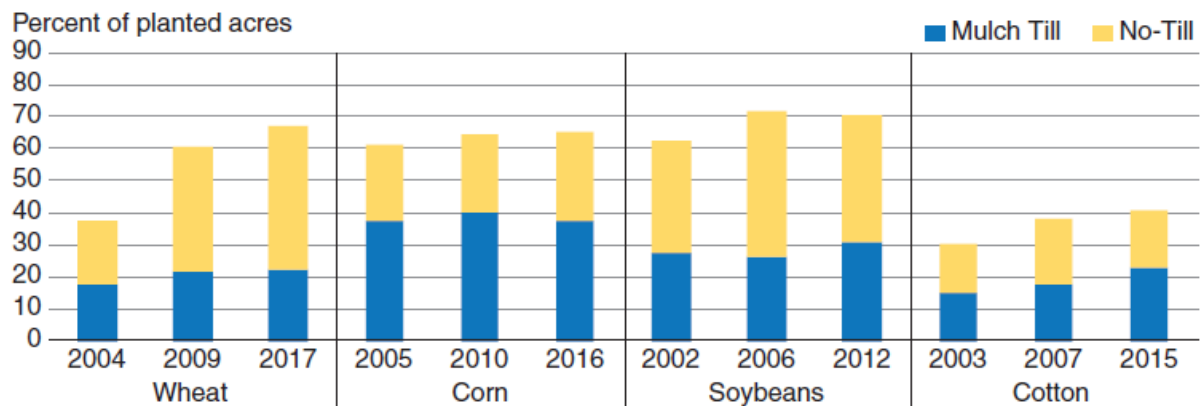


Figure 3-3. Conservation Tillage Practices in Cotton, 2003 – 2015.

Note: No-till is based on the absence of tillage operations reported in the Agricultural Resource Management Survey. Mulch till is a type of conservation tillage that leaves more than 30% crop residue cover after planting, and the soil surface disturbed by noninversion tillage. This practice benefits soil by increasing organic matter, improving soil tilth and increases productivity as the constant supply of organic material left on the soil surface is decomposed by a healthy population of earth worms and other organisms.

Source: (Claassen et al. 2018)

3.1.2.3 Fertilizers

Soils in many areas of the United States where cotton is produced are naturally deficient in nitrogen, phosphorus, and other nutrients, requiring fertilizer inputs, to include manure, to produce crops efficiently, and the yields necessary, to meet market demand. Given the importance of nutrient availability to cotton growth, fertilization with nitrogen, phosphorus, and potassium is practiced widely in the United States.

Since 1975, about 75-90% of cotton acreage has been treated annually with nitrogen. The average rate of application has increased from about 72-110 lbs/acre from 1975 to 2017 (USDA-ERS 2019d). Phosphate has been applied to about 40-65% of cotton acreage at an average rate of about 45 lbs/acre (USDA-ERS 2019d). The acreage treated with potash (potassium) has increased since 1975 from 30% to the current estimate of about 45% at application rates between 40-80 lbs/acre (USDA-ERS 2019d). Inputs reported for the most recent crop year available (2017) are listed in (Table 3-4). While nitrogen and phosphorus are important agricultural inputs in crop production, the introduction of amounts exceeding recommended rates can have a number of undesirable impacts on water and air quality (discussed in Section 3.2 – Physical Environment).

Fertilizer	% of Planted Acres	Avg. Rate for Year (lbs/acre)	Total Applied (million lbs)
Nitrogen (N)	78	94	821.5
Phosphate (P2O5)	59	45	298.4
Potash (K2O)	45	64	325.3

Source: (USDA-NASS 2018a)

3.1.2.4 Pest and Pest Resistance Management

In all cotton production regions in the United States, mite and insect pests are a common and continuous problem (Table 3-5). More than 100 different pests have been reported to attack cotton. If plant pests are left unmanaged, cotton crops can be badly damaged, resulting in yield losses, reductions in cotton quality, and increased production costs. Consequently, large scale use of commercial insecticides has been an integral component of cotton crop production since the advent of synthetic insecticides in the 1940s (before that, various other insecticides such as arsenic-based pesticides, sodium chlorate, and nitrophenols were used). Until its eradication, the cotton boll weevil was the most economically important pest of U.S. cotton, and insecticide applications to control it accounted for nearly half of all those made to control agricultural pests. Combined with widespread adoption of transgenic cotton, the eradication program allowed farmers to significantly reduce the number of insecticide applications made annually, while increasing yields by 30% (Smith 2014). Currently, the most economically damaging insect pests of cotton are those that attack the squares (flower bud stage) or maturing bolls (the ovary containing developing seeds and fibers) (Gianesi and Carpenter 1999).

In 2018, the total cost of U.S. cotton yield losses from insect damage was estimated at \$567 million (about \$42.45/acre) (Williams 2019). The highest yield losses were associated with a bollworm/budworm complex (1.16%), lygus bugs (0.66%), stink bugs (0.27%+ 0.37%), spider mites (0.27%), thrips (0.24%), and cotton fleahoppers (0.21%).

Table 3-5. Cotton Insect Losses and Costs, 2018								
Pest	Acres Infested	% Acres Infested	Acres Treated	% Acres Treated	% loss /acre infested	overall % reduction	Bales lost / pest	Loss + cost
Bollworm/Budworm	8,384,053	62.8%	3,100,987	23.2%	1.85%	1.16%	553,110	\$252,931,977
Beet Armyworm	518,538	3.9%	2,051	0.0%	0.00%	0.00%	101	\$37,028
Fall Armyworm	811,444	6.1%	60,983	0.5%	0.24%	0.01%	8,001	\$2,948,659
Loopers	516,953	3.9%	1,091	0.0%	0.00%	0.00%	9	\$3,273
Cutworms	435,248	3.3%	564,232	4.2%	0.03%	0.00%	524	\$376,860
Cotton Leaf Perforator	3,309	0.0%	0	0.0%	0.00%	0.00%	0	\$0
Saltmarsh Caterpillar	150,947	1.1%	380	0.0%	0.00%	0.00%	0	\$0
Lygus	5,449,810	40.8%	3,127,011	23.4%	1.62%	0.66%	335,992	\$175,270,947
Cotton Fleahopper	5,112,002	38.3%	1,902,061	14.2%	0.54%	0.21%	86,467	\$42,673,473
Stink Bugs (other)	5,221,696	39.1%	2,744,459	20.5%	0.96%	0.37%	152,115	\$67,406,989
Brown Stink Bug	4,347,300	32.5%	2,043,637	15.3%	0.83%	0.27%	108,982	\$45,843,706
Clouded Plant Bug	1,129,341	8.5%	128,498	1.0%	0.13%	0.01%	5,100	\$1,988,335
Leaf Footed Bugs	837,842	66.3%	215,071	1.6%	0.11%	0.01%	2,163	\$819,284
Spider Mites	3,128,000	23.4%	1,110,529	8.3%	1.15%	0.27%	148,229	\$59,501,424
Thrips	11,161,091	83.6%	3,705,744	27.7%	0.29%	0.24%	115,234	\$66,976,144
Aphids	7,295,752	54.6%	1,235,085	9.2%	0.10%	0.05%	26,728	\$17,537,945
Grasshoppers	1,164,589	8.7%	52,700	0.4%	0.03%	0.00%	750	\$288,181
Banded Winged Whitefly	441,922	3.3%	569	0.0%	0.00%	0.00%	45	\$17,581
Silverleaf Whitefly	1,147,836	8.6%	248,961	1.9%	0.13%	0.01%	5,505	\$2,174,122
Darkling Beetles	253,548	1.9%	0	0.0%	0.00%	0.00%	0	\$0
Pale-Striped Flea Beetle	270,727	2.0%	171	0.001%	0.01%	0.00%	61	\$22,165
Empoasca leafhoppers	18,068	0.1%	0	0.0%	0.03%	0.00%	22	\$8,188
Mealybugs	76	0.001%	0	0.0%	0.00%	0.00%	0	\$0
Kurtoma Thrips	235,129	5.0%	0	0.0%	0.00%	0.00%	0	\$0
Wireworms	235,129	5.0%	0	0.0%	0.00%	0.00%	0	\$0
Boll Weevil	277,414	2.1%	277,414	2.1%	0.00%	0.00%	0	\$0
TOTAL						3.29%	1,549,137	\$736,826,279

Source: (Williams 2019)

Insecticide Use in GE IR Cotton

The USDA National Agricultural Statistics Service (NASS) collects data about fertilizer and pesticide use. In 2017 (most recent available data), NASS surveyed nine states that collectively accounted for 89% of the 12.6 million U.S. cotton acres: Alabama, Arkansas, Georgia, Mississippi, Missouri, North Carolina, Oklahoma, Tennessee, and Texas. An estimated 4.47 million pounds (lbs) of insecticides (active ingredient) were applied to about 43% of cotton acreage (Table 3-6). In 2018, 3.1 million cotton acres (about 23.4% of the total planted) were treated for lygus bug control—the pest MON 87708 cotton is designed to resist—and the total cost of treatments plus yield losses was estimated at more than \$175 million (Table 3-5).

Table 3-6. Insecticide Use in Cotton: 2017*					
Insecticide Active Ingredient		Application: lbs a.i./yr	Application: lbs a.i./acre/yr	Cotton Acres Treated	Target Pests-Foliar Applied
Zeta-Cypermethrin	Pyrethroid	1,000	0.01	nd	lygus bug, beet armyworm, loopers
Abamectin	biological (macrocyclic lactones)	3,000	0.02	2%	mites
Cyfluthrin	Pyrethroid	7,000	0.05	1%	lygus bug, beet armyworm, looper
Methoxyfenozide	Diacylhydrazine	7,000	0.15	nd	beet armyworm, other caterpillars
Flupyradifurone	butenolide/neonicotinoid	11,000	0.14	1%	aphids, psyllids, stink bugs,
Acetamiprid	Neonicotinoid	12,000	0.2	1%	aphids
Cypermethrin	Pyrethroid	15,000	0.09	1%	lygus bug, beet armyworm, loopers
Pyriproxyfen	Hormone mimic/growth regulator	24,000	0.06	3%	whiteflies
Novaluron	Hormone mimic/growth regulator	34,000	0.08	4%	lygus bug, beet armyworm, loopers
Sulfoxaflor	Nicotinic acetylcholine receptor (nAChR) modulator	36,000	0.08	4%	aphids, mealybugs, psyllids, whiteflies
Chlorantraniliprole (Rynaxypyr)	Ryanoid	48,000	0.08	6%	primarily caterpillars
Lambda-cyhalothrin	Pyrethroid	53,000	0.05	9%	lygus bug, beet armyworm, looper
Thiamethoxam	Neonicotinoid	56,000	0.09	6%	whiteflies, aphids
Imidacloprid	Neonicotinoid	204,000	0.17	11%	lygus bug, aphids
Bifenthrin	Pyrethroid	267,000	0.16	15%	lygus bug, whiteflies, beet armyworm, looper
Diclotophos	Organophosphate	525,000	0.53	9%	aphids, thrips, stink bugs and plantbugs
Acephate	Organophosphate	3,101,000	1.08	25%	thrips, lygus bug, loopers, whiteflies
Total		4,469,000		43%	

* This is an approximation of total insecticide use. Not all use data is reported for each year, and each insecticide. Source: (USDA-NASS 2019d)

While insect pest control remains a significant issue in cotton production, studies conducted by USDA-ERS (Fernandez-Cornejo et al. 2014c; Fernandez-Cornejo et al. 2014b), the National Academy of Sciences (NAS 2016), and others (Fleming et al. 2018) have found that insecticide use has declined in

cotton production in part because of adoption of Bt cotton. A combination of use of integrated pest management strategies, Bt crops, and the success of the boll weevil eradication program have resulted in a significant reduction in the number of insecticide applications (Smith 2014). Insecticide use for cotton, which peaked at 9.5 pounds per planted acre in 1967 has declined to less than 1 pound per planted acre in recent years (Figure 3-4). As of 2017, cotton insecticide use by farmers was near an all-time low of 0.35 lbs a.i./acre (USDA-NASS 2019d). Insecticide use for Bt corn production, which peaked in the late 1970s and 1980s at 0.35-0.45 pounds per acre, likewise declined throughout the 1990s and 2000s to under 0.03 pounds per planted acre in 2017. In general, farmers have used less insecticide when they have cultivated Bt cotton and Bt corn crops.

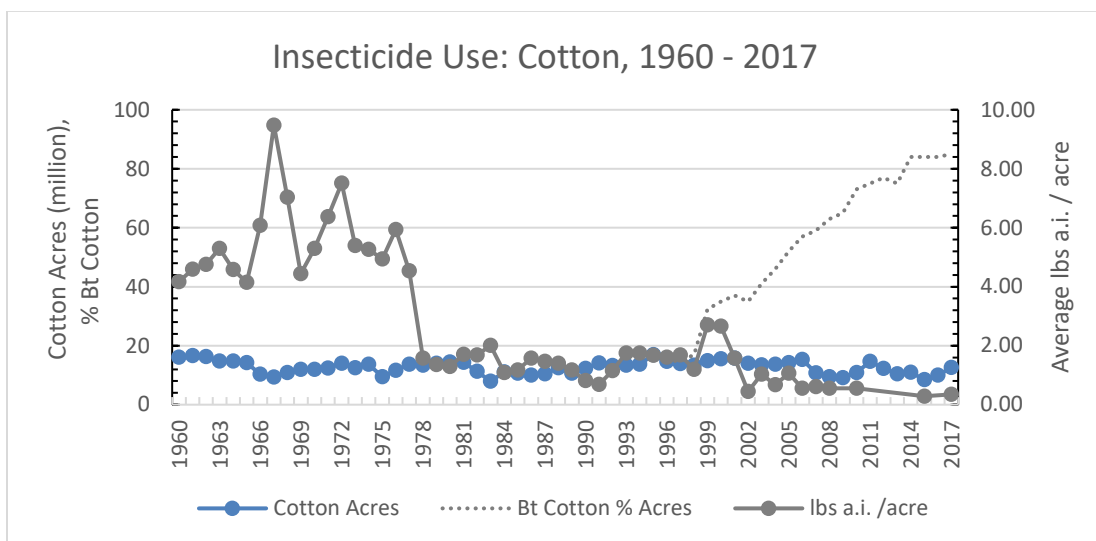


Figure 3-4. Insecticide Use in Cotton Production

Source: (USDA-NASS 2017b, 2018b)

In areas where cultivation of Bt corn and Bt cotton is high, the use of Bt crop varieties has also been associated with reduced insecticide use in adjacent cropping systems cultivating non-Bt varieties, a result of the area-wide suppression of insect pest populations (Hutchison et al. 2010; NAS 2016). A 25-year study of cotton pests in China found that Bt crops led to a major reduction in insecticide use, and an improvement in aphid biological control, caused in part by reduced insecticide use for bollworm control, which helped to conserve aphid natural enemies (Zhang et al. 2018). In general, current peer review literature and other reports indicate that cultivation of Bt crops can potentially provide tangential benefits to adjacent farms by reducing the prevalence of certain insect pest populations, which reduces the need for insecticide use to control the Bt crop targeted pest in nearby cropping systems (Carrière et al. 2003; Wu et al. 2008; Hutchison et al. 2010; NAS 2016; Dively et al. 2018). This benefit considered, when insecticide use is reduced for target pests, other secondary pests that may have been controlled by those insecticide applications could potentially increase. For example, Zhang et al. (2018) found that reduced insecticide use against bollworm was responsible for increasing mirid bug severity in cotton. Many of the insecticides used to control lygus and thrips in major cotton producing states of the U.S. (Table 3-6) may also be used to control beet armyworm, loopers, whiteflies, aphids, and stink bugs. Where secondary pest outbreaks occur, there could be an increase in insecticide use for their control.

GE IR Crops and Pest Resistance and Management

As with herbicide resistant weeds, continued exposure of insect pests to insecticides can result in the development of resistant insect populations. This is also an important concern for GE crop plants that have insecticidal traits (plant incorporated protectants; PIPs). The potential for development of insect population resistance to Bt trait proteins is ever present and has occurred in some areas. For example, resistance of *H. zea* (corn earworm) to several Bt toxins has emerged in the eastern and central Cotton Belt (Fleming et al. 2018). Development of resistance has also been reported in association with the use of Bt sprays, which are one of the most widely used foliar applied insecticides on non-GE crops (Tabashnik et al. 2013). While insects are capable of developing resistance to most insecticides (discussed in following subsection), for Bt PIPs this risk may be increased by the fact that:

- Bt proteins are expressed at high levels in most or all plant tissues;
- Bt protein expression levels are too low to be lethal to the target pest;
- The proteins are produced by the plant continually during the growing season (i.e., throughout the lifespan of the plant);
- Some of the major target pests, such as European corn borer, corn rootworm, and pink bollworm, feed almost exclusively on corn or cotton.

These factors can increase insect exposure to the insecticidal Bt protein and thereby increase selection pressure for development of resistant populations (US-EPA 2019i).

While the use of Bt based crops has been effective as part of integrated pest management (IPM) programs used in commercial crop production, their efficacy may wane if a pest population adapts to the mechanism of action of the particular introduced Cry protein and becomes less susceptible. The cumulative number of cases⁷ of resistance to Bt toxins in GE crops increased from three in 2005 to 16 in 2016 (Tabashnik and Carrière 2017). These 16 cases represent practical resistance⁸ in populations of seven major pests in five countries to each of the nine Cry toxins produced by widely grown Bt crops: Cry1Ab, Cry1Ac, Cry1A.105, Cry1Fa, Cry2Ab, Cry3Bb, mCry3A, eCry3.1Ab, and Cry34/35Ab. For these 16 cases, the average time from the first commercial planting of a Bt crop in a region to the first sampling of field populations in the region that provided evidence of resistance was 5.2 years (Tabashnik and Carrière 2017). By contrast, in 17 other cases there was no decrease in pest susceptibility to Bt crops, including the recently introduced transgenic corn that produces a Bt vegetative insecticidal protein (Vip) (Tabashnik and Carrière 2017). In the United States, populations of cotton bollworm (*H. zea*) have developed resistance to Cry1Ab, Cry1Ac, Cry1A.105, and Cry2Ab (Table 3-7).

⁷ Each case represents the responses of one pest species to one insecticidal protein from *Bacillus thuringiensis* (Bt).

⁸ The criteria for practical resistance are that >50% of individuals in a population are resistant and the efficacy of the Bt crop is reduced in the field.

Table 3-7. Insect Resistance to Bt Crops in the United States						
Scientific Name	Common Name	Crop	Toxin	Year marketed ^a	Years ^b	High dose ^c
<i>Diabrotica virgifera virgifera</i>	Western corn rootworm	Corn	Cry3Bb	2003	6	No
<i>Diabrotica virgifera virgifera</i>	Western corn rootworm	Corn	Cry34/35Ab	2006	7	No
<i>Diabrotica virgifera virgifera</i>	Western corn rootworm	Corn	mCry3A	2007	4 ^d	No
<i>Diabrotica virgifera virgifera</i>	Western corn rootworm	Corn	eCry3.1Ab	2014	0 ^d	No
<i>Helicoverpa zea</i>	corn earworm, cotton bollworm	Corn	Cry1Ab	1996	8	No
<i>Helicoverpa zea</i>	corn earworm, cotton bollworm	Corn	Cry1A.105	2010	6 ^d	No
<i>Helicoverpa zea</i>	corn earworm, cotton bollworm	Cotton	Cry1Ac	1996	6	No
<i>Helicoverpa zea</i>	corn earworm, cotton bollworm	Cotton	Cry2Ab	2003	2 ^d	No
<i>Striacosta albicosta</i>	Western bean cutworm	Corn	Cry1Fa	2003	10	No
<i>Spodoptera frugiperda</i>	fall armyworm	Corn	Cry1F	2003	4	No

a. First year of commercial planting of a Bt crop in the region monitored.

b. Years from the first commercial planting of a Bt crop in the region to the first sampling of field populations in the region yielding evidence of resistance.

c. Test for the high-dose standard based on direct or indirect evidence.

d. Cross-resistance suspected or known as a factor contributing to resistance.

Source: (Tabashnik and Carrière 2017)

In many instances, development of resistance has been attributed to insufficient levels of expression of the Cry protein—levels too low to be lethal (Tabashnik and Carrière 2017; Fleming et al. 2018). Cry/Vip protein expression levels need to be enough such that the quantity of ingested protein is high enough to kill all, or almost all, of the heterozygous insects that feed on Bt plants (Tabashnik and Carrière 2017). Lastly, both Bt cotton and Bt corn were first introduced around 1996, and many of the same Bt genes used in Bt cotton have been used in Bt corn to control various lepidopteran pests, including *H. zea*, which is a pest of both crops. Thus populations of *H. zea* occurring in areas where both Bt crops are grown are potentially exposed to the Cry1A, Cry1F, Cry2A and Vip3A toxins in both crops (Fleming et al. 2018).

Tabashnik et al. (2013) concluded that pests can evolve resistance to Bt crops in as few as two years, although efficacy can be sustained for 15 years or more, where proper IRM practices are implemented. Therefore, if not used judiciously, GE IR crops may become less efficacious over time, which would also contribute to increasingly limited pest management options for GE, conventional, and organic cropping systems. For instance, Bt bio-insecticide formulations are used in organic farming, either as an aerial spray or ground application, to help control insect pests. Bt is one of the few pesticides permitted for use on crops produced in compliance with USDA Organic Standards. Insect resistance management in Bt

crops remains a critical concern and will continue to be an essential aspect of GE IR cropping systems (Tabashnik and Carrière 2017).

Several strategies, such as the use of multiple Cry proteins/toxins, spatial or temporal refuges, and high or ultrahigh doses of a Cry toxin are used to delay the development of insect resistance to PIPs. The primary IRM practice that has received the most attention from both industry and regulatory agencies involves a high dose/refuge” (HDR) concept (Bates et al. 2005; Siegfried and Hellmich 2012). In this strategy, a GE crop variety that expresses a high dose of Bt toxin is grown intermixed with a non-GE variety that does not express the toxin, the latter being the refuge. The ratio between the GE and refuge varieties is designed to ensure that if Bt-toxin-resistant pests develop, the refuge will provide enough non-resistant pests for mating to prevent the resistance trait from becoming fixed in the population, which could result in a Bt-resistant pest strain. This practice essentially dilutes resistance genes in populations while sustaining populations of susceptible insects. In two supporting studies (Bates et al. 2005; Siegfried and Hellmich 2012), 30 cases, where data were available to evaluate the dosage, the high dose standard was met in 69% (9 of 13) of the cases with no loss of susceptibility, and with none of the 17 cases showing either practical resistance or early indications of resistance. Therefore, this pattern demonstrates a significant association between using the high-dose standard to achieve a lower risk of rapid resistance evolution.

Management of resistance to insecticidal PIPs increasingly uses combinations of different Cry proteins, especially proteins that have different receptors or independent modes of action. Pyramided Bt crops are a special type of multi-toxin crops designed to delay evolution of resistance. To minimize the risk of resistance development, pyramided crops produce two or more distinct Bt toxins that kill the same pest (Carrière et al. 2015). Pyramided cotton crops include those that express mCry1Ab + Vip3Aa, Cry1Ab + Cry2Ae, and Cry1Ac + Cry1Fa + Vip3Aa toxins (Carrière et al. 2015). Refuge requirements mandated by EPA have become less stringent as more pyramid crop varieties have become available (Carrière et al. 2015). For most cases, a structured refuge (5% or 20% refuge untreated or treated with insecticides, (US-EPA 2019i)) is not required.

Implementation of insect resistant management (IRM) practices in cultivation of Bt crops is required to protect and effectively sustain their use (US-EPA 2019i). One of the primary goals of EPA oversight is to prevent or mitigate the development of resistance to PIPs in target pests (US-EPA 2019i). To counter the development of resistance, since the 1990s, EPA has mandated the implementation of an IRM plan for each commercially registered Bt Cry protein (US-EPA 2019i). The goal of an IRM plan is to prevent or delay the development of resistant insect populations. In 2017, EPA issued PRN 2017-1, *Guidance for Pesticide Registrants on Pesticide Resistance Management Labeling* (US-EPA 2017a), for conventional pesticides and resistance management. PRN 2017-1 revises and updates PRN 2001-5, and applies to all conventional pesticides (i.e., fungicides, bactericides, insecticides, and acaricides). The guidance is intended to provide:

- Additional guidance for resistance management on pesticide labels;
- References to external technical resources for guidance on resistance management;
- Updated instructions on how to submit changes to existing labels to enhance resistance-management language.

Guidance on FIFRA Section 6(a)(2) Regulations for Pesticide Product Registrants, established a requirement and guidelines for reporting any substantiated incidents of pest resistance to any pesticide product regulated by EPA.⁹ This reporting requirement is in accordance with FIFRA Adverse Effects Reporting Section 6(a)(2), which requires pesticide product registrants to submit adverse-effects information about their products to EPA.

In 2018, USDA announced updated guidance to the National Road Map for Integrated Pest Management. The update is the product of the Federal Integrated Pest Management Coordinating Committee (FIPMCC), a joint effort that is coordinated by the Office of Pest Management Policy in the Office of USDA's Chief Economist with representatives of all federal agencies with responsibilities in IPM research, implementation, or education programs. These agencies/departments include USDA, Environmental Protection Agency (EPA), Department of the Interior (DOI), and Department of Defense (DoD) (USDA 2018).

3.1.2.5 Weed and Herbicide Resistant Weed Management

Because MON 88702 cotton only expresses resistance to certain insect pests, APHIS anticipates that it's likely to be crossed with one or more HR cotton varieties to develop stacked-trait cultivars that combine both types of traits (Figure 3-3). HR cotton volunteers from a previous cotton crop can create problems as a weed in subsequent plantings of cotton or other crops grown in the same fields. This can develop from the prevalence of the same HR traits (especially 2,4-D resistance) in both cotton and other crops planted in rotation with cotton because cotton volunteers must be controlled to achieve eradication or to prevent the re-establishment of cotton boll weevil. Because of these concerns, weed management in cotton is discussed in this section.

The difficulty and cost of controlling weeds is a major challenge to cotton growers because they compete and deprive a crop of resources (e.g., soil moisture and nutrients, access to sunlight) that would otherwise be available to the crop plant. Weeds in cotton can (a) reduce fiber quality, (b) reduce crop yield, (c) increase production costs, (d) reduce irrigation efficiency, and (e) serve as hosts/ habitat for insect pests and disease-causing pathogens (Ashigh et al. 2012). The slow, early growth of cotton does not permit crop plants to aggressively compete against weeds that often grow more rapidly (UGA 2016). Across the Cotton Belt, many annual and perennial weeds occur, causing economic losses (Ashigh et al. 2012). Table 3-8 summarizes the most common weeds in cotton reported in the United States. Prior to the development of synthetic chemical pesticides in the 1940s, farmers controlled weeds by tillage, mowing, site selection, crop rotation, and hoeing or pulling by hand. While tillage is effective, it can contribute to the erosion and compaction of topsoil, reducing soil capacity to absorb water, and promoting runoff that can pollute surface waters with sediments and agronomic inputs. U.S. farmers began using synthetic chemical pesticides after their commercial introduction in the 1940's because they were inexpensive, effective, easy to apply, lower in labor costs, required less tillage, and increased crop yields (Fernandez-Cornejo et al. 2014c). Because herbicides are effective, they remain the most commonly used option among weed management tools, and are expected to remain so for the foreseeable future. In 2012 (latest use/cost data available), herbicides accounted for 57% of all pesticide uses, and 58% of pesticide expenditures; farmers spent roughly \$5.1 billion on herbicides in 2012 (Atwood and Paisley-Jones 2017).

⁹ See <https://www.epa.gov/pesticide-registration/prn-98-3-guidance-final-fifra-6a2-regulations-pesticide-product-registrants>

Table 3-8. Common Weeds in Cotton Production: 2019

Scientific Name	Common Name	States Present
<i>Abutilon theophrasti</i>	velvetleaf	MO
<i>Amaranthus blitoides</i>	prostrate pigweed	AZ
<i>Amaranthus Palmeri</i>	Palmer amaranth	AL, AZ, AK, FL, GA, LA, MS, MO, MT, NC, OK, TN, TX
<i>Amaranthus tuberculatus</i>	waterhemp	LA, MS, MO, TX
<i>Ambrosia artemisiifolia</i>	common ragweed	NC
<i>Ambrosia tenuifolia</i>	false ragweed	TX
<i>Bassia scoparia</i>	kochia	MO, MS, OK, TX
<i>Chloris spp.</i>	fingergrass spp.	OK
<i>Commelina benghalensis</i>	Benghal dayflower	AL, FL, GA
<i>Convolvulus arvensis</i>	field bindweed	TX
<i>Convolvulus spp.</i>	bindweed spp.	TX
<i>Cucumis melo</i>	Small melon	TX
<i>Cyperus esculentus</i>	yellow nutsedge	FL, LA, LO, MI, NC
<i>Cyperus rotundus</i>	purple nutsedge	OK
<i>Cyperus spp.</i>	nutsedge spp.	AL, GA
<i>Scientific Name</i>	<i>Common Name</i>	<i>States Present</i>
<i>Digitaria sanguinalis</i>	large crabgrass	MO, NC
<i>Digitaria spp.</i>	crabgrass spp.	GA, MT
<i>Dinebra panicea</i>	red sprangletop	OK
<i>Echinochloa colona</i>	junglerice	AZ, TN
<i>Echinochloa crus-galli</i>	barnyard grass	AK, LA, MS, MO, MT, TX
<i>Echinochloa spp.</i>	barnyard grass spp.	MS
<i>Eleusine indica</i>	goosegrass	FL, GA, MT, NC, TN
<i>Erigeron canadensis</i>	horseweed	LA, MO, NC, OK, TN, TX
<i>Ipomoea hederacea</i>	Ivy leaf morning glory	AZ, MS, MO, NC, TX
<i>Ipomoea lacunosa</i>	pitted morning glory	MO, TN, NC
<i>Ipomoea spp.</i>	morning glory spp.	AL, AK, GA, LA, MS, NC, OK, TN, TX
<i>Jacquemontia tamnifolia</i>	Small flower morning glory	GA, MS
<i>Lolium perenne</i>	perennial ryegrass	TN
<i>Lolium spp.</i>	ryegrass spp.	AK
<i>Mollugo verticillata</i>	carpetweed	NC
<i>Parthenium hysterophorus</i>	ragweed parthenium	TX
<i>Poa spp.</i>	annual grass spp.	AK
<i>Proboscidea louisianica</i>	devil's-claw	TX
<i>Salsola tragus</i>	Russian-thistle	TX
<i>Senna obtusifolia</i>	sicklepod	AL, FL, NC
<i>Setaria viridis</i>	green foxtail	MO
<i>Sida spinosa</i>	prickly sida	LA, MS, MT, TN
<i>Solanum carolinense</i>	Horse nettle	MO
<i>Solanum elaeagnifolium</i>	silverleaf nightshade	TX
<i>Sorghum halapense</i>	johnsongrass	AZ, OK, TN
<i>Trianthema portulacastrum</i>	horse purslane	TX
<i>Urochloa platyphylla</i>	broadleaf signalgrass	LA, MS, MO
<i>Urochloa texana</i>	Texas millet	AL, FL, GA, NC, TX
<i>Xanthium strumarium</i>	common cocklebur	MS
<i>Xanthium strumarium</i>	common cocklebur	MT

Source: (WSSA 2020) (Webster et al. 2009; Monsanto 2013)

Herbicide Resistant Weeds in U.S. Cotton Crops

HR weed populations are present in all states where cotton is produced. Currently, the majority of HR weed populations in cotton exhibit resistance to a single herbicide MOA. However, HR weed populations exhibiting resistance to two MOAs are increasingly present in cotton (Heap 2019). Table 3-9 lists weeds with resistance to one or more herbicides that occur in U.S. cotton crops.

Table 3-9. Herbicide-Resistant Weeds in Cotton with Resistance to One or More Herbicides		
Mode of Action (MOA)	Weed-Common Name	States Present
ACCase inhibitors	Johnsongrass	Louisiana, Mississippi, Tennessee
ALS inhibitors	Palmer Amaranth	South Carolina, Tennessee
	Spiny Amaranth	Mississippi
	Tall Waterhemp	Missouri
	Horseweed	Kansas, Oklahoma
EPSP synthase inhibitors	Palmer Amaranth	Arkansas, Florida, Georgia, Kansas, Louisiana, Mississippi, Missouri, North Carolina, South Carolina, Tennessee, Texas
	Spiny Amaranth	Mississippi
	Tall Waterhemp	Arkansas, Louisiana, Tennessee, Texas
	Common Ragweed	Alabama, North Carolina
	Giant Ragweed	Tennessee
	Horseweed	Alabama, Arkansas, Kansas, Mississippi, Missouri, North Carolina, Tennessee
	Junglerice	California
	Goosegrass	Mississippi
	Kochia	Kansas
	Italian Ryegrass	Louisiana, Mississippi, North Carolina
Microtubule inhibitors	Palmer Amaranth	South Carolina, Tennessee
	Goosegrass	Alabama, Arkansas, Georgia, Mississippi, North Carolina, South Carolina, Tennessee
	Johnsongrass	Mississippi
Nucleic acid inhibitors	Common cocklebur	Alabama, Arkansas, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee
Multiple Resistance: Up to 5 MOAs - ALS inhibitors, PPO inhibitors, EPSP synthase inhibitors, Microtubule inhibitors, Long chain fatty acid inhibitors	Palmer Amaranth	Arkansas, Arizona, Georgia, Mississippi, South Carolina, Tennessee
	Tall Waterhemp	Missouri

Source: (Heap 2019)

HR Weeds—Environmental Concerns and Management

Herbicide resistant (HR) weeds are more of an agronomic than ecological concern. However, HR weed populations may have environmental impacts. This may result when HR weed control requires an increase in herbicide applications and/or tillage, when it causes an increase in soil erosion and run-off of non-point source pollutants (e.g., sediments, herbicide residue).

In cotton, cultivation/tillage can be used to effectively manage small Palmer amaranth and other weeds between rows, but eliminating cultivation for weed control reduces equipment and labor demands (i.e., cost). It also reduces subsequent weed flushes, destruction of residual herbicide activity, moisture loss, and root damage (Whitaker et al. 2018).

Most plants, including weeds, have a natural capacity to withstand some exposure to herbicides and survive. While herbicides are an important tool for weed control, they impart selection pressure on these inherent natural survival mechanisms, which are usually described as a plant's "tolerance."¹⁰ Repeated exposure of weed populations to herbicide pressure results in the survival of those more resistant plants (Owen 2011; Owen 2012; Vencill et al. 2012). They differ slightly in genetic makeup from the rest of the population, but remain reproductively compatible. Those most resistant plants initially are present in a weed population in extremely small numbers: about 1 in 100 thousand to fewer than 1 in 1 million (Campbell et al. 2015). The repeated use of one herbicide mode of action (MOA)¹¹ promotes survival of these few naturally resistant plants, which selects for a resistant weed population (Sherwani et al. 2015).

Weed populations can also develop "evolved" resistance to an herbicide a.i. when a weed adapts to an external chemical stressor. Key to understanding the evolution of HR traits is identifying the mechanism(s) of resistance, which are broadly classified into target-site resistance (TSR) and/or non-target-site resistance (NTSR). Most TSR mechanisms involve mutations in the target site of action of an herbicide, resulting in an insensitive or less sensitive target protein of the herbicide (Jugulam and Shyam 2019). For example, evolved TSR can emerge from mutations in genes/proteins involved in the herbicide's MOA. A genetic mutation can cause a minor change in the structure of the target enzyme of an herbicide, resulting in an herbicide no longer having an adverse effect on the enzyme's function, rendering the plant "resistant" to the herbicide (e.g., (Yang et al. 2016; Rey-Caballero et al. 2017)). Development of over-expression or amplification of the target gene is another TSR mechanism (Jugulam and Shyam 2019).

NTSR to herbicides in weeds can result from the alteration of one or more physiological processes, such as herbicide absorption, translocation, sequestration, and/or metabolism. Compared to TSR, NTSR mechanisms are typically more complex, so are more difficult to elucidate. They can impart cross-resistance to herbicides with different modes of action, which further complicates resistance management strategies (Jugulam and Shyam 2019).

Over-reliance on herbicides and increasing problems caused by the development of HR weed populations has aroused debate on how to best incorporate herbicides into sustainable cropping systems (Vencill et al. 2012; Duke 2015; Owen 2016). Currently, 48 states report the presence of HR weed populations. This is not a recent concern, nor is it unique to GE crops. HR weed populations have been occurring since the

¹⁰ Note that "Resistance" to herbicides is defined by the Herbicide Resistance Action Committee (HRAC) as the inherited ability of a plant population to survive and reproduce following repeated exposure to a dose of herbicide normally lethal to the wild type. "Tolerance" is distinguished from resistance and defined by HRAC as the inherent ability of a plant to survive and reproduce following exposure to an herbicide treatment. This implies that there was no selection or genetic manipulation to make the plant tolerant; it is naturally tolerant. In reference to GE crops, the terms "resistance" and "tolerance" are often used interchangeably. Throughout this EA, APHIS will use the term "resistance" and "resistant", and "herbicide-resistant" (HR), when referring to GE cotton.

¹¹ The MOA is the unique biological mechanism at the cellular/molecular level by which an herbicide is lethal to a plant.

advent and wide-spread use of chemical herbicides in the 1950s. As illustrated in Table 3-9, HR weed populations occur in multiple states in cotton growing regions in the United States. By 1999, there were 166 unique cases of HR weeds in the United States (weed species by herbicide mode of action [MOA]) (Heap 2019).

Strategies for managing and avoiding the development of HR weed populations in U.S. agriculture are steadily being refined (see for example: Norsworthy et al. 2012; Vencill et al. 2012; Garrison et al. 2014; Owen 2016). A combination of preventive, cultural, mechanical, biological, and chemical methods are required for effective weed, and weed resistance management (Norsworthy et al. 2012; Garrison et al. 2014; Owen 2016). The coordinated use of these is termed integrated weed management (IWM). Crop producers are advised to, and are implementing IWM strategies to address development of HR weeds. These practices are recommended by the crop protection and seed industries, USDA, university extension services, EPA, state departments of agriculture, the Weed Science Society of America (WSSA), and others. In 2017, EPA issued PR Notice 2017-2, *Guidance for Herbicide-Resistance Management, Labeling, Education, Training and Stewardship* (US-EPA 2017b), which provides registrants and growers detailed information on slowing the development and spread of HR weeds. EPA guidance is part of a more holistic, proactive approach involving crop consultants, agricultural commodity organizations, professional /scientific societies, researchers, and the pesticide registrants themselves.

3.2 Physical Environment

3.2.1 Soil Quality

Overview

In an agricultural setting, concerns regarding soils are the potential for agronomic practices and inputs to affect soil fertility; erosional capacity; off-site transport of topsoil (sediments), pesticides, and fertilizers; and disturbance of soil biodiversity. Tillage, cover crops, crop rotation, and pesticide and fertilizer inputs can influence the biological, physical, and chemical properties of soil. All of these can substantially impact soil fertility, crop yield potential, and soil erosion (Baumhardt et al. 2015). Loss of soil quality occurs through declines in soil organic matter (SOM), vital minerals (magnesium, calcium), essential nutrients (i.e., nitrogen, phosphorus, and potassium), soil biota, and physical alteration of soil structure (compaction).

Soil Erosion on U.S. Croplands

Because of the slow rate of soil formation (on the order of millimeters per year), soil is considered a nonrenewable resource that requires conservation and stewardship for sustainable crop production. Soil erosion not only increases fertilizer requirements and production costs, it leads to impaired air and water quality. Soil erosion occurs in all areas of the United States but is more concentrated in those regions where the percentage of total area in cropland is highest and a larger proportion of the land is highly erodible (Magleby et al. 1995; Baumhardt et al. 2015; USDA-NRCS 2018a). Excessively eroding cropland soils are concentrated in the Midwest, southern High Plains of Texas, and the northern plains states. Cropland in the Cotton Belt is susceptible to wind and water erosion (Figure 3-5). Where soil erosion occurs through natural processes, the rates of which are determined by soil type, local ecology,

and weather; certain tillage and cover crop practices have substantial impacts on the erosion potential of soils.

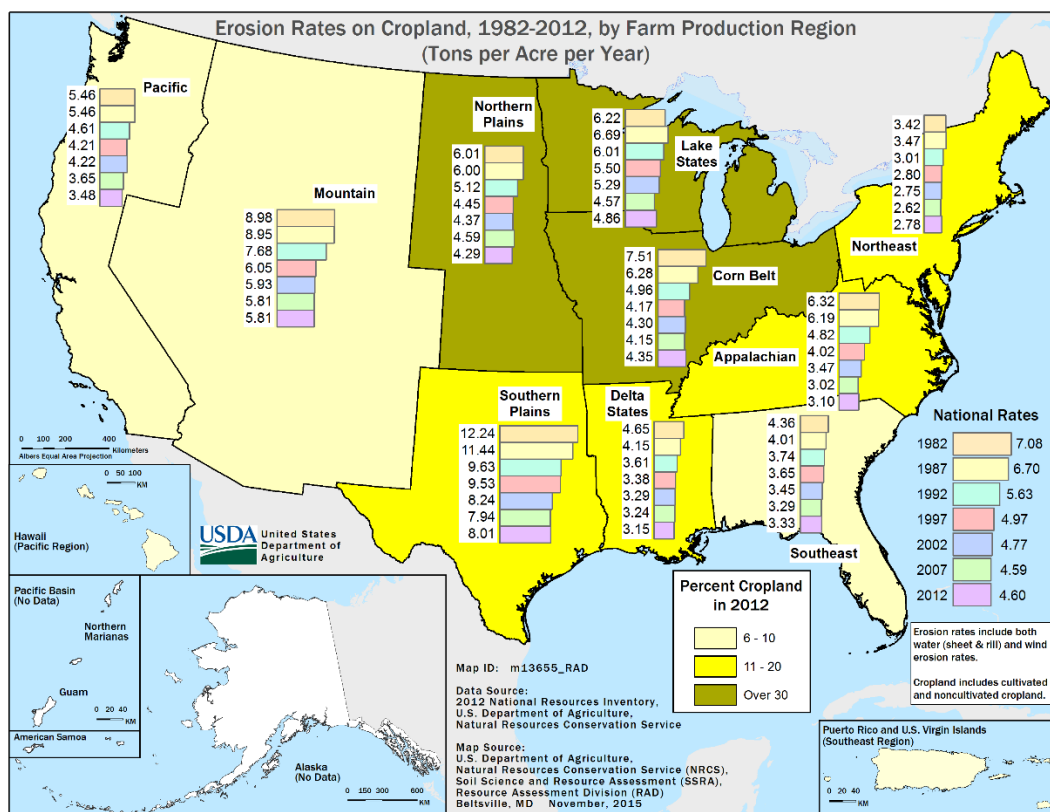


Figure 3-5. Locations and Status of U.S. Croplands Subject to Water and Wind Erosion
Source: (USDA-NRCS 2018b)

Conservation programs began specifically targeting highly erodible lands in the United States in 1985. As these conservation tillage and cover cropping practices have increased, soil erosion has declined (USDA-NRCS 2010, 2018a). Soil erosion rates on U.S. cropland decreased 34% between 1982 and 2015 (USDA-NRCS 2018a). In 1982, total annual water erosion (sheet and rill) on cultivated cropland was 3.82 tons per acre per year, versus 2.71 in 2015. For wind erosion, erosion rates reduced from 3.21 to 1.91 tons per acre over the same time period (USDA-NRCS 2018a). Since 2002, water sheet and rill erosion has remained fairly steady at around 2.90 to 3.03. Any decrease in erosion of cropland soils carries with it a corresponding decrease in run-off and introduction of non-point source pollution (NPS) pollutants such as sediments, fertilizer, and pesticides into surface waters.

Because susceptibility to erosion is a key concern on more than half of U.S. cropland (USDA-NRCS 2010), soil management and conservation is a basic component of crop production. Since 1985, conservation programs have specifically targeted highly erodible lands in the United States. Cover crops are being adopted primarily to conserve soils and soil quality (SARE/CTIC 2017). A 2017 survey of U.S. farmers primarily targeting cover crop users found that among the 1,582 cover crop users who responded, 41% of surveyed farmers applied continuous no-till practices, 14% rotational no-till, 27% reduced tillage, and 4% vertical tillage (a type of conservation tillage), with only 14% using conventional tillage

(SARE/CTIC 2017). Overall, in USDA –NASS surveys, conservation tillage and cover crop adoption rates have increased on U.S. cropland from 2012 to 2017. U.S. farmers applied no-till on 32.64% (104.4 million acres), reduced tillage on 30.54% (97.7 million acres), conventional tillage on 25% (80 million acres), and; and cover crops to 4.81% (15.4 million acres) of harvested cropland in 2017 (Table 3-10). The use of conservation tillage, to include no-till, is attributed, in part, to cultivation of GE HR crops, which provide for effective chemical means of weed control, and can reduce reliance on tillage for control of weeds (Fernandez-Cornejo et al. 2014a). Thirty-two percent of GE HR cotton acres were planted using conservation tillage (including no-till) in 2007 compared to 17% of conventional cotton acreage (Fernandez-Cornejo et al. 2014a). However, the availability of GE HR crops is not the only driving factor in adoption of conservation tillage practices, as many growers adopted conservation tillage well before GE HR varieties were introduced to the market (Givens et al. 2009). As shown in Figure 3.4 conservation tillage practice in cotton have trended lower than those for wheat, corn, and soybean.

	Total Harvested Cropland	Cropland with reduced tillage, excluding no-till	Cropland with no-till practices	Cropland with intensive tillage practices	Cropland planted to a cover crop (excluding CRP)
2017	320,041,858	97,753,854 30.54%	104,452,339 32.64%	80,005,292 25.00%	15,390,674 4.81%
2012	314,964,600	76,639,804 24.33%	96,476,496 30.63%	105,707,971 33.56%	10,280,793 3.26%

Source: (USDA-NASS 2014, 2019c)

In summary, land management practices for crop cultivation can affect soil quality and erosion relative to the tillage, pesticide application, crop rotation, soil amendment, and cover cropping practices applied. GE HR crops are correlated with use of conservation tillage practices, which sustain soil health and water retention, and reduce runoff (Fernandez-Cornejo et al. 2014a; Claassen et al. 2018). There are no adverse effects on soil health unique to GE HR crops that have been identified since their adoption in the late 1990s. All growers producing crops on highly erodible land are required to maintain and implement a soil conservation plan that substantially reduces soil loss, and is approved by the USDA National Resources Conservation Service (NRCS). These plans are prepared by the grower pursuant to the Food Security Act of 1985 (P.L. 99-198, Farm Bill), which included a number of provisions designed to conserve soil and water resources, and minimize erosion. The 2014 and 2018 Farm Bills have continued the requirement that producers adhere to conservation compliance guidelines to be eligible for conservation programs administered by the USDA Farm Service Agency and USDA-NRCS. State agencies also provide assistance in development and implementation of soil conservation plans.

3.2.2 Water Resources

Agronomic inputs, and in many areas tillage and irrigation, are necessary for efficient crop production. These practices and inputs can, however, lead to the impairment of surface waters and coastal waters and bays through runoff of pesticides, fertilizers (nutrients), and soil sediment (Bricker et al. 2008; CENR 2010). Groundwater can also be impacted by agronomic inputs from leaching and withdrawals for irrigation.

While pollutants come from various sources, the National Water Quality Assessment indicates that agricultural nonpoint source (NPS) pollution is a leading cause of impairment of surveyed rivers and streams; the third largest source for lakes/ponds; the second largest source of impairments to wetlands; and a major contributor to contamination of surveyed estuaries, coastal areas, and groundwater (US-EPA 2019b). The most common NPS contaminants in agricultural run-off are sediment, nutrients such as nitrogen and phosphorus, and pesticide residues (Table 3-10), all of which can adversely affect aquatic ecosystems.

Table 3-11. Causes of Impairment in Assessed Waters, 2019								
	Rivers, Streams		Lakes, Reservoirs, Ponds		Bays, Estuaries		Wetlands	
	Miles	Rank	Acres	Rank	Miles	Rank	Acres	Rank
Nutrients	118831	3rd	3943395	2nd	18279	2nd	67849	6th
Sediment	138874	2nd	502200	12th	400	18th	1237	15th
Pesticides	18069	16th	412672	13th	7543	8th	202	21st

Shown are national water quality data reported by the states to EPA under Section 305(b) and 303(d) of the Clean Water Act. The data shown is the most current available, which varies widely among states, spanning the years from 2004 to 2016. The EPA lists around 34 different factors that are causes of impairment of U.S. waters. For rivers and streams, EPA lists sediments as the second most frequent cause of impairment; nutrients, third; and pesticide residues, sixteenth. For lakes, reservoirs, and ponds: nutrients are second, sediments, twelfth; and pesticide residues, thirteenth. For bays and estuaries: nutrients are second; sediments, eighteenth; and pesticide residues, eighth. For wetlands: nutrients are sixth; sediments, fifteenth; and pesticides, twenty-first.

Source: (US-EPA 2019b)

Excess sediment in runoff can adversely affect aquatic ecosystems by covering fish breeding substrates, increased turbidity, and impairing growth of aquatic plants. Nutrient runoff (e.g., nitrogen and phosphorus) runoff from agricultural fields can contribute to eutrophication of surface waters. Nearly two-thirds of the U.S. estuaries have moderate to high levels of eutrophication. Eutrophication causes impairments to human uses and to living resources, including harmful algal blooms and hypoxic/anoxic conditions¹² that lead to fish kills, fish consumption warnings (to prevent human health problems), declines in tourism, and impacts on fisheries (Bricker et al. 2008; CENR 2010). These conditions occur in estuaries along all coasts, but are most prevalent in estuaries along the Gulf of Mexico and mid-Atlantic coasts (Figure 3-7). Watersheds with a high potential to discharge nitrogen from agriculture to estuaries are located primarily in the Heartland, Mississippi Portal, and Southern Seaboard regions (Wiebe and Gollehon 2006; CENR 2010).

¹² Hypoxia means low dissolved oxygen concentrations. Anoxia means a total depletion of dissolved oxygen. Both conditions are harmful to aquatic biota.

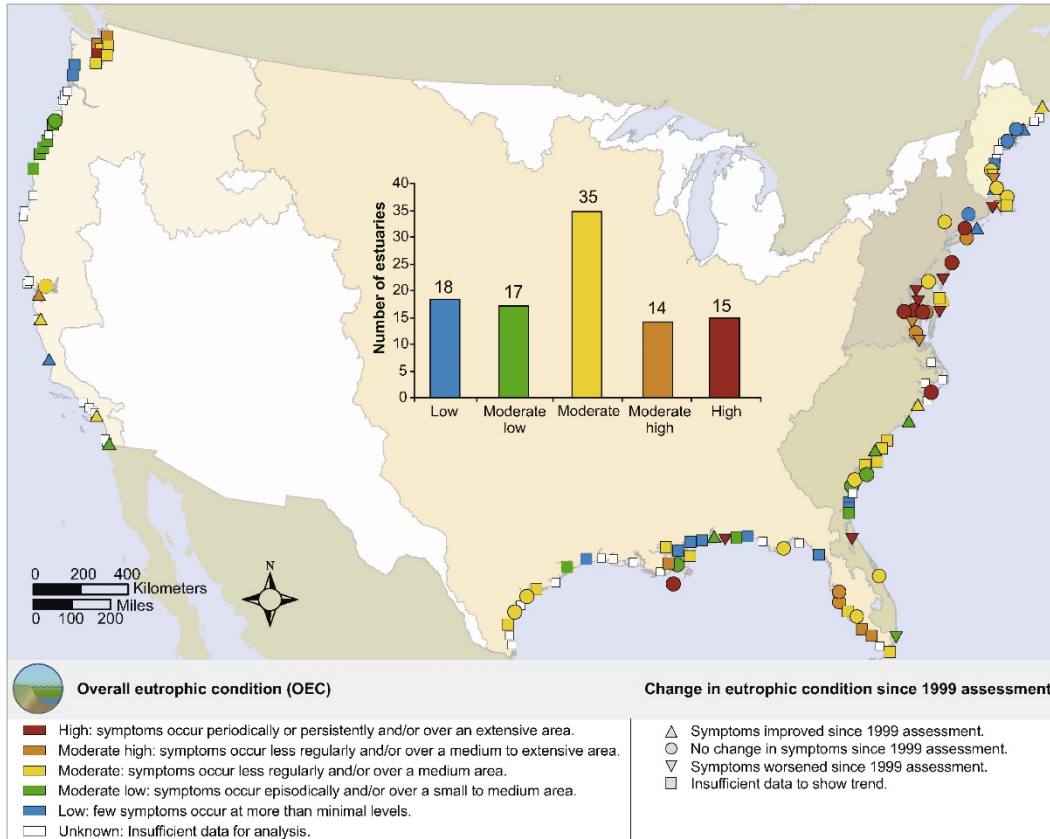


Figure 3-6. Overall Eutrophic Conditions on a National Scale

Source: (Bricker et al. 2008)

Human uses impacted by impairment of surface waters for all regions include commercial and recreational fishing, shellfish harvesting, fish consumption, swimming, aesthetics, and tourism (CENR 2010). The overall top four causes of these use impairments were listed as agriculture (crops and animal operations), wastewater treatment plants, urban runoff, and atmospheric deposition (Bricker et al. 2008; Boesch 2019). Animal operations and crop agriculture were noted mostly for systems in the mid- and South Atlantic regions, while exurban development (outside boundaries of urban and usually suburban areas) was reported in the South Atlantic region. In all regions except for the North Atlantic, non-point sources remain a primary focus (CENR 2010).

Agricultural management practices and factors that determine erosion and NPS pollution include the type of crop cultivated; tillage and irrigation practices; pesticide and fertilizer application practices (e.g., type, quantity, methods); weather; regional environment; and federal and state requirements (summarized below). Efforts to increase resource use efficiency have been largely successful in the United States and have increased cotton yields approximately 42% from 1980-2015 (FTM 2016). On a per pound of lint basis, the following resource use metrics have improved from 1980 to 2015: land use 48%; soil conservation, 36%; and irrigation water applied, 78% (FTM 2016). Volume of water applied per incremental pound of lint produced as a result of irrigation was reduced from over 0.09 acre-inches to 0.02 acre-inches by the end of the 1980-2015 period. Much of the increased yields and resource use efficiencies have been possible by: research and advances made to eradicate pests; implementation of

precision agriculture technologies; creation of higher performing cotton varieties; and development of integrated pest management strategies (Deguine et al. 2008).

3.2.2.1 Water Quality Regulation

Point and Non-Point Source Discharges

Under Section 404 of the Clean Water Act (CWA), it is unlawful to discharge any pollutant from a point source into navigable waters without a permit authorized under the CWA. The EPA's National Pollutant Discharge Elimination System (NPDES) permit program controls these point source discharges (US-EPA 2019g). NPS pollution, which is the primary type of discharge from cropping systems, is not regulated under the CWA. It is regulated mostly under voluntary controls implemented by states and local authorities. Therefore, many crop production activities do not require a Section 404 permit, even where they involve discharges of dredged or fill materials into waters of the United States. To be exempt, the farming activity must be part of an ongoing farming operation and cannot be associated with bringing a wetland into agricultural production or converting an agricultural wetland to a non-wetland area.

Diffuse runoff from nonpoint sources, such as agriculture fields, can be difficult to control, although improved production methods that reduce tillage, optimize fertilizer application and buffer fields from waterways, can mitigate water quality impairments. Because of potential impacts of agriculture on water resources, various national and regional efforts are underway to reduce NPS contaminants in agricultural run-off, and run-off itself, such as EPA's Mississippi River/Gulf of Mexico Hypoxia Task Force (US-EPA 2019e) and USDA-NRCS National Water Quality Initiative (NWQI) (USDA-NRCS 2019c). For example, through the NWQI, the NRCS and partners such as local and state agencies, and nongovernmental organizations, work with producers and landowners to implement voluntary conservation practices that improve water quality. The NWQI program began in 2012 and has been extended through 2023. It provides funding for financial and technical assistance for conservation practices, and in 2018 NRCS invested \$30 million in targeted assistance to help farmers and ranchers improve water quality in high priority streams and rivers. State water quality agencies and other partners contribute additional resources for watershed planning, program implementation, and outreach and for monitoring efforts to track water quality improvements over time. In FY19, NRCS expanded the scope of NWQI to include source water protection, including both surface and groundwater systems.

Several other legislative drivers also influence how federal agencies work on coastal water quality including the Clean Water Act; the Food, Conservation, and Energy Act ("Farm Bill"); the Energy Independence and Security Act of 2007; and the Coastal Zone Management Act, and The Harmful Algal Bloom and Hypoxia Research and Control Act. Responsibility for resolving hypoxia spans several federal agencies (U.S. Department of Agriculture, U.S. Geological Survey, U.S. Environmental Protection Agency, and National Oceanic and Atmospheric Administration), which oversee research and management/control programs. States play a critical role in monitoring and managing eutrophication (CENR 2010).

Pesticides

The EPA determines use requirements for pesticides that are intended to be protective of water quality (US-EPA 2019n, 1). The EPA provides label use restrictions and guidance for product handling intended to prevent impacts to surface and groundwater. There are also national and local programs to reduce NPS contaminants in agricultural runoff, and runoff itself, such as the USDA-NRCS National Water Quality

Initiative (NWQI). The United States Geological Survey (USGS) monitors and maintains information on pesticide concentrations in surface and groundwater in its Pesticide National Synthesis Project (USGS 2018).

3.2.3 Air Quality

National Ambient Air Quality Standards

Because air pollution can adversely affect human health and the environment, maintaining air quality is a primary U.S. regulatory goal. The EPA establishes National Ambient Air Quality Standards (NAAQS) pursuant to the Clean Air Act (CAA) that are intended to protect public health and the environment. NAAQS are established for six criteria pollutants: ozone (O₃), nitrogen dioxide (NO₂), carbon monoxide (CO), sulfur dioxide (SO₂), lead (Pb), and particulate matter (PM). In addition to criteria pollutants, EPA regulates 187 other air pollutants considered hazardous, such as ammonia and hydrogen sulfide.

All areas of the nation are classified based on their status with regard to attainment of NAAQS. States enforce the NAAQS through creation of state implementation plans (SIPs), which are designed to achieve EPA-established NAAQS. The EPA designates a region as being in attainment for a criteria pollutant if atmospheric concentrations of that pollutant are below the NAAQS, or being in nonattainment if criteria pollutant concentrations exceed the NAAQS.

Crop production practices can generate air pollutants that can potentially affect the environment and human health, and challenge regional NAAQS. Agricultural emission sources include: smoke from agricultural burning (PM); fossil fuels associated with equipment used in tillage and harvest (CO₂, NO_x, SO_x); soil particulates from tillage (PM); soil nitrous oxide (N₂O) emissions from the use of fertilizers/manure; and atmospheric emissions through the volatilization of pesticides, and gases and odors from manure (Aneja et al. 2009; US-EPA 2020c).

Prescribed burning is a land treatment used under controlled conditions to accomplish resource management objectives. Prescribed burning used for preparing fields for the next growing season is an efficient and economical method for eliminating pests and diseases that can be detrimental to future crops. Burning crop residue also allows for no-till or reduced-till during the next growing season. Open combustion produces particles in a wide range of sizes. The size range depends to some extent on the rate of energy release of the fire (US-EPA 2019j). Smoke management planning prior to the application of prescribed fires helps to reduce the impact of smoke on roadways, nearby towns, and sensitive areas like schools, nursing homes, churches, and other facilities occupied by people. The extent to which agricultural and other prescribed burning may occur is regulated by individual state implementation plans to achieve compliance with the NAAQS. Prescribed burning of fields would likely occur only as a pre-planting option based on individual farm characteristics. Little or no field burning is performed for cotton production. Emission from field burning of residue are a relatively small share of total emissions from agricultural production. However, in cases where residue is burnt, the impact can be significant (FTM 2016).

While EPA establishes NAAQS, the standards do not set emission control requirements for any particular industry, including agriculture. USDA and EPA provide guidance for regional, state, and local regulatory agencies, and farmers, on how to best manage agricultural emissions sources and limit NAAQS emissions (USDA-EPA 2012). These measures allow stakeholders the flexibility in choosing which measures are

best suited for their specific situation. These measures allow stakeholders the flexibility to choose those measures best suited for their specific situations/conditions and desired purposes. The EPA has also developed USDA-approved measures to help manage air emissions from cropping systems to help satisfy State Implementation Plan requirements. The EPA recommends that in areas where agricultural activities have been identified as a contributor to a violation of NAAQS, USDA-approved conservation systems and activities be implemented to limit emissions. The USDA Environmental Quality Incentives Program Air Quality Initiative provides financial and technical assistance to help farmers and ranchers limit air pollution (USDA-NRCS 2019d).

Other conservation practices, as required by USDA to qualify for crop insurance, and federal loans and programs, effectively reduce crop production impacts to air quality through the use of windbreaks, shelterbelts, reduced tillage, and cover crops that promote soil protection on highly erodible lands.

Pesticides

Apart from NAAQS emissions, spray drift, and volatilization of pesticides from soil and plant surfaces, can result in the introduction of constituent chemicals into the air; which can present human health risks, and risks to nearby crops. Therefore, drift and volatilization of pesticides can be a source of concern to both farmers and the general public because of the potential environmental and human health effects. Volatilization is dependent on pesticide chemistry, soil wetness, humidity, and temperature (US-EPA 2019h). Drift is dependent on wind conditions and applicator practices, including application equipment features such as boom height, nozzle type and droplet size (US-EPA 2019d).

The EPA's Office of Pesticide Programs, which regulates the use of pesticides, introduced initiatives to help pesticide applicators minimize off-target pesticide drift. The EPA's voluntary Drift Reduction Technology Program was developed to encourage the manufacture, marketing, and use of spray technologies that reduce pesticide drift. The EPA is also working with pesticide manufacturers through the registration and reregistration review programs to develop improvements to pesticide label instructions that will reduce drift and volatilization (e.g., see (US-EPA 2019d)).

3.3 Biological Resources

3.3.1 Soil Biota

Soil biota consist of microorganisms (bacteria, fungi, archaea and algae), soil animals (protozoa, nematodes, mites, springtails and other insects, spiders, and earthworms), and plants (e.g., algae) living all or part of their lives in or on the soil, or pedosphere (Fortuna 2012). Soil biota are critical for the formation and turnover of soil organic matter (including mineralization), biodegradation of anthropogenic substances (e.g., pesticides), nutrient cycling, suppression of plant diseases, promotion of plant growth, soil structure formation, and most biochemical soil processes (Gupta et al. 2007; Fortuna 2012; Parikh and James 2012). Plant roots release a variety of compounds into the soil creating a unique environment for microorganisms in the rhizosphere (root zone). Millions of species of soil organisms exist but only a fraction of them have been cultured and identified (Fortuna 2012).

Some microorganisms can cause plant diseases, which can result in substantial costs from losses in crop production, and soil treatments to control plant pathogens. Serious soil-borne cotton crop diseases include those caused by fungi (e.g., verticillium wilt, fusarium wilt, and cotton root rot); and bacteria (e.g., bacterial blight) (UA 2020).

Potential changes to the soil microbial community as a result of cultivating GE crops has been a subject of much research interest since their introduction in the late 1990s (e.g., Motavalli et al. 2004; Locke et al. 2008; Kremer and Means 2009). Potential direct impacts could possibly include changes to the structural and functional community near the roots of GE plants from altered root exudation or the transfer of novel proteins into soil, or a change in microbial populations caused by changes in agronomic practices used to produce GE crops (e.g., pesticides, fertilizers, and tillage practices). The majority of these studies have focused on Bt crops, including Bt cotton, because of research interest in their insecticidal activity. Most studies have found no significant effect of Bt crop traits on soil community structures (Kowalchuk et al. 2003; Hannula et al. 2014; Zaman et al. 2015; Xie et al. 2016; Yasin et al. 2016).

Relative to crop production, the main factors affecting soil biota populations and diversity include soil type (texture, structure, organic matter, aggregate stability, pH, and nutrient content), plant type (providers of specific carbon and energy sources into the soil), and agricultural management practices (crop rotation, tillage, pesticide and fertilizer application, and irrigation (Kowalchuk et al. 2003; Garbeva et al. 2004; Gupta et al. 2007). Climate, particularly the water and heat content of soil, is a principal determinant of soil biological activity.

Pesticides

The continued use of pesticides is considered necessary to commercial crop production if global demands for food are to be met (FAO 2017). The capacity of the soil to filter, buffer, degrade, immobilize, and detoxify pesticides is a function of soil biota, particularly soil microbiota.

Some pesticides used on cotton crops can, relative to the application rates, mode of action (toxicity), and frequency of exposure of soil biota to a pesticide, potentially impact soil communities (Locke and Zablutowicz 2004). Changes in community structure are known to be the most significant effects of pesticides (FAO 2017). A recent assessment at the global level of the impact of plant protection products on soil functions and soil ecosystems concluded that most agricultural inputs can cause changes in the amount, activity, diversity, and community structures of soil organisms (FAO 2017).

In general, the effects of pesticides can lead to both significant decreases and significant increases in the attributes of soil organisms such as biomass, enzymatic activity, respiration, and species composition. The challenge lies in interpreting these changes relative to adaptive responses in soil organisms/communities versus harmful effects, such as decreased species diversity, impeded soil functions, and diminished soil productivity (FAO 2017). There is very limited evidence that the observed effects of pesticides on soil organisms have led to significant and long-lasting decreases in soil functions (FAO 2017). However, the inability to clearly link the observed effects of pesticides on organisms with soil functions is a major limitation of the current literature (FAO 2017).

There is more evidence for significant harmful effects of pesticides on earthworms. Specifically, the negative effects of copper-based fungicides are well-established, and recent evidence indicates that neonicotinoids are particularly toxic to earthworms (FAO 2017). Generally, earthworms are subject to pronounced, long-term effects when exposed to fungicides and insecticides, while herbicides have limited or no effects (FAO 2017).

While the application of a pesticides may lead to the local suppression of a taxonomic unit of soil organisms, the resilience of soil organisms, or ability to adapt, and functional redundancy across taxa, serve to limit the effects of pesticides on soil community dynamics (FAO 2017). Fundamentally, the vast majority of soil organisms have yet to be identified, and hence, a comprehensive assessment of the effects of pesticides on soil biota is not possible at this time (FAO 2017).

In terms of GE Bt crops, the potential ecological impacts considered are in regard to (1) the potential effects of GE trait genes and/or gene products on soil biota which could be transferred to soils via plant litter and detritus; or (2) via root exudates (Broeckling et al. 2008; Hu et al. 2018).

3.3.2 Animal Communities

3.3.2.1 Vertebrate Wildlife

Highly managed monocrops such as cotton provide limited food sources and habitat for wildlife, as compared to that found in natural areas. As such, the types and numbers of animal species found in and around cotton fields will be fewer and less diverse as compared to unmanaged lands. Cotton plants may, however, serve as a food source for some mammals, as well as birds.

Raw cottonseed contains gossypol and cyclopropanoid fatty acids (CPFAs), naturally occurring compounds that can be toxic to non-ruminant animals at high doses (Scarpelli 1974; Poore and Rogers 1998; Dowd et al. 2010). Gossypol occurs in the stems, leaves, seeds, and flower buds; it is distributed throughout the cotton plant but with greatest concentration in the seeds (Gadelha et al. 2014). CPFAs occur primarily in the seeds and roots (Fisher and Cherry 1983). Gossypol poisoning has been reported in a variety of animals, including broiler chicks, pigs, dogs, sheep, goats, and cattle (Gadelha et al. 2014). Monogastric animals, such as pigs, birds, and rodents, are more susceptible to gossypol toxicity than ruminants. General signs of acute toxicity are similar among animal species and include respiratory distress, impaired body weight gain, anorexia, weakness, apathy, and death after several days (Gadelha et al. 2014). CPFAs cause growth retardation and reduce fertility in hens (Shone 1966).

There is little information in the scientific and lay literature about wildlife feeding on cotton. Many wildlife species may avoid feeding on cotton plants because of the toxic effects of gossypol and CPFAs. However, wildlife feeding preferences for cotton has not been systemically studied. Birds may transit cotton fields seeking prey (e.g., raptors), although they are not expected to utilize fields for nesting because of frequent human activities associated with crop production and lack of suitable habitat. Many birds feed on insects that live on and among cotton plants. Orioles are known to prey on boll weevils directly on cotton plants, and crows, mockingbirds, and cardinals will eat insect larvae found on cotton plants (Beal et al. 1941). A study of Northern bobwhite quail found that the birds selected against cottonseed meal in favor of other game bird feed and scratch grains (Farthing et al. 2018).

Feral hogs damage cotton and some other row crops.¹³ They are destructive invasive animals in North America (Engeman et al. 2018). Although they tend to prefer other crops such as peanuts, damage to

¹³ The *Sus scrofa* populations in the United States are descendants of a common ancestor, the Eurasian wild boar. The term wild boar is typically used to describe Eurasian wild boar from Europe or Asia. Feral hogs are those that originated from domestic breeds but may be the result of a few or many, many generations in the wild. In the United

cotton can begin shortly after planting and may be extensive. Based upon observational evidence, when feral swine track through cotton fields to get to peanut fields, they do not cause much damage. However, severe damage requiring replanting following swine foraging usually results from rooting behavior when swine target grasses within the planted rows of cotton seed (Engeman et al. 2018). Focused feral swine control efforts by professionals may greatly reduce feral swine consumption of newly planted crops including cotton (Engeman et al. 2018).

While most mammals do not tend to utilize cotton plants directly for food presumably because of a lack of palatability, deer will eat cottonseed readily (e.g., (Taylor et al. 2013)). In North Carolina, 92% of cotton growers surveyed reported crop damage from white-tailed deer feeding (NCDA&CS 2010), suggesting that deer will forage on cotton plants. Cottonseed is often used by deer managers as a supplemental feed because it is cheaper than protein pellets, and raccoons will not consume it (DeYoung 2005; Taylor et al. 2013). Some studies have reported that feral swine will feed on cotton seed; others report that feral swine avoid cotton seed, when other food sources are present (Campbell et al. 2010).

3.3.2.2 Invertebrates: Non-Target Organisms

Arthropods (insects, arachnids [spiders, mites]) are the predominant invertebrates that feed on cotton plants or prey upon other insects living on cotton plants. More than 1,326 species of insects have been reported in commercial cotton fields worldwide (GTR 2002; Knutson and Ruberson 2005). While certain invertebrates are target pests of Bt cotton plants and/or synthetic insecticides, most are beneficial to cotton production, providing services such as predation and parasitism on plant pests (Table 3-12). Other beneficial invertebrate organisms, including earthworms, termites, ants, beetles, millipedes, and others contribute to the decay of organic matter and the recycling of soil nutrients (Stewart et al. 2007; Ruiz et al. 2008).

Species considered pests likewise feed on beneficial insects or other pest species. For example, Western flower thrips (*Frankiniella occidentalis*) usually feed on leaf tissue and on plant pollen, but may also attack eggs of predatory mites, their natural enemies, and eggs of the two-spotted spider mite (*Tetranychus urticae*) and greenhouse whitefly (*Trialeurodes vaporariorum*), two competitor species (van Maanen et al. 2012). *Lygus hesperus* and *Lygus lineolaris*, economically important plant bugs on many crops worldwide, are also facultative predators on a wide variety of Lepidoptera, Hemiptera, and beneficial species (Champlain and Sholdt 1967; Lindquist and Sorensen 1970; Hagler and Naranjo 1994; Pfannenstiel and Yeagan 2002; Hagler et al. 2010).

Most cotton is self-pollinating and does not require pollinators to set a crop. However, bees can increase yield via wild pollinator-mediated fruit set, significantly in some instances (Cusser et al. 2016). Major pollinators of *G. hirsutum* are bumble bees (*Bombus* spp.), black bees (*Melissodes* spp.), and honey bees (*Apis mellifera*) (Cusser and Jha 2016; Cusser et al. 2016).

States, the best descriptor is wild pigs. The Eurasians and domestics will interbreed successfully resulting in “hybrids.” None of these should be confused with the javelina, a native pig-like mammal found in the American southwest that is not closely related to wild boars/wild pigs/feral hogs. In this document the terms wild pig, wild boar, feral hog, feral swine, and free ranging swine are considered synonymous (Texas A&M University Extension Service, Coping with Feral Hogs, accessed December 30, 2019: <https://feralhogs.tamu.edu/frequently-asked-questions/frequently-asked-questions-wild-pigs/>)

Table 3-12. Examples of Beneficial Insects that Prey on Pest Species of Cotton Plants	
Pest Species	Natural Enemies (Beneficial Predator and Parasitoid Insects)
Thrips (Thysanoptera)	Minute pirate bug (N,A), Insidious flower bug (N,A)
Mirids (Pant bugs) <i>(Lygus hesperus, Lygus lineolaris)</i>	Big-eyed bug (N,A), Leafhopper assassin bug (N,A), Spined assassin bug (N,A), Jumping spiders (N,A), Lynx spiders (N,A), Celer crab spider (N,A), Minute pirate bug (N,A), Insidious flower bug (N,A), Damsel bugs (N,A), Spined soldier bug (N,A), Fire ants (N,A)
Cotton Aphid <i>(Aphis gossypii)</i>	Seven-spotted lady beetle (N,A), Harmonia or Asian lady beetle (N,A), Convergent lady beetle (N,A), Pink spotted lady beetle (N,A), Scymnus lady beetle (N,A), Green lacewings (N,A), Brown lacewings (N,A), Hover flies (N,A)
Boll Weevil <i>(Anthonomus grandis)</i>	Fire ants (L), Leafhopper assassin bug (A), Spined assassin bug (A), Jumping spiders (A)
Tobacco Budworm <i>(Heliothis virescens)</i>	Seven-spotted lady beetle (E,L), Harmonia lady beetle (E,L), Convergent lady beetle (E,L), Pink spotted lady beetle (E,L), Scymnus lady beetle (E), Green lacewings (E,L), Brown lacewings (E,L), Big-eyed bugs (E,L), Leafhopper assassin bug (L), Spined assassin bug (L), Jumping spiders (E,L), Lynx spiders (L), Celer crab spider (L), Minute pirate bug (E,L), Insidious flower bug (E,L), Damsel bugs (E,L), Spined soldier bug (E,L), Fire ants (E,L), Collops beetle (E,L), Earwigs (E,L), Ground beetles (E,L), Parasitic wasps (E), Other tachinid flies (L),
Cotton Bollworm, Corn Earworm <i>(Helicoverpa zea)</i>	Seven-spotted lady beetle (E,L), Harmonia lady beetle (E,L), Convergent lady beetle (E,L), Pink spotted lady beetle (E,L), Scymnus lady beetle (E), Green lacewings (E,L), Brown lacewings (E,L), Bigeyed bugs (E,L), Leafhopper assassin bug (L), Spined assassin bug (L), Jumping spiders (E,L), Lynx spiders (L), Celer crab spider (L), Minute pirate bug (E,L), Insidious flower bug (E,L), Damsel bugs (E,L), Spined soldier bug (E,L), Fire ants (E,L), Collops beetle (E,L), Earwigs (E,L), Ground beetles (E,L), Parasitic wasps (E), Other tachinid flies (L)
Pink Bollworm <i>(Pectinophora gossypiella)</i>	Parasitic wasps (E)
Beet Armyworm/ Fall Armyworm <i>(Spodoptera exigua, Spodoptera frugiperda)</i>	Seven-spotted lady beetle (E,L), Harmonia lady beetle (E,L), Convergent lady beetle (E,L), Pink spotted lady beetle (E,L), Scymnus lady beetle (E), Green lacewings (E,L), Brown lacewings (E,L), Big-eyed bugs (E,L), Leafhopper assassin bug (L), Spined assassin bug (L), Jumping spiders (L), Lynx spiders (L), Celer crab spider (L), Minute pirate bug (E,L), Insidious flower bug (E,L), Damsel bugs (E,L), Spined soldier bug (L), Fire ants (E,L), Collops beetle (E), Earwigs (E), Ground beetles (E,L), Other tachinid flies (L)
Soybean Looper/ Cabbage Looper (Copidosoma is specific to soybean looper)	Seven-spotted lady beetle (E,L), Harmonia lady beetle (E,L), Convergent lady beetle (E,L), Pink spotted lady beetle (E,L), Scymnus lady beetle (E), Green lacewings (E,L), Brown lacewings (E,L), Big-eyed bugs (E,L), Leafhopper assassin bug (L), Spined assassin bug (L), Jumping spiders (L), Lynx spiders (L), Celer crab spider (L), Minute pirate bug (E,L), Insidious flower bug (E,L), Damsel bugs (E,L), Spined soldier bug (L), Fire ants (E,L), Collops beetle (E), Earwigs (E), Ground beetles (E,L), Parasitic wasps (E)
Pentatomids (e.g., stink bugs) <i>(Halyomorpha halys)</i>	Parasitic wasps (E)
Spider Mites <i>(Tetranychus urticae)</i>	Six-spotted thrips (E), Western predatory mite (E,N,A), Stethorus (E,N,A), Minute pirate bug (E,N,A), Insidious flower bug (E,N,A),

Table 3-12. Examples of Beneficial Insects that Prey on Pest Species of Cotton Plants	
Pest Species	Natural Enemies (Beneficial Predator and Parasitoid Insects)
	Green lacewings (E,N,A)
Whiteflies (<i>Bemisia argentifolii</i>)	Minute pirate bug (N,A), Green lacewings (N,A), Collops beetles (N,A), Big-eyed bugs (N,A), Whitefly parasites (N), Convergent lady beetles (N,A)

Source: (Knutson and Ruberson 2005; USDA-NRCS 2014)

Notes: Parenthetical letters designate life stages of the pest attacked by the natural enemy: (E) = eggs, (N) = nymphs, (L) = larvae, (A) = adults

3.3.2.3 Aquatic Species

Aquatic ecosystems potentially impacted by cotton production include freshwater and marine systems adjacent to, nearby, or downstream of cotton fields. These include ponds, lakes, streams, and rivers, and marine environments such as the Gulf of Mexico. Aquatic species may be exposed to sediments, nutrients, and pesticides from agricultural runoff or particulate deposits. These species would include freshwater and estuarine/marine fish and invertebrates, amphibians, as well as marine mammals.

3.3.3 Plant Communities

Plant diversity in surrounding field areas is an important component of a sustainable agricultural system (Scherr and McNeely 2008; CBD 2019b). Hedgerows, woodlands, fields, and other surrounding habitat serve as important reservoirs for beneficial insects, as well as plant pests. Cotton fields and field edges are also habitat for weeds that adversely impact crop production directly through interference and resource competition (discussed below), and can also harbor both beneficial or damaging insects and plant microbes. Most weeds, however, provide valuable ecosystem services. By providing habitat, pollen and nectar resources, and serving as hosts, plants adjacent to cotton fields can support a suite of beneficial arthropod species that serve as pollinators of insect-pollinated crops, and biological control agents, insects that prey on cotton plant pests (as in Table 3-11 above), such as lady beetles, spiders, and parasitic wasps (Scherr and McNeely 2008; Nichols and Altieri 2012). However, for cotton production, pollinators would not be as valued from an agronomic perspective, as cotton is primarily self-pollinating. Surrounding plant communities can also help regulate run-off, reduce soil erosion, and improve water quality. Hence, effective management of surrounding plant communities can provide benefits to cotton crop production via control of some insect pests and agricultural run-off (Altieri and Letourneau 1982), and provide pollinator services to other plants that benefit from insect pollination (Nichols and Altieri 2012).

Members of the plant communities in and around cotton fields that adversely affect cotton cultivation are generally characterized as weeds, and weed control programs are fundamental components of crop production in maximizing crop yield and quality. Following planting, cotton requires 8 weeks of weed-free growth to make maximum yields. Good yields require greater than 95% weed control, excellent yields require 99% or better control (CI 2020). Such, near perfect control is needed to avert difficulties with picking, excess trash in the harvested lint, and a recurring cycle of heavy weed seed fall, followed by emergence of high populations of weeds the next spring (CI 2020). Controlling weeds of cotton, especially those that are herbicide resistant, in field edges that produce prolific numbers of seeds before

plants flower or before seeds mature is an important management practice to prevent weed seed dispersal into the production field ((Norsworthy et al. 2012; UGA 2018).

Most relevant to environmental review and GE crops are sexually compatible plant communities with which the GE crop plant interbreed, discussed following.

3.3.4 Gene Flow and Weediness of Cotton

Weediness of Cotton

Upland cotton (*G. hirsutum*) is a domesticated perennial plant cultivated as an annual in the United States, grown from Virginia southward and westward to California. Cotton is self-pollinating, as well as pollinated by insects. Insect pollination is primarily carried out by bumble bees, Melissodes bees, and honey bees, while flies, butterflies, and beetles can also contribute to pollination (Cusser et al. 2016; Muhammad et al. 2020). Cotton pollen is not readily dispersed by the wind because it is sticky and heavy.

Gossypium hirsutum, upland cotton, can be weedy according to the USDA-NRCS Introduced, Invasive, and Noxious Plants list (USDA-NRCS 2019a). The USDA PLANTS database lists it as a U.S. weed with a single reference to a Southern Weed Science Society (SWSS) CDROM titled "Weeds of the United States and Canada" (USDA-NRCS 2019a). From APHIS' prior communication with the SWSS business manager, cotton as listed on that CD is not considered a weed in the true sense, only that they can occur as volunteers or feral plants (USDA-APHIS 2015). The World Weeds database has no *Gossypium* species listed as invasive weeds (ISSG 2019).

Modern upland cultivars are high-yielding, day-length neutral, early-cropping plants ("annuals") with easily ginned and abundant fiber (Brubaker and Wendel 1994). These "improved" characteristics resulted from human selection from perennial ancestors. This domestication process is widely believed to have been accompanied by an extreme reduction in genetic diversity, relative to the less "improved" forms. It is unclear whether any truly wild *G. hirsutum* populations exist, although naturally occurring wild or feral forms are found in beach strand and other littoral environments in many parts of the species' range (Brubaker and Wendel 1994). Many of these wild populations exhibit one or more features suggestive of human selection (e.g., in lint characteristics), implying that they represent feral, self-seeding escapes from some earlier period in domestication (Brubaker and Wendel 1994).

While perennial forms *G. hirsutum* are widely distributed, albeit in isolated areas, throughout Mesoamerica and the Caribbean (Coppens d'Eeckenbrugge and Lacape 2014), the probability of *G. hirsutum* occurring as wild or feral is considered negligible in all regions of the continental United States above South Florida (USDA-APHIS 2015). In general, modern varieties of upland cotton are domesticated plants that do not typically persist in areas outside of cultivation. Upland cotton does not exhibit characteristics that are found in weeds, such as the production of highly persistent seeds or other propagules that can remain for long periods in the soil, or an ability to disperse over long distances, spread widely and invade habitats, or become a dominant highly competitive species in areas outside of cultivation. Commercial cultivars do not survive freezing conditions, which limits their potential range and ability to overwinter.

In the United States, in areas below 29° N latitude, such as southern Florida, Hawaii, and Puerto Rico, upland cotton can persist become locally feral, i.e., naturalize (Wozniak and Martinez 2011; Coppens

d'Eeckenbrugge and Lacape 2014). In the very south of Florida, feral *G. hirsutum* have been reported to exist in apparently self-sustaining populations (USDA-APHIS 2015; Wunderlin et al. 2019). There is documentation of feral *G. hirsutum* in Hawaii (USDA-APHIS 2015; USDA-NRCS 2019a). Cotton is no longer widely grown as an agricultural commodity in Hawaii, but *G. hirsutum* survives as feral escapes from earlier periods of commercial cultivation. There are native indigenous and feral populations of *G. hirsutum* in Puerto Rico and the U.S. Virgin Islands. The naturalized *G. hirsutum* growing in Puerto Rico appears to derive from primitive cultivars that naturalized centuries ago, at least some of which appear to have undergone substantial hybridization with *G. barbadense* (USDA-APHIS 2015).

G. hirsutum is cultivated as an annual in the United States, and the biology of the plant does not support it persisting in the environment as a perennial in colder temperatures found above 29 ° N latitude. In these areas in the United States the risk of *G. hirsutum* being weedy is negligible as the plant is highly domesticated, and grown in the U.S for over 200 years without feral or self-sustaining populations recorded as escapes from that cultivation (USDA-APHIS 2015).

Gene Flow

There are four wild/feral species of cotton that occur in the United States and its territories; *G. hirsutum*, *G. barbadense*, *G. tomentosum*, and *G. thurberi*. Upland cotton, *G. hirsutum* L., is known to have sexually compatible wild relative species in the form of indigenous and feral populations of *G. hirsutum* and *G. barbadense* L. (Pima cotton) in the Florida Keys, Puerto Rico, Hawaii, and the U.S. Virgin Islands (Wozniak and Martinez 2011; Coppens d'Eeckenbrugge and Lacape 2014). *G. barbadense* survives as feral escapes from earlier periods of commercial cultivation in Hawaii. *G. barbadense* is still grown commercially in Arizona, California, New Mexico, and Texas. In many instances indigenous populations of *G. hirsutum* and *G. barbadense* L exist as hybrid swarms and are difficult to distinguish phenotypically and genetically. Both species are allotetraploid ($4x = 52$) and capable of interbreeding with each other and feral escapes (Brubaker and Wendel 1994; Wozniak and Martinez 2011). Thus, unassisted outcrossing and gene introgression could potentially occur in areas where these species are co-located.

G. tomentosum (Hawaiian cotton) is endemic to the Hawaiian archipelago; present on all of the main Hawaiian Islands except Hawaii and Kauai. Upland (*G. hirsutum*) and Hawaiian (*G. tomentosum*) cotton are both tetraploids that can crossbreed – interspecific hybrids are easily formed and are fully fertile. However, extensive genetic breakdown occurs in second generation hybrids (F₂) giving rise to unbalanced types of low viability. While hybrids of *G. tomentosum* and *G. hirsutum* are easily formed and fertile, no evidence of natural introgression in Hawaii between the two species has been presented. No information was found to indicate that hybrids of *G. tomentosum* and *G. hirsutum* are considered weedy or invasive (US-EPA 2001; Coppens d'Eeckenbrugge and Lacape 2014; USDA-APHIS 2015).

G. thurberi (Arizona cotton) occurs in the mountains of southern Arizona and northern Mexico. While this cotton species is known to exist in the United States, it is not being considered as a sexually compatible relative since any gene exchange between plants of *G. hirsutum* and *G. thurberi*, if it did occur, would result in sterile triploid ($3x=39$ chromosomes) plants because *G. hirsutum* is an allotetraploid ($4x = 52$ chromosomes), and *G. thurberi* is a diploid ($2x = 26$ chromosomes) (Wozniak and Martinez 2011; USDA-APHIS 2015). While sterile hybrids have been produced under controlled conditions; it would be highly unlikely such hybrids would reproduce and form a persistent population in

the wild. Attempts to deliberately cross *G. hirsutum* with *G. thurberi* as the female parent have been unsuccessful ((Brubaker and Wendel 1994; USDA-APHIS 2015).

Outcrossing rates reported for upland cotton can vary depending on location but are relatively low, even at short distances from neighboring fields in commercial settings (Van Deynze et al. 2011). Generally, gene flow is less than 1% at distances beyond 10 m but can be detected at very low levels (<0.05%) at distances up to 1625 m (1 mile) (Llewellyn et al. 2007; Van Deynze et al. 2011). In general, buffers of 20 m of conventional cotton surrounding GE fields, if needed, prove to be highly effective in isolating GE cotton crops, unless bee or other pollinator numbers are unusually high (Llewellyn et al. 2007).

Volunteer Cotton

In some crop rotation systems, cotton can volunteer in a subsequent crop cycle, which can be problematic for growers (Fromme et al. 2011). These volunteer cotton plants are unwanted and considered weeds, as they compete for essential nutrients, water, and light with the crop and can cause harvest problems. The primary methods for removing volunteer cotton are tillage and/or herbicides. Where herbicides may be more economical than tillage, special attention must be paid to the herbicide selection, application equipment, timing, and the HR traits in the volunteer cotton (Morgan et al. 2011b). Management of volunteers is also important for boll weevil (*Anthonomus grandis* L.) eradication efforts, namely in areas of Texas that have a Boll Weevil Eradication Program, as volunteer cotton plants can serve as a host for boll weevil (Morgan et al. 2011a; Morgan et al. 2011b). In quarantined zones of the Texas Boll Weevil Eradication Program, there is a zero tolerance for volunteer cotton plants (6-8 leaf plants or larger) in non-cotton fields (Morgan et al. 2011b). 2,4-D, and to a lesser extent dicamba herbicides have long been used to control volunteer cotton and for destruction of overwintered cotton stalks, but with the launch of cotton varieties with resistance to these herbicides (also stacked with glufosinate and glyphosate resistance) other management options have been developed to control regrowth and are highly dependent on environmental conditions and amount of regrowth (Bowen 2018; Corteva 2019).

3.3.5 Biodiversity

Biological diversity in the context of agriculture encompasses the variety of species that are capable of existing in a given agricultural setting. Various taxa contribute to essential ecological functions upon which agriculture depends, such as pollinators, soil biota, and predators of crop pests (CBD 2019b). Plant diversity in particular has been shown to create a wider array of foraging niches for different functional groups of pollinators. Cusser et al. (2016) found that crop yields in South Texas cotton agroecosystems can be increased through the management of natural areas supporting pollinator abundance and richness. For example, this study concluded that if all farmers engaged in management practices to increase their pollination service, cotton growers could potentially gain as much as an 18% increase in cotton seed weight. Cusser et al. (2016) concluded the increased production could be worth a regional gain of over \$1.1 million USD (Cusser et al. 2016).

Modern conservation practices incorporated in cotton cultivation have brought a positive impact to animal and plant communities through reduced tillage, more carefully controlled and targeted chemical placement (fertilizers and pesticides), and better control of irrigation systems (Ward et al. 2002). Conservation tillage practices that leave greater amounts of crop residue serve to increase the diversity and density of local bird and mammal populations (Sharpe 2010). Increased residue also provides habitat for insects and other arthropods, increasing prey species for insect predators. The increased use of

conservation tillage practices can benefit birds, mammals, and other wildlife through sustaining water quality, the availability of waste grain, retention of cover in fields, and increased populations of invertebrates (Sharpe 2010; Towery and Werblow 2010) .

Relative to GE crops, specifically, by facilitating conservation tillage (HR crops), decreasing insecticide use (IR crops), use of more environmentally benign herbicides, and increasing yield—which alleviates pressure to convert additional land into agricultural use—some GE crops can contribute to reducing the impacts of agriculture on biodiversity (Storer et al. 2008; Carpenter 2011). A U.S. National Research Council assessment of the relationship between GE crop adoption and farm sustainability in the United States (NRC 2010), and review of GE IR crops by Storer et al. (2008) concluded that, generally, GE IR crops have had fewer adverse effects on the environment than non-GE crops produced conventionally. Pesticide risks of adversely impacting non-target organisms is managed through those aspects of the EPA pesticide registration process for developing labeling requirements to reduce drift, volatilization, and other types of off-site movement.

While biodiversity will be inherently limited in commercial cotton crops due to frequent disturbance, tillage, mechanized planting, planting of a monoculture crop, and application of fertilizers and pesticides, growers, as well as federal and state programs, well recognize the need for maintenance of some degree of cropland biodiversity. A variety of federally supported programs, such as the USDA funded Sustainable Agriculture Research and Education Program (SARE), and partnership programs between EPA and the agricultural community support sustainable agricultural practices that are intended to protect the environment, conserve natural resources, and promote cropland biodiversity (i.e.,(USDA-NIFA 2017; US-EPA 2019f). The USDA Natural Resources Conservation Service, through its Conservation Stewardship Program, Landscape Initiatives, Environmental Quality Incentives Program, Landscape Planning, and other services provides technical and financial support to growers to assist in managing the complex interaction of cropping systems and the natural environment (USDA-NRCS 2019b). In 2018, the USDA-NRCS allocated \$137 million for biodiversity improvements in partnership with farmers in states that grow cotton (CL 2019). Tools are also developed by the industry. For example, *Field to Market: The Alliance for Sustainable Agriculture* has developed an agricultural sustainability program that helps farmers and the food supply chain benchmark sustainability performance, and promote biodiversity (Field-to-Market 2019).

3.4 Human Health and Worker Safety

Human health considerations associated with GE crops are those related to (1) the safety and nutritional value of GE crops and their products for consumers (e.g., cottonseed oil), and (2) the potential health effects of pesticides that may be used in association with GE crops. As for food safety, consumer health concerns center on the potential toxicity or allergenicity of the introduced genes/proteins, the potential for altered levels of existing allergens in plants, or the expression of new antigenic proteins. Some consumers may be concerned about the potential consumption of pesticides on/in foods derived from GE crops. Occupational exposure to pesticides is also considered.

The safety assessment of GE crop plants, summarized following, includes characterization of the physicochemical and functional properties of the introduced gene(s) and gene products, determination of the safety of the gene products (e.g., proteins, enzymes), and evaluation of the potential health effects of

food derived from the GE crop plant. The safety of the Cry protein (mCry51Aa2) introduced into MON 88702 cotton is reviewed below.

3.4.1 Food Safety

Relative to human consumption, cottonseed oil is mainly used in processed foods such as margarine and salad dressings, and for canning. Because raw cottonseed oil contains gossypol and cyclopropenoid fatty acids (CPFAs), naturally occurring compounds that can be toxic to humans and non-ruminant animals at high doses (Scarpelli 1974; Poore and Rogers 1998; Dowd et al. 2010), only highly refined cottonseed oil is used for food purposes. The refining process substantially reduces the levels of gossypol and CPFAs, as well as other undesired compounds (AOCS 1990).

As summarized in Section 1.3—Coordinated Framework for the Regulation of Biotechnology, FDA regulates the safety of plant-derived foods pursuant to the FFDCa and FSMA.¹⁴ The FDA created a voluntary plant biotechnology consultation process in the 1990's to work cooperatively with GE plant developers to ensure food made from GE plant varieties are safe (US-FDA 1992, 2006). In such a consultation, a developer who intends to commercialize food or feed derived from a GE plant meets with FDA to identify and discuss relevant safety, nutritional, or other regulatory issues regarding the food product(s). The FDA evaluates the food safety data presented by developers and responds to the developer by letter with any concerns it may have or additional information it may require.

Monsanto concluded its consultation with FDA on MON 88702 cotton (BNF 000160) in September 2018. The FDA agreed with Monsanto's conclusion that MON 88702 cotton does not raise any safety or regulatory issues with respect to its uses in human or animal food (US-FDA 2019).

In addition to FDA consultation, foods derived from GE plants undergo a safety evaluation among international agencies before entering foreign markets, such as reviews by the European Food Safety Agency and the Australia and New Zealand Food Standards Agency. The Codex Alimentarius, established by the World Health Organization and Food and Agriculture Organization of the United Nations, is a set of international standards, principles, and guidelines for the safety assessment of foods derived from modern biotechnology. These standards help countries coordinate and harmonize review and regulation of foods derived from GE plants to ensure public safety and facilitate international trade (FAO/WHO 2019). Currently, the Codex Alimentarius Commission is comprised of 188 member countries, to include the United States. Most governments incorporate Codex principles and guidelines in their review of foods derived from GE crop plants.

Food safety reviews for GE crop plants commonly compare the compositional characteristics of the GE crop plant with non-transgenic, conventional varieties of that crop. Compositional analyses include characteristics such as moisture, protein, fat, carbohydrates, ash, minerals, dietary fiber, essential and non-essential amino acids, fatty acids, vitamins, and antinutrients (NAS 2016). The food and feed safety reviews of GE crops introduced into the market to date have generally concluded that there are no significant nutritional differences in conventional versus GE plants for food or animal feed, beyond those intended (NAS 2016; Delaney et al. 2017).

¹⁴ Under the Federal Food, Drug, and Cosmetic Act, food is defined as “food or drink for man or other animals.”

3.4.2 Pesticides Used in Cotton Production

As indicated in Section 1.3, EPA is responsible for regulating the sale, distribution, and use of pesticides, including pesticides that are produced by GE organisms (e.g., pesticides produced *in planta*), termed plant incorporated protectants (PIPs) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136 *et seq.*). Before a pesticide may legally be used in the United States, EPA must evaluate the pesticide to ensure that it will not result in an unreasonable risk to human health or the environment. Pesticides that complete this evaluation are issued a "registration" that permits their sale and use according to requirements set by U.S. EPA.

Before a pesticide can be used on a food crop, under the authorizations of the FFDCA and the Food Quality Protection Act of 1996 (FQPA), EPA establishes a tolerance limit, which is the amount of pesticide residue allowed to remain in or on each treated food commodity (21 U.S. Code § 346a–Tolerances and exemptions for pesticide chemical residues). Pesticide tolerance limits established by EPA are to ensure the safety of foods and feed for human and animal consumption (US-EPA 2019c). If pesticide residues are found above the tolerance limit, the commodity will be subject to seizure by the government.

Section 408(c)(2)(A)(i) of the FFDCA allows EPA to establish an exemption from the requirement for a tolerance if EPA determines that the exemption is “safe.” Safe is defined as meaning that there is a "reasonable certainty that no harm will result from aggregate exposure to the pesticide residue." To make a safety finding, EPA considers, among other things: the toxicity of the pesticide and its break-down products, aggregate exposure to the pesticide in foods and from other sources of exposure, and any special risks posed to infants and children. Some pesticides are exempted from the requirement to have a tolerance. The EPA may grant exemptions in cases where the pesticide residues do not pose a dietary risk under reasonably foreseeable circumstances.

A permanent exemption from the requirement for a tolerance for the Cry protein introduced into MON 88702 cotton (mCry51Aa2) was issued by EPA in January, 2018 (US-EPA 2018e).

The EPA conducts periodic pesticide reregistration reviews for each pesticide every 15 years, as required by FIFRA, to ensure that each continues to meet the statutory standard of no unreasonable adverse effects. Other applicable EPA regulations include 40 CFR part 152 - Pesticide Registration and Classification Procedures, part 174 - Procedures and Requirements for Plant Incorporated Protectants (PIPs) and part 172 - Experimental Use Permits.

Both FDA and USDA monitor foods for pesticide residues to enforce these tolerance limits, and ensure protection of human health. For example, the USDA Pesticide Data Program (PDP) collects data on pesticides residues on agricultural commodities in the U.S. food supply, with an emphasis on those commodities highly consumed by infants and children (USDA-AMS 2019). The Monitoring Programs Division administers PDP activities, including the sampling, testing, and reporting of pesticide residues on agricultural commodities in the U.S. food supply, with an emphasis on those commodities highly consumed by infants and children. The program is implemented through cooperation with state agriculture departments and other federal agencies. PDP data enable EPA to assess dietary exposure; facilitate the global marketing of U.S. agricultural products; and provide guidance for FDA and other governmental agencies to make informed decisions.

The EPA also sets limits for potential drinking water contaminants that need to be regulated in order to protect public health (40 CFR part 141). These contaminant limits are required by the Safe Drinking Water Act (SDWA). The EPA works with States, Tribes, and many other partners to implement SDWA standards.

3.4.3 Worker Safety

Agriculture is considered one of the most hazardous industries in the United States. Worker hazards include those associated with the operation of farm machinery, vehicles, and pesticide application. Agricultural operations are covered by several Occupational Safety and Health standards including Agriculture (29 CFR 1928), General Industry (29 CFR 1910), and the General Duty Clause. Further protections are provided through the National Institute of Occupational Safety and Health (NIOSH), which in 1990 began development of an extensive agricultural safety and health program to address the high risks of injuries and illnesses experienced by workers and families in agriculture.

In consideration of the risk of pesticide exposure to field workers, EPA's Worker Protection Standard (WPS) (40 CFR Parts 156 & 170) was issued in 1992 to require actions to reduce the risk of pesticide poisonings and injuries among agricultural workers, and pesticide handlers. The WPS contains requirements for pesticide safety training, notification of pesticide applications, use of personal protective equipment, restricted entry intervals following pesticide application, decontamination supplies, and emergency medical assistance. The Occupational Safety and Health Administration (OSHA) also requires employers to protect their employees from hazards associated with pesticides and herbicides.

On November 2, 2015, EPA revised the WPS to implement more protections for agricultural workers, handlers, and their families (80 FR 211, November 2, 2015, p. 67495). The WPS revisions are intended to decrease pesticide exposure incidents among farmworkers and their family members. Fewer incidents means a healthier workforce and avoiding lost wages, medical bills, and absences from work and school. Most of the revised WPS requirements became effective on January 2, 2017 (US-EPA 2016b). Farmworkers are required to use pesticides consistent with instructions provided on the EPA-approved pesticide labels, which may include instruction on personal protective equipment, specific handling requirements, pesticide equipment application specifications, and field reentry requirements.

3.5 Animal Feed

The presence of gossypol and cyclopropenoid fatty acids in cottonseed limits its use as animal feed. Whole cottonseed is used as a protein source for beef cattle, although its use is apportioned due to high fat content and the potential for gossypol toxicity. As indicated in Section 3.4.1, removal or inactivation of gossypol and cyclopropenoid fatty acids during seed processing enables the use of cottonseed meal for aquaculture, poultry, and swine feed, as well as for cattle. The hulls of cottonseed can also be used for cattle feed, serving primarily as a roughage source.

In addition to foods for human consumption, FDA regulates animal feed safety under the FFDCa and FSMA. It is the responsibility of feed manufacturers to ensure that their products are safe for animal consumption.

As discussed for public health, Monsanto concluded its consultation with FDA on MON 88702 cotton (BNF 000160) in September 2018. The FDA agreed with the conclusion that MON 88702 cotton does not raise any safety or regulatory issues with respect to its uses in animal food (US-FDA 2019).

3.6 Socioeconomics

3.6.1 Domestic Economic Environment

U.S. Cotton Commodities

Cotton yields five products of commercial value: fiber, linters (fine, silky fibers that cling to the seed after ginning), hulls, cottonseed oil, and meal. Among these, cotton fiber is one of the most valuable textile fibers in the world. In the United States, fiber typically accounts for approximately 85% of the value of harvested cotton. After fiber, oil is the most valuable product, followed by meal, which itself is worth more than the combined value of hulls and linters. Linters serve as a source of cellulose and are used to produce a variety of products such as plastics, rocket propellants, rayon, cosmetics, photography and X-ray film, and paper products (NCPA 2018).

Domestic and global vegetable oil markets and markets for livestock feed ingredients all play major roles in determining the value of cottonseed. For every 100 pounds of fiber produced by cotton plants, there is around 162 pounds of seed. Annual cottonseed production typically comes to about 6.5 billion tons, of which about two-thirds is fed whole to livestock. The remaining seed is crushed, producing the oil and high protein meal used for livestock, dairy, and poultry feed. The oil is further processed to produce food grade cooking oil, which is used in salad dressings, shortenings, margarine, and some canned fish products. Limited quantities of the oil are used in soaps, pharmaceuticals, cosmetics, textile finishes, and other products (NCCA 2017).

The United States is the world’s third-largest cotton producer, after China and India, and the leading cotton exporter, accounting for one-third of global trade in raw cotton fiber (USDA-ERS 2019c). During the past decade annual cotton production in the United States has varied from approximately 12 to 20 million bales (480 pounds/bale), and net value has ranged from around \$3.0 billion to \$7 billion, annually. The direct value of cotton crop products was 6.7 billion in 2017 (Table 3-10). The average U.S. crop moving from the field through cotton gins, warehouses, oilseed mills, and textile mills to the consumer accounts for more than \$35 billion annually in products and services, collectively (NCCA 2017). Thus, the cotton industry is a vital part of economies in the 17 major cotton producing states (NCCA 2017).

Table 3-13. Market Value of Cotton Products Sold Including Landlord's Share, Food Marketing Practices, and Value-Added Products: 2017, 2012		
	2017	2012
Farms	16,149	18,155
Acres	11,401,965	9,384,080
Bales	20,413,180	16,534,302
Value (\$1000)	6,685,609	1,491,208

Source: (USDA-NASS 2019c)

GE IR Crops

In all cotton production regions in the United States, insect and mite pests are a common and continuous problem that can increase the cost of production. In 2018, yield losses to insects amounted to costs totaling \$567,047,283; around \$42.45/acre (Williams 2019). The highest yield losses were associated with a bollworm/budworm complex (1.16%), lygus bugs (0.66%), stink bugs (0.27% + 0.37%), spider mites (0.27%), thrips (0.24%), and cotton fleahoppers (0.21%) (Williams 2019).

GE IR cotton has proven effective in control of insect pests. The average yield gains for GE IR cotton from 1996–2016 has been reported to be 9.9% in the United States. The average farm income benefit from GE IR cotton (after deduction of cost of technology) is reported to be around \$111/hectare (\$45/acre) (Brookes and Barfoot 2018). In 2016, at the aggregate level, the global gross farm income gains from using GE IR cotton was estimated to be \$3.7 billion. Cumulatively, since 1996, the global gains are estimated to be \$54 billion for GE IR cotton (Brookes and Barfoot 2018).

Another economic benefit derived from GE IR cotton varieties is the potential for area wide suppression of insect pest populations. In areas where cultivation of Bt corn and Bt cotton is high, there has been observed an associated reduction in insecticide use in adjacent cropping systems cultivating non-Bt varieties, a result of the area-wide suppression of insect pest populations (Carrière et al. 2003; Wu et al. 2008; Hutchison et al. 2010; NAS 2016; Dively et al. 2018). For example, in U.S. cotton, the average number of insecticide applications used against the budworm-bollworm complex decreased from 4.6 in 1992–1995 to 0.8 in 1999–2001, largely owing to the introduction of Bt cotton (FAO 2004). A 25-year study in China found Bt cotton led to major reduction in pesticide use, and improvement in aphid biological control (Zhang et al. 2018). Treatment for bollworm in China declined from an average of 9.3 sprays during 1991–1996 to less than 3 sprays per year after 2006 (Zhang et al. 2018). In general, current peer review literature and other reports indicate that cultivation of Bt crops can potentially provide tangential benefits to adjacent farms by tempering the prevalence of certain insect pest populations, reducing the need for insecticide use, and associated costs, in nearby cropping systems. However, it is also noted that in some instances where area-wide suppression has occurred, relative to the particular Cry/Vip toxin, emergence of secondary pests and need for insecticide use for their control can negate the gains of area-wide pest suppression.

Organic Cotton Production

While organic cotton production in the United States (in terms of bales produced) has steadily increased from 2011 through 2018, there remain a small number of farms, relative to conventional cotton production (USDA-AMS 2018). This is likely due in part to the fact that growing organic cotton in the United States is a highly specialized and problematic endeavor. A few isolated regions of the United States have conditions that make it possible: well-drained soil, a long growing season, moderate rainfall, and a late freeze that minimizes pests and defoliates the plants for harvest (OTA 2014). While demand for organic seeds is strong, limited availability of non-GE seed for organic upland and pima cotton continues to be an issue for organic farmers (USDA-AMS 2018).

A primary factor limiting yields in organic cotton is effective weed control. In wet regions or years, early season weeds can choke out an emerging cotton crop. Later in the season, weeds can adversely impact yields and quality. Mechanical weeding is standard practice for organic farmers. Surveyed cotton growers—particularly those new to farming organic cotton—have expressed concerns that the lack of

available labor is a hindrance to expanding their production (OTA 2014; McNeil). Commercial availability of organic seed has also been a problem for organic cotton producers. Among major seed companies, non-GE and non-treated cottonseed offerings are limited, and there has not been significant effort dedicated to improving cottonseed by traditional breeding techniques (OTA 2014). Most surveyed cotton farmers report using at least a portion of their own saved cottonseed from year to year. In 2018, the price premium for organic cottonseed prices range from \$400 to \$525 per ton, compared to \$155 to \$225 per ton for conventional cotton (USDA-AMS 2018).

While production of organic cotton is limited, comprising around 14,000 acres across 36 farms, the value of certified organically grown cotton commodities was \$8.24 million (Table 3-11). The Texas Organic Cotton Marketing Cooperative, based in the West Texas High Plains, grew 85% of the organic cotton in the United States in 2016. Organic cotton— mostly Pima—is also grown in New Mexico and minor amounts in California and North Carolina (OTA 2015). Since 2000, small and sporadic acreages of organic cotton have been cultivated in Missouri, Illinois, Kansas, Tennessee, and Colorado (USDA-ERS 2019b).

Table 3-14. Certified Organic Cotton Crops Harvested and Value of Sales	
	2016
Farms	36
Acres	14,599
Bales	19,244
Value (\$)	8,236,217

Source: (USDA-NASS 2017c)

3.6.2 International Trade

Cotton is a global commodity with robust trading in raw and finished products. Much of the world’s cotton crosses international borders before finally arriving at its end-use destination, and factors that affect the trade and marketing of cotton have far-reaching impacts.

The United States is the leader in global cotton exports, making up approximately 38% of the world’s export market for raw cotton fiber. Annual values of U.S. cotton sold overseas have averaged more than \$2 billion. U.S. cotton exports vary year-to-year due to various factors such as pricing and yields across countries, although currently ranges from around 10 to 15 million bales/yr (USDA-FAS 2018).¹⁵ U.S. cotton demand (mill use plus exports) in 2020/21 is forecast at 18.9 million bales, the highest in three years (Meyer 2020). Exports are expected to increase to 16.0 million bales, 1 million above the previous year. In 2020/21, U.S. cotton exports are forecast to account for nearly 85% of U.S. cotton demand (Meyer 2020).

Organic cotton production in the United States currently represents approximately 0.4% of global organic cotton production. Around 19 countries produce organic cotton, although the top six countries (India (47%), China (21%), Kyrgyzstan (12%), Turkey (6%), Tajikistan (5%), the United States (3%)) account for more than 94% of production (OTA 2018). Global production of organic cotton saw impressive

¹⁵ 1 bale of cotton = 480 lbs

growth between 2016/17 and 2017/18, increasing 56% to 180,971 metric tons (831,193 bales) (OTA 2018). Organic cotton was planted on 356,131 hectares (880,018 acres), with total volumes reaching the highest level since 2010/11. Organic cotton now makes up 0.7% of global cotton production (OTA 2018).

4 ENVIRONMENTAL CONSEQUENCES

This chapter provides an evaluation of the potential environmental impacts that could derive from the alternatives considered in this EA; denying the petition, or issuing a determination of nonregulated status for MON 88702 cotton. Pursuant to CEQ regulations APHIS considers the direct, indirect, and cumulative impacts of both alternatives. Potential direct and indirect impacts are discussed in this Chapter, and potential cumulative impacts in Chapter 5.

4.1 Scope of Analysis

An impact would be any change, beneficial or adverse, from existing (baseline) conditions described for the affected environment in Chapter 3. A direct impact is one that derives immediately from APHIS' decision on the petition, without intermediate steps or processes. An example of a direct impact would be, on approval of the petition, the availability of MON 88702 cotton to commercial markets, subject to any EPA requirements, FDA consultation, and/or state requirements. Indirect impacts are those related to, but removed from the Agency's decision in space and time. Examples would include emissions of air pollutants from farm equipment used in MON 88702 cotton production, and potential impacts on water quality resulting from runoff comprised of soil sediment, pesticides, and fertilizers used in MON 88702 cotton production.

Where possible, APHIS used data that supported a quantitative analysis of the impacts of selecting either the No Action Alternative or the Preferred Alternative. When data were not available or were insufficient to support a quantitative assessment, APHIS provides qualitative assessments of the impacts of an Agency regulatory decision for MON 88702 cotton. APHIS focused its environmental analyses to the geographic areas that currently support U.S. cotton production.

4.1.1 Assumptions and Uncertainties used in Analysis

It is APHIS' understanding that MON 88702 cotton will be used for seed production and breeding of stacked-trait IT cotton varieties. MON 88702 cotton was registered with EPA for limited seed increase/breeding in 2018 (US-EPA 2018b). Monsanto registered MON 88702 (mCry51Aa2) x MON 15985 (Cry1Ac and Cry2Ab) x COT 102 (Vip3Aa19) in 2020 (US-EPA 2020a). It is the latter stacked-trait variety that will be marketed and grown for commercial purposes (Monsanto 2019).

Based on agronomic, phenotypic, and environmental data, MON 88702 cotton is no different from other conventional cotton varieties other than the insect-resistance trait (US-EPA 2018b; Monsanto 2019). The agronomic practices and inputs used for production of MON 88702 cotton would not substantially differ from that of other cotton varieties. It is assumed, for the purposes of this EA, that the only potential impacts that could derive from production of MON 88702 cotton, or its progeny, that would be considered potentially unique, are relative to the modified Bt trait gene and gene product, which are summarized below. In regard to introduced Bt insecticidal traits in crop plants, potential uncertainties commonly concern:

- Phenotypic, biochemical, and molecular characteristics of the GE plant
- Potential for increased toxicity, allergenicity, and weediness

- For stacked-trait/pyramided Bt crop plants—potential toxicity to an increased range of insects, particularly beneficial non-target organisms. This could derive from multiple insecticidal traits targeting different genera, as well as synergism among traits.

To address these uncertainties Monsanto provided data on the genetic insert (T-DNA); MON 88702 cotton compositional characteristics; phenotypic, agronomic, and environmental studies; and potential impacts on nontarget organisms (Monsanto 2019). Weediness potential has been addressed in this EA and the PPRA (USDA-APHIS 2019). The EPA has evaluated MON 88702 cotton, and concluded it unlikely that MON 88702 cotton presents any human or animal health risk (US-EPA 2018b, e; Monsanto 2019). The potential for toxicity to an increased range of insects, particularly beneficial non-target insects, is discussed below.

4.1.1.1 Bt Proteins, Mode of Action, and Target Invertebrate Populations

Bacillus thuringiensis (Bt) is a naturally occurring soil bacterium that produces proteins that are toxic to certain orders of insects. The insecticidal proteins synthesized by *B. thuringiensis* include crystal proteins (Cry) and cytolytic proteins (Cyt), which are produced during sporulation. Cry and Cyt toxins are also referred to as delta(δ)-endotoxins (Palma et al. 2014). *B. thuringiensis* and *B. cereus* strains also produce proteins during vegetative growth (Vip toxins). Currently, there are 78 Cry groups and 3 Cyt groups. Among both groups, over 800 individual toxins have been identified and characterized (Berry and Crickmore 2017; Crickmore et al. 2018). Corn and cotton plants have been genetically modified to contain transgenic DNA sequences from Cry and Vip toxins, most utilizing 3 different classes of Cry proteins (Cry1, Cry2, Cry3) (ISAAA 2020a). GE IR soybeans that have been developed utilize only Cry toxins; there are to date no VIP based IR soybean crops grown commercially. Cyt proteins have not been used in any GE crops, to date.

The primary classes of Cry proteins that have been used in GE crops (Cry1, Cry2, Cry3) are toxic to the insect orders Lepidoptera (moth and butterfly larvae) and Coleoptera (beetles) (Palma et al. 2014; ISAAA 2020a). Cyt toxins are primarily active in Diptera (e.g., mosquitoes); however, Cyt toxins also display relatively low toxicity against other insect orders such as coleopteran, hemipteran and hymenopteran suggesting that Cyt toxins could be potentially useful for the control of insect pest different from mosquitoes (Torres-Quintero et al. 2018). Vip proteins are classified into four families; Vip1, Vip2, Vip3, and Vip4 according to their degree of amino acid similarity (Palma et al. 2014). The binary toxin comprising Vip1 and Vip2 proteins (Warren et al. 1998; Palma et al. 2014) exhibit insecticidal activity against Coleoptera and Hemiptera (*Aphis gossypii*), whereas Vip3 toxins are toxic against lepidopterans (Donovan et al. 2006; Palma et al. 2014). Their homology to other bacterial binary toxins suggests that Vip1 and Vip2 form typical A+B type binary toxins, where Vip2 is the cytotoxic A-domain and Vip1 the receptor-binding domain responsible of the translocation of the cytotoxic Vip2 into the host cell (de Maagd et al. 2003; Barth et al. 2004). The host spectrum of the Vip4Aa1 toxin remains to date unknown (Palma et al. 2014; Chakroun et al. 2016).

While Bt toxins are generally recognized as having biological activity within specific orders of insects (e.g., for Lepidoptera (Cry1), Coleoptera (Cry3), Diptera (Cry4) and Lepidoptera and Diptera (Cry2)), some Cry proteins can also affect organisms outside their primary order of specificity (van Frankenhuyzen 2013; Hilbeck and Otto 2015). van Frankenhuyzen (2013) concluded that of 140 Bt crystal proteins and 8 Vip proteins for which toxicity data are available, 95 (64%) demonstrated toxicity

to one order only (however only 27.5% of the 87 Lepidoptera-, Coleoptera- or Diptera-active proteins were actually tested against species outside their primary order), and 27 were toxic across orders or higher ranking taxa. Among these, activity was limited to the phylum Arthropoda, with Cry1Ac, Cry1Ba, Cry3Aa, Cry51Aa putatively affecting species in three orders, Cry2Aa and Cyt1Aa affecting species in four orders, Cyt1Ba affecting species in five orders, and Cry1Ab affecting species in six orders (van Frankenhuyzen 2013). Similarly, the binary Vip1A/Vip2A toxin affects not only corn rootworms (*D. virgifera*, *D. longicornis*, *D. undecimpunctata*) but also the cotton aphid (Hemiptera: *Aphis gossypii*) (Warren 1997; Sattar and Maiti 2011; van Frankenhuyzen 2013). Thus, the characterization of Cry/Cyt/Vip toxins by “order-specificity” is relatively accurate, but should be regarded as a general functional concept.

Additionally, when evaluating the ecological relevance of the “specificity” of Bt proteins—potential effects on non-target insects—it is important to likewise consider that the majority of available data on the toxicity of Cry, Cyt, and Vip toxins is based on mortality as the “efficacy” or “specificity” endpoints. However, sub-lethal effects such as growth inhibition, changes in larvae development, and other parameters that may affect fitness may occur at doses lower than those inducing mortality (Hilbeck and Otto 2015).

4.1.1.2 Cry/Cyt Toxins and Modes of Action

Both Cry and Cyt are pro-toxins, meaning they are only toxic after activation by interaction with other compounds in the insect’s gut. Cry toxins cause the formation of pores in midgut epithelial cells of insect larvae, resulting in osmotic disruption and cell lysis (Bravo et al. 2013). To induce pore formation the pro-toxins have to be ingested, solubilized by the pH conditions of the insect gut, alkaline in the case of lepidopteran and dipteran insects and acidic in the case of coleopteran, and cleaved/modified by midgut proteases to yield the activated toxin—toxic portion of the Cry protein (Bravo et al. 2013). The activated toxic fragment binds to specific receptors on midgut epithelium cells, and cause formation of pores in the cell membrane. These pores enable excess cations to enter the cell creating an osmotic imbalance. The affected midgut cells swell and lyse, eventually resulting in death of the insect (Aronson and Shai 2001; de Maagd et al. 2001; Bravo et al. 2007). Different sized fragments of the same Cry class have been shown to exhibit different activities in different ranges of affected insects (Haider and Ellar 1987). Various steps, proteins, and cell receptor types may be involved in cell membrane binding such as cadherins, aminopeptidases, and alkaline phosphatases as well as glycolipids (Sanchis 2011; Vachon et al. 2012). For example, Cry1A toxins undergo a sequential binding mechanism with glycosyl-phosphatidylinositol anchored proteins such as alkaline phosphatase (ALP) or aminopeptidase-N (APN), and cadherin-like protein, resulting in pore formation (Bravo et al. 2013). Receptor recognition by Cry toxins has been recognized as a key aspect in Cry toxicity, and insect specificity (Bravo et al. 2011).

4.1.1.3 Modification of Bt Toxins

Before being inserted into plant genomes, *cry* gene sequences are modified to optimize gene expression *in planta* and the efficacy of the toxin against target plant pests. These changes can be introduced by protein domain swapping,¹⁶ or modification of amino acids in the Cry protein. For example, the properties of

¹⁶ A protein domain is an evolutionarily conserved amino acid sequence that determines a structural and functional unit that can exist independently of the rest of the protein structure. Some Cry proteins are modified using a process

domain III in Cry proteins have been used for the development of chimeric toxins with broader target specificities by exchanging domain III regions between different Cry proteins. Examples of modified proteins expressed in commercially available insect-protected crops include Cry3.1Ab (Walters et al. 2010), mCry3Aa (Walters et al. 2008), Cry3Bb (Vaughn et al. 2005), and Cry1A (Pardo-López et al. 2013).

Site-directed mutagenesis is also used for the modification of Cry toxins. For example, in Cry1Ac1, a mutation of arginine to serine in domain II results in increased toxicity three-fold towards cabbage moth (*Mamestra brassicae*) larvae (Lightwood et al. 2000).

Selected amino acid modifications (i.e., substitutions and deletions) in the Cry51Aa2 protein (variant Cry51Aa2.834_16) in MON 88702 cotton increased the toxicity to hemipteran (*Lygus* spp.) and thysanopteran (*Frankiniella* spp.) insect pests, relative to the unmodified Cry51Aa2 protein (Gowda et al. 2016; Huseth and DA 2020). The modifications to mCry51Aa2 consisted of eight amino acid substitutions and 3 amino acid deletions (see Gowda et al. (2016) and Figure III-3 in the Monsanto petition (Monsanto 2019)). The modified mCry51Aa2 protein expressed by MON 88702 cotton shares approximately 96% amino acid sequence similarity to wild-type Cry51Aa2.

The structure of the closely related Cry51Aa1 protein was published by Xu et al. (2015). The structure of mCry51Aa2 closely resembles that of Cry51Aa1, which is expected as these two proteins have high sequence homology (97.7% identity) (Gowda et al. 2016). The Cry51Aa1 protein differs from the mCry51Aa2 protein at seven amino acid positions. Cry51Aa1 was reported to exhibit toxicity to larvae of the silkworm moth, *Bombyx mori* larvae (Huang et al. 2007). However, 500 ppm preparations of the unmodified Cry51Aa2 caused no larval mortality in diet assays with other lepidopteran pest species, which included tobacco budworm (*Heliothis virescens*), black cutworm (*Agrotis ipsilon*), fall armyworm (*Spodoptera frugiperda*), and European corn borer (*Ostrinia nubilalis*) (Baum et al. 2012). The potential effects of the mCry51Aa2 protein on non-target species are discussed further below in 4.1.1.6—mCry51Aa2 Target Pests and Expression in MON 88702 Cotton).

Jerga et al. (2016) characterized the mode of action (MOA) of the mCry51Aa2 protein. The full-length mCry51Aa2 forms a stable non-toxic molecular complex (dimer) comprised of two identical units (monomers). Activation of mCry51Aa2 occurs through exposure to enzymes in *Lygus* saliva, which results in proteolytic cleavage and dissociation of the dimer into two separate monomers (Jerga et al. 2016). In the gut, the activated mCry51Aa2 monomeric forms bind to *Lygus* brush border cell membrane proteins and disrupt cell membrane integrity, which results in midgut epithelium cell sloughing and mortality (Jerga et al. 2016). Thus, disassociation of the mCry51Aa2 dimer into monomers is required for cell membrane binding, and the subsequent cell membrane pore forming steps which culminate in insect toxicity. This MOA is consistent with observations of other insecticidal Bt Cry proteins. It is noted however that many the Bt proteins expressed in crop plants are expressed in the proteolytically cleaved, active form, while mCry51Aa2 is not—it is expressed in the plant as a nontoxic dimer.

termed domain swapping—this involves swapping portions of domains, or whole domains, from one Cry protein with portions or whole domains from another Cry protein. Domain swapping has been shown to be an effective way to change the spectrum of activity of a native Cry protein, to include increased toxicity for targeted pest species.

4.1.1.4 Advantages of Bt Toxin and Potential Risks Posed

B. thuringiensis preparations (powder, sprays) have been used as an insecticide in conventional crops, to include organic, for over 40 years. Bt based insecticides are allowed in organic farming because *B. thuringiensis* is a bacterium that is found naturally in the soil. A major environmental advantage of Bt toxins, used as Bt powders and sprays, as well as PIPs in transgenic crops—as compared with use of many synthetic chemical insecticides—is the greater specificity of Bt toxins for target species (Bravo et al. 2007; Palma et al. 2014; Hilbeck and Otto 2015); adverse impacts on non-target insects and other organisms can be significantly reduced.

A disadvantage of Bt sprays and powders is their low environmental persistence. Bt sprays persist for only a few days on the leaf surface due UV light degradation, weather, and the presence of proteinases that contribute to degradation of Cry proteins (Sanahuja et al. 2011). In rain events spores can be washed off the leaf surface into the soil (Sanahuja et al. 2011). GE IR plants expressing genes encoding Bt toxins, however, produce the toxin for the duration of the crop cycle, resulting in prolonged exposure of insects to the toxins (PIPs). A potential disadvantage with Bt crops is that the extended exposure of insects to Cry/Vip proteins, relative to foliar applied Bt sprays or powders, and relatively higher amounts of Bt toxin *in planta* as compared to microbial foliar sprays/powders, may increase selection pressure for insects that are resistant to one or more of the Bt toxins, thus potentially reducing the usefulness of the BT based PIP, as well as Bt sprays and powders comprised of the Cry toxin (Devine 2009; Brevault et al. 2013; Gassmann et al. 2016; Few and Kerns 2019).

In addition, there has been some concern raised in the scientific literature and lay press regarding the safety of Cry or similar Bt proteins that have been modified, as summarized above, and introduced into GE crop plants. Some consider modified Cry proteins as not “natural,” arguing that their safety is unknown and they should be subjected to chronic animal testing as is done for chemical pesticides (e.g., (Séralini et al. 2011)). Concerns have also been expressed in that modified Cry proteins in GE crops may have a broader host range presenting risk to non-target species, enhanced toxicity as compared to parent proteins, and that extended exposure might affect insect populations (Latham et al. 2017).

One reason cited for these concerns is that wild-type Cry proteins, as they occur in *B. thuringiensis*, are tightly bound within crystalline inclusion bodies and are, in that form, inactive, whereas GE plant Cry toxins exist in non-crystalline active forms. If the toxin is ingested as a nontoxic parasporal crystalline body it must undergo solubilization to liberate a pro-toxin form, which is generated after sequential proteolysis of the pro-toxin form in the insect gut. Thus, wild-type crystalline Cry proteins require more proteolytic steps to convert them into the activated toxin. However, many GE IR crop plants (e.g., Bt11, Bt-176, TC1507, DBT418, and T304) express modified non-crystalline forms of Cry proteins that are either in toxic form, or require fewer/differing steps for activation. For example, many commercial plant Cry proteins are truncated in such a way that the carboxy-terminal domain that inhibits toxicity is lost (Hilbeck and Otto 2015; Latham et al. 2017). Since both solubilization and proteolysis are activation steps that require specific conditions (e.g., proper pH and specific proteases) that differ among potentially affected organisms, it has been suggested that GE IR plant Cry proteins may have broader host ranges or greater toxicity (Hilbeck and Otto 2015; Latham et al. 2017). The potential impacts of GE Bt based IR crops on non-target organisms are summarized below.

As for potential beneficial effects, planting of GE Bt crop varieties tends to result in higher insect biodiversity in/around Bt crop fields, as compared to similar non-Bt varieties treated with synthetic insecticides (NAS 2016).

4.1.1.5 mCry51Aa2 Target Pests and Expression in MON 88702 cotton

MON 88702 cotton is intended to provide protection against lygus bugs (*Lygus hesperus*, *Lygus lineolaris*: Hemiptera) and thrips (*Frankliniella* spp.: Thysanoptera) (Monsanto 2019). The mCry51Aa2 protein produced by MON 88702 cotton also affects limited species of Coleoptera (Table 4-1). Larger-scale field studies conducted to further explore the potential efficacy of MON 88702 cotton against *P. seriatus* demonstrated variable efficacy of. Therefore, commercial scale activity of MON 88702 cotton against *P. seriatus* has not been confirmed at this time (Monsanto 2019). Neither *L. decemlineata* nor *D. u. howardi* are typically pests in cotton fields and therefore their exposure, and risk would be negligible (Monsanto 2019). Activity was also observed against *O. insidiosus*, another Hemiptera. This was not unexpected due to its relatedness to *Lygus* spp. (Monsanto 2019).

Table 4-1. Activity Spectrum Results from Feeding Assays with the mCry51Aa2 Protein in Invertebrates Representing Target and Non-target Invertebrate Species				
Order	Common Name	Genus species	Representative Function	Mean LC50 or Maximum Concentration Tested
Hemiptera	Lygus bug	<i>Lygus hesperus</i>	Herbivore (Target pest)	3.009 µg/mL diet
Hemiptera	Lygus bug	<i>Lygus lineolaris</i>	Herbivore (Target pest)	Plant expression*
Hemiptera	Cotton fleahopper	<i>Pseudatomoscelis seriatus</i>	Herbivore	Plant expression*
Thysanoptera	Thrips	<i>Frankliniella</i> spp.	Herbivore (Target pest)	Plant expression*
Coleoptera	Colorado potato beetle	<i>Leptinotarsa decemlineata</i>	Herbivore	400 µg/mL diet (1)
Coleoptera	Southern corn rootworm	<i>Diabrotica undecimpunctata howardi</i>	Herbivore	200 µg/mL diet (2)
Hemiptera	Anthocoridae	<i>Orius insidiosus</i>	Predator	400 µg/g diet (3)

* See plant tissue expression level data in Table 4-2

1. The corrected survival response was near 50% in treatment concentrations from 50 to 400 µg mCry51Aa2/mL diet treatment for *L. decemlineata*.

2. The corrected survival response was 64% in the 200 µg mCry51Aa2/mL diet treatment for *D. u. howardi*.

3. The survival response was 67% in the 400 µg mCry51Aa2/g diet treatment which was the highest concentration tested for *O. insidiosus*.

Source: (Monsanto 2019)

The expression levels in plant tissue during various growth stages of MON 88702 cotton are provided in Table 4-2.

Table 4-2. mCry51Aa2 Protein Expression Levels in MON 88702 Corn Tissues			
Tissue Type ¹	Development		Mean (SE)
	Stage ²	Range (µg/g : ng/mg dwt) ³	
OSL1	Pre-Flower	1300 - 2300	1900 (63)
OSL2	Pre-Flower	1700 - 2400	2000 (53)
OSL3	Peak Bloom	790 - 2700	1600 (120)
OSL4	Cutout	1000 - 2300	1500 (76)
Square 1	Pre-flower	1500 - 2800	2200 (88)
Square 2	Pre-flower	2100 - 4000	3000 (130)
Square 3	Peak Bloom	1800 - 3600	2600 (110)
Square 4	Cutout	1900 - 3600	2700 (110)
Pollen	Peak Bloom	2.8 - 5.0	4.0 (0.65)

1. OSL = over season leaf

2. The crop development stage at which each tissue was collected.

3. Protein levels are expressed as the arithmetic mean and standard error (SE) as microgram (µg) of protein per gram (g) of tissue on a dry weight basis (dwt). The means, SE, and ranges (minimum and maximum values) were calculated for each tissue across all sites (n=16 except in OSL1 where n=15 due to one sample expressing <LOQ) and for pollen where n=3 (pooled)).

Source: (Monsanto 2019)

Additional activity spectrum studies with representatives of the orders Hemiptera, Coleoptera, Lepidoptera, Hymenoptera, Collembola, Haplotaxida, Diptera demonstrated no adverse effects from continuous dietary exposure to the mCry51Aa2 protein (Table 4-3).

Table 4-3. Activity Spectrum Results from Feeding Assays with the mCry51Aa2 Protein in Invertebrates Where No Effects Where Observed				
Order	Common Name	Genus species	Representative Function	Maximum Concentration Tested
Hemiptera	Stink bug	<i>Euschistus heros</i>	Herbivore	5000 µg/ml
Coleoptera	Western corn rootworm	<i>Diabrotica virgifera</i>	Herbivore	1000 µg/mL diet
Coleoptera	Mexican bean beetle	<i>Epilachna varivestis</i>	Herbivore	400 µg/mL diet
Lepidoptera	Fall armyworm	<i>Spodoptera frugiperda</i>	Herbivore	400 µg/mL diet
Lepidoptera	Corn earworm	<i>Helicoverpa zea</i>	Herbivore	400 µg/mL diet
Lepidoptera	European corn borer	<i>Ostrinia nubilalis</i>	Herbivore	400 µg/mL diet
Lepidoptera	Diamondback moth	<i>Plutella xylostella</i>	Herbivore	400 µg/mL diet
Hemiptera	Insidious flower bug	<i>Orius insidiosus</i>	Predator	400 µg/g diet
Coleoptera	Spotted lady beetle	<i>Coleomegilla maculata</i>	Predator	400 µg/mL diet
Hymenoptera	Western honey bee	<i>Apis mellifera</i>	Pollinator	2000 µg/mL diet
Hymenoptera	Parasitoid wasp	<i>Pediobius foveolatus</i>	Parasitoid	400 µg/mL diet
Collembola	Springtail	<i>Folsomia candida</i>	Decomposer	400 µg/g diet
Haplotaxida	Tiger worm	<i>Eisenia andrei</i>	Decomposer	400 µg/g soil dwt
Diptera	Mosquito	<i>Aedes aegyptii</i>	Decomposer	800 µg/mL diet

Source: (Bachman et al. 2017; Monsanto 2019)

4.1.1.6 Ecological and Non-Target Organism Effects

Over the past 20 years there has been considerable focus on the potential effects of GE IR plants containing Bt based insecticidal proteins on non-target populations, and more broadly, local ecology. Various ecological consequences have been considered, such as pest adaptation to the insecticidal

proteins; pest population suppression; non-target population reduction through direct effects or indirect trophic effects; increase in populations of non-target species (including pest and beneficial species) through insecticide reduction; alteration of soil biota populations; and reduction of use of cultural pest control techniques such as crop rotation (Betz et al. 2000; Cannon 2000; Obrycki et al. 2001; Storer et al. 2008).

The assessment of any ecological effects should be conducted from the perspective of sustainability of agricultural ecosystems and in the context of existing agricultural practices.

In general, while potential effects of some Cry toxins on non-target insects have been identified (see reviews by van Frankenhuyzen (2013), Hilbeck and Otto (2015)), GE Bt crop varieties that have been commercially produced, to date, have not been found to have significant adverse effects on non-target insect populations (Marvier et al. 2007; Storer et al. 2008; Wolfenbarger et al. 2008; Naranjo 2009; Yu et al. 2011; Koch et al. 2015). The EPA has reviewed all currently registered Bt derived PIPs and determined that these GE PIP products do not pose a significant risk to non-target species (US-EPA 2018c).

The potential landscape-level effects of Bt crops on predatory and parasitoid arthropods are not qualitatively different from chemical insecticides; however, potential quantitative differences derive from the full season presence of the Bt protein *in planta*, and in most cases the near elimination of a member, or members, of the herbivore community within Bt fields (Storer et al. 2008). Tempering this potential for more long-term effects on predators and parasitoids is the lack of off-crop exposure (chemical spray drift, run-off), and the comparatively narrow spectrum of activity of Bt proteins (Storer et al. 2008).

While removing an herbivorous pest, or several, from the agro-ecosystem is expected to have secondary effects through the food web, non-target populations do not appear to be significantly affected either directly or indirectly at current levels of Bt crop use, in contrast to the effects commonly seen with broad-spectrum insecticides. Collectively, meta-analyses and reviews have concluded that few harmful non-target effects of Bt crops have been demonstrated in field studies (Marvier et al. 2007; Storer et al. 2008; Wolfenbarger et al. 2008; Naranjo 2009; Yu et al. 2011).

Fundamentally, cotton producers seek to maximize yield by optimizing agricultural practices and inputs (fertilizers, pesticides—both chemical and PIPs) and reducing competition from other plants, insect pests, and pathogens. Tillage practices, field margin management, planting density, irrigation, weed management, and crop rotation practices all significantly affect the diversity and abundance of species within crop fields and nearby habitats (Storer et al. 2008). It is in this context of the highly managed and disturbed agricultural ecosystem that the impact of a GE Bt based crop is evaluated.

While Bt based crops produced to date have not been found to have substantive impacts on non-target populations in field studies (Marvier et al. 2007; Storer et al. 2008; Wolfenbarger et al. 2008; Naranjo 2009; Yu et al. 2011), each individual new Bt IR trait, as well traits in combination, must be assessed on a case-by-case basis as the spectrum of activity differs among proteins, levels of protein expression differ among each GE IR cotton variety, and potential synergistic effects need consideration when evaluation stacked-trait varieties. The potential for the mCry51Aa2 protein to impact non-target organisms is evaluated in 4.3.3.2.1–Non-Target Organisms.

4.2 No Action Alternative – Deny the Petition

Because APHIS concluded in its PPRA that MON 88702 cotton is unlikely to pose plant pest risk (USDA-APHIS 2019), denial of the petition for nonregulated status would be inconsistent with the Agency’s statutory authority under the plant pest provisions of the PPA, implementing regulations at 7 CFR part 340, and federal policies embodied in the Coordinated Framework. Because it would be unreasonable to implement an alternative absent any jurisdiction to do so, this alternative is not a practicable option.

While implementing the No Action alternative is not feasible, APHIS provides a summary evaluation for denial of the petition – where MON 88702 cotton would remain a regulated article and require APHIS authorization for importation, interstate movement, or release into the environment.

APHIS’ continued regulation of MON 88702 cotton, which would effectively preclude commercial production of this variety, would have no effect on the acreage and areas used for U.S. cotton production, nor the current practices and inputs used for the commercial production of cotton. Likewise, denial of the petition would have no effect on physical or biological resources, human or animal health, or domestic or international cotton commodities markets.

Any field testing or interstate movement of MON 88702 cotton would require APHIS authorization, which would be provided via permit, or an acknowledgment of notification pursuant to 7 CFR part 340 and APHIS guidance. For both permits and notifications, USDA-BRS prescribes criteria and conditions that must be met in order to ensure that the regulated article is introduced in such a way that it is not inadvertently released beyond the proposed introduction site, and it or its progeny do not persist in the environment. Applicants submit documents for releases, such as design protocols, that address how the required conditions will be met.

The regulations in § 340.4(a) provide that any person may submit an APHIS permit application for the introduction of a regulated article, for example, field testing of a GE crop plant. When APHIS receives a permit application, the Agency is required to make a decision to either grant or deny the permit after review of the application and any data submitted with the application.

Notification is an administratively-streamlined alternative to the permit. GE plants must meet specified eligibility criteria, and the introduction must meet certain pre-defined performance standards. For notifications, the notifier must meet eligibility requirements specified in 7 CFR part 340.3 (b)(4)(ii) and 7 CFR part 340.3 (6). APHIS reviews notifications to verify that the GE plants meet the eligibility criteria, and evaluates whether the proposed importation, interstate movement, or environmental release can be done in a manner that meets the required performance standards described in the regulation. When APHIS receives a notification application, it is reviewed by APHIS for completeness to verify that the GE organisms proposed for introduction meet the eligibility criteria for a notification and that performance standards can be met. If APHIS completes the review process and finds that all regulatory requirements have been met, the notification is authorized in a process termed “acknowledgement,” and the applicant may proceed with the proposed introduction under the terms of the notification as prescribed in 7 CFR §340.3.

If a regulated article does not meet the eligibility criteria for notification, a more stringent APHIS permit is required (7 CFR § 340.4). In addition to the information required for notification, permit applicants must describe how developers of GE organisms will perform field testing, including specific measures to keep the GE organism confined to the authorized field site and measures to ensure that it does not persist after completion of the field test. The permitting provisions found in § 340.4 describe the information required for permit applications, the standard permit conditions, and administrative information. Standard permit conditions are listed in the regulation, and APHIS can supplement these with additional conditions or requirements, as necessary, e.g. APHIS can specify appropriate conditions for confinement and monitoring to ensure that confinement is working as expected and that the regulated article or its progeny do not persist in the environment.

Actions taken by APHIS on permit applications and notifications are subject to NEPA. APHIS performs a variety of functions to ensure compliance with NEPA. Issuance of permits and acknowledgement of notifications are typically authorized under a categorical exclusion from the requirement to conduct an EA or EIS,¹⁷ consistent with APHIS' NEPA implementation regulations (7 CFR part 372). This process complies with CEQ and USDA regulations for implementing NEPA.¹⁸

There are no impacts on the human environment that would derive from a denial of the petition. To the extent individuals comply with current APHIS notification and permit requirements, EPA requirements for pesticide use, and ESA requirements, there would be little risk of harm to wildlife or natural resources as a result of APHIS authorized field testing of MON 88702 cotton. Interstate movement or importation of MON 88702 cotton would present negligible environmental risks.

4.3 Preferred Alternative – Approve the Petition

4.3.1 Agricultural Production of Cotton

4.3.1.1 Acreage and Area of Cotton Production

MON 88702 cotton will not be used for production of cotton commodities, directly; its purpose is for breeding stacked-trait IR cotton varieties. Stacked-trait MON 88702 cotton progeny, if adopted by growers, would be expected to replace other cotton varieties currently cultivated, namely GE IR cotton varieties, as opposed to augmenting current cotton crops. This would especially be expected in areas where the target pests tarnished plant bugs (*Lygus hesperus* and *L. lineolaris*) and thrips (*Frankliniella* spp.) are causing damage. Approval of the petition would have negligible impact on commercial cotton acreage; acreage would be determined by market demand for cotton based fiber, food, feed, and industrial commodities, independent of APHIS' regulatory status decision.

Seed and hybrid production is standard practice for both GE and non-GE varieties, conducted regularly on an annual basis. Monsanto submitted an Experimental Use Permit ((EUP No. 524-108) for MON 88702 cotton to EPA in 2016, for production on 2,510 acres in Alabama, Arizona, Arkansas, California, Florida, Georgia, Louisiana, Mississippi, Missouri, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia and Puerto Rico. The EUP spanned from March 1, 2017, and continue until

¹⁷ See 7 CFR 372.5(c) for more information about the APHIS categorical exclusion process.

¹⁸ CEQ regulations for implementing NEPA at 40 CFR 1500); USDA regulations implementing NEPA at 7 CFR part 1b; and APHIS regulations at 7 CFR part 372.

February 28, 2019 (US-EPA 2016a). Monsanto registered MON 88702 x MON 15985 x COT 102 in 2020, for breeding purposed only (MON 88702 x MON 15985 x COT 102 will be referred to as MON 88702 cotton progeny from here on out) (US-EPA 2020a). COT 102 produces the Vip3Aa19 protein and MON 15985 produces the Cry1Ac and Cry2Ab2 proteins. Both COT 102 and MON 15985 are currently authorized for production in other countries in several different hybrid varieties (Table 4-4). While both COT 102 and MON 15985 are authorized for use in the United States, there are to date no hybrid cotton varieties comprised of COT 102 and MON 15985 produced in the United States. Cultivation of MON 88702 x MON 15985 x COT 102 would be the first GE IR crop to provide, to some degree, protection against thrips and lygus bugs, in addition to lepidopteran insect pests.

Table 4-4. Current GE Cotton Varieties Utilizing COT 102 and MON 15895 Cotton		
Varietal	Tradename	Trait
COT102 (IR102)*	VIPCOT™ Cotton	vip3A(a)
MON15985*	Bollgard II™ Cotton	Cry1Ac, Cry2Ab2
COT102 x COT67B	VIPCOT™ Cotton	cry1Ab, vip3A(a)
COT102 x COT67B x MON88913	VIPCOT™ Roundup Ready Flex™ Cotton	cry1Ab, vip3A(a), glyphosate resistance
COT102 x MON15985	Bollgard® III	cry1Ab2, cry1Ac, vip3A(a)
COT102 x MON15985 x MON88913	Bollgard® III x Roundup Ready™ Flex™	cry1Ab2, cry1Ac, vip3A(a), glyphosate resistance
COT102 x MON15985 x MON88913 x MON88701	N/A	cry1Ab2, cry1Ac, vip3A(a), dicamba resistance, glufosinate resistance
T304-40 x GHB119 x COT102	N/A	cry2Ae, cry1Ab, vip3A(a), glufosinate resistant
GHB811 x T304-40 x GHB119 x COT102	N/A	cry2Ae, cry1Ab, vip3A(a), HPPD-inhibitor resistant, glufosinate resistant
GHB614 x T304-40 x GHB119 x COT102	Glytol™ x Twinlink™ x VIPCOT™ Cotton	cry2Ae, cry1Ab, vip3A(a), glyphosate resistant, glufosinate resistant
3006-210-23 x 281-24-236 x MON88913 x COT102 x 81910	N/A	cry1Ac, cry1F, vip3A(a), glufosinate resistant, glyphosate resistant, 2,4-D resistant
3006-210-23 x 281-24-236 x MON88913 x COT102	Widestrike™ x Roundup Ready Flex™ x VIPCOT™ Cotton	cry1Ac, cry1F, vip3A(a), glufosinate resistant, glyphosate resistant
281-24-236 x 3006-210-23 x COT102 x 81910	N/A	cry1Ac, cry1F, vip3A(a), glufosinate resistant, 2,4-D resistant
281-24-236 x 3006-210-23 x COT102	N/A	cry1Ac, cry1F, vip3A(a)

* Authorized for use in the United States

Source: (ISAAA 2020b)

4.3.1.2 Agronomic Practices and Inputs Used in Cotton Production

The agronomic practices and inputs used for cultivation of MON 88702 cotton, and MON 88702 x MON 15985 x COT 102 progeny, would be no different than for other cotton varieties, save that MON 88702 cotton/progeny, as GE IR varieties, could potentially utilize fewer insecticide applications. Based on Monsanto data, insecticide applications with MON 88702 cotton are reduced by 1 to 1.5 applications per crop cycle with MON 88702 cotton (discussed further below). Because MON 88702 x MON 15985 x COT 102 progeny will also be lepidopteran resistant (cotton bollworm (*Helicoverpa zea*), tobacco

budworm (*Heliothis virescens*), pink bollworm (*Pectinophora gossypiella*), beet armyworm (*Spodoptera exigua*), and fall armyworm (*Spodoptera frugiperda*)), the stacked-trait progeny could further reduce insecticide requirements for pest control.

4.3.1.2.1 Pest and Pest Resistance Management

Efficacy of MON 88702 cotton

The mCry51Aa2 trait in MON 88702 cotton has been found to be effective in management of thrips and plant bugs, although not total control (Graham and Stewart 2018; Graham et al. 2019). In field tests mCry51Aa2 cotton reduced total thrips numbers by 71.3% (Graham and Stewart 2018). Akbar et al. (2019) found similar efficacy in control of lygus bugs and thrips. MON 88702 cotton provided a significant reduction in the numbers of lygus nymphs and subsequent yield advantage. MON 88702 cotton also had fewer thrips and minimal injury. The level of control demonstrated by the mCry51Aa2 trait was significantly better compared with its non-transgenic near-isoline, receiving insecticides at current commercial rates (Akbar et al. 2019).

Based on field trials, yields were found to be higher when there was some type of thrips control, with either insecticide seed treatment (IST) or the Bt trait, compared with non-Bt cotton without an IST. The IST for thrips was a combination of imidacloprid and thiodicarb. MON 88702 cotton also received a treatment of acephate at the first true leaf stage. In terms of both thrips number and thrips injury ratings, there was a benefit of using an IST plus the foliar insecticide application in conjunction with the Bt Cry51Aa2. Non-Bt cotton without an IST had more thrips injury (3.02 ± 0.08) than all other treatments (Fig. 1, Supp. Table S1). Bt Cry51Aa2 cotton without an IST had less thrips injury than non-Bt cotton treated with an IST and a foliar insecticide application, and Bt Cry51Aa2 cotton treated with an IST and a foliar application of acephate had the least injury (0.64 ± 0.03) (Graham and Stewart 2018).

Although mCry51Aa2 reduced the need for insecticide applications, foliar-applied insecticide applications were needed to provide adequate plant protection from tarnished plant bugs (Graham and Stewart 2018). Based on current threshold recommendations for tarnished plant bug, one to seven insecticide applications were needed to manage tarnished plant bug depending on the year and test location, and the overall pre-bloom tarnished plant bug infestations were considered low to moderate (Graham and Stewart 2018). On average, based on field trials, Bt Cr51Aa2 cotton required 1.25 fewer insecticide applications (range 0-3) for tarnished plant bug than non-Bt cotton to achieve similar yields (Graham and Stewart 2018). Thus, the use of this trait, especially in areas with high tarnished plant bug pressure, may reduce the total number of insecticide application made during the growing season.

The level of efficacy demonstrated in field trials suggests that MON 88702, when incorporated into IPM programs, could become a valuable additional tool for management of lygus bugs and thrips in cotton cropping systems experiencing challenges with chemical control strategies (Akbar et al. 2019).

Insect Resistance Management

The behavioral responses of lygus bugs and thrips when exposed to the mCry51Aa2 trait will determine the potential for resistance evolving in these insect populations, and insect resistance management strategies (Graham and Stewart 2018; Graham et al. 2019). Of consideration, field studies have shown that plant bugs and thrips tend to avoid plants comprised of the mCry51Aa2 trait. Thus, the trait may

function more as a deterrent, and less as an insecticide. The possibility of the mCry51Aa2 protein has a non-preference effect on thrips, leading to thrips preferring to feed on plants other than MON 88702 cotton, is described by (Graham and Stewart 2018). This suggests that the mCry51Aa2 protein expressed in MON 88702 cotton leads to deterrence of exposed thrips, resulting in reduced plant damage. Such a non-preference effect on thrips has previously been documented for imidacloprid, a neonicotinoid seed treatment frequently used by cotton growers to control insect pests (Huseth et al. 2017). Huseth and DA (2020) found that in no-choice assays, cotton plants expressing mCry51Aa2 suppress oviposition, when compared to a non-Bt cotton. MON 88702 cotton was not found to kill a large proportion of *F. fusca* larvae or adults, but killed most *F. occidentalis* larvae. Time series experiments with *F. occidentalis* larvae documented significant developmental lags for mCry51Aa2 exposed individuals. These studies also found that female thrips preferred to oviposit on non-Bt cotton when provided a choice (Huseth and DA 2020).

Huseth et al. (2017) demonstrated that several foliar and seed treatments such as cyantraniliprole and imidacloprid reduced the average eggs laid per female tobacco thrips (*F. fusca*), another indicator of a non-preference effect.

Adult tarnished plant bugs also exhibited a non-preference for MON 88702 cotton, although to a lesser extent. More nymphs were found in non- mCry51Aa2 flowers than were found on mCry51Aa2 squares and mCry51Aa2 bolls (Graham et al. 2019). No difference was observed between the number of nymphs found on non-mCry51Aa2 flowers, non- mCry51Aa2 bolls, non- mCry51Aa2 squares, and mCry51Aa2 flowers (Graham et al. 2019). Also, no difference was found in the numbers of tarnished plant bug nymphs observed on non-mCry51Aa2 squares, mCry51Aa2 flowers, or mCry51Aa2 squares (Graham et al. 2019). Adult tarnished plant bug exhibited a non-preference for diet containing lyophilized Bt Cry51Aa2.834_16 leaves and for excised Bt Cry51Aa2.834_16 squares in choice tests with non-Bt squares (Graham et al. 2019).

Because the efficacy of the mCry51Aa2 trait appears to be based, to some extent, on repellency (non-preference and avoidance) as opposed to lethality—for both thrips and plant bugs—this could potentially reduce selection for resistant insects, as they may prefer to migrate to other plant hosts, limiting exposure to the mCry51Aa2 trait (Graham and Stewart 2018; Graham et al. 2019). If most of mCry51Aa2 activity on thrips is related to avoidance, it may also have implications on insecticide resistance management strategies, although the specific impacts are not clear. Another consideration is that the efficacy of cotton varieties expressing mCry51Aa2 could be reduced in large fields if efficacy is partly based on avoidance, as opposed to lethality (Graham et al. 2019). In other words, there may be limited impact on populations of thrips and lygus bugs. It is known that it takes about 6 days for the mCry51Aa2 to kill nymphs of tarnished plant bugs (Baum et al. 2012). Further data will be required to determine how deployment of mCry51Aa2 cotton in large fields may affect populations of thrips and tarnished plant bug.

These factors considered, insect resistance management will remain a key issue for all Cry toxins, and other insecticidal PIPs. Any cultivation of in MON 88702 cotton/progeny (the Bt Cry protein) would be subject to implementation of EPA mandated IRM plans (US-EPA 2019i), the goal of which is to prevent or delay the development of resistant insect populations. In 2017, EPA issued PRN 2017-1, *Guidance for Pesticide Registrants on Pesticide Resistance Management Labeling* (US-EPA 2017a) for conventional pesticides and resistance management. In EPA's *Guidance on FIFRA Section 6(a)(2) Regulations for*

Pesticide Product Registrants, any substantiated incidents of pest resistance for any regulated pesticide product must be reported to the U.S. EPA.¹⁹ This reporting requirement is in accordance with FIFRA Adverse Effects Reporting Section 6(a)(2), which requires pesticide product registrants to submit adverse-effects information about their products to EPA.

4.3.2 Physical Environment

4.3.2.1 Soil Quality

The agronomic practices and inputs used for MON 88702 cotton/hybrid production that can impact soil quality would be no different from those currently used for both GE and non-GE cotton, apart from potential reductions in insecticide use with MON 88702 cotton, and MON 88702 cotton progeny. Consequently, any potential impacts on soil quality resulting from MON 88702 cotton/hybrid cultivation would be similar to those resulting from cultivation of current cotton crops. Any reductions in insecticide use (discussed in 4.3.1.2.1) would be of benefit to soils, relative to non-IR cotton crop production (discussed in 4.3.3.1–Soil Biota).

For all cropping systems, GE and non-GE alike, growers producing crops on highly erodible land would be required to maintain and implement a soil conservation plan that reduces soil loss—a plan approved by the USDA National Resources Conservation Service (NRCS).

4.3.2.2 Water Resources

Because the agronomic practices and inputs utilized for MON 88702 cotton/hybrid production would be similar to or no different than those currently used (92% of cotton crops are IR), the sources of potential impacts on water resources, namely NPS pollutants in agricultural run-off, would not be expected to substantially differ. Runoff from MON 88702 cotton/hybrid production fields would likely be comprised of lesser quantities of insecticides, to some degree, reducing risks to surface waters and groundwater, as compared to non-IR cotton crops. Insecticides used for control of lygus bugs include flonicamid (pyridine organic compound), novaluron (benzoylphenyl urea), indoxacarb (oxadiazine), pyrethroids (bifenthrin, beta-cyfluthrin, imidacloprid plus cyfluthrin, lambda-cyhalothrin, zeta-cypermethrin), and aldicarb combined with organophosphates (dimethoate, acephate) (UC-IPM 2015b). Thrips are controlled with acepahtae and spinetoram (UC-IPM 2015c). On average, based on field trials, mCry51Aa2 cotton required 1.25 fewer insecticide applications for tarnished plant bug control, as opposed to non-Bt cotton (Graham and Stewart 2018). Because MON 88702 x MON 15985 x COT 102 progeny will also be lepidopteran resistant (cotton bollworm (*Helicoverpa zea*), tobacco budworm (*Heliothis virescens*), pink bollworm (*Pectinophora gossypiella*), beet armyworm (*Spodoptera exigua*), and fall armyworm (*Spodoptera frugiperda*)), stacked-trait progeny could further reduce insecticide requirements for lepidopteran pest control.

Various National and regional efforts are underway to reduce NPS contaminants in agricultural run-off, and run-off itself (US-EPA 2019e; USDA-NRCS 2019c). For example, in 2012, the USDA-NRCS launched the National Water Quality Initiative (NWQI) in collaboration with EPA and state water quality agencies to reduce nonpoint sources of nutrients, sediment, and pathogens related to agriculture in high-priority watersheds in each state (USDA-NRCS 2019c).

¹⁹ See <https://www.epa.gov/pesticide-registration/prn-98-3-guidance-final-fifra-6a2-regulations-pesticide-product-registrants>

4.3.2.3 Air Quality

There are no risks to air quality that would derive from MON 88702 cotton/hybrid production. The emission sources associated with MON 88702 cotton/hybrid production would be the same as for other cotton varieties (i.e., tillage, fossil fuel burning equipment, the application of fertilizers and pesticides). As a GE IR crop there would be reductions in insecticide use, relative to non-Bt cotton, which would reduce use of fossil fuel use in the machinery used for insecticide application, and thereby volume of fossil fuel based emissions. There would also be commensurate reductions in potential insecticide drift and volatilization from MON 88702 cotton crops.

4.3.3 Biological Resources

4.3.3.1 Soil Biota

Soil biota include organisms such as earthworms, nematodes, protozoa, fungi, bacteria, arthropods, as well as burrowing mammals like voles and moles. Potential impacts on soil biota resulting from the practices and inputs used in MON 88702 cotton/hybrid cultivation would be the same as or similar to that of other cotton varieties. Generally, potential adverse effects on soil biota are largely associated with use of insecticides and fungicides, less so for herbicides. Insecticides used for control of lygus bugs include flonicamid (pyridine organic compound), novaluron (benzoylphenyl urea, growth regulator), indoxacarb (oxadiazine), sulfoximines (insect nicotinic acetylcholine receptor agonists), pyrethroids (cypermethrin, bifenthrin, beta-cyfluthrin, imidacloprid, cyfluthrin, cyhalothrin), and aldicarb combined with organophosphates (dimethoate, acephate, dicotophos) (UC-IPM 2015b; Shepard 2018). Thrips are controlled with acepahtae (organophosphate), spinetoram (nicotinic/gamma amino butyric acid (GABA)-gated chloride channel inhibitor), dicotophos (organophosphate), or dimethoate (organophosphate) (Storer et al. 2008; UC-IPM 2015c; Shepard 2018).

Insecticides can influence the number and metabolic activity of soil microbial and faunal communities (e.g., arthropod larvae and earthworms), and in turn soil nutrient cycling, and physico-chemical properties (Kalia and Gosal 2011; Wang et al. 2012). The most commonly applied pesticides, i.e. insecticides (organochlorines, organophosphates and carbamates), act primarily by disrupting nervous system function in insects, in particular, four nerve targets, acetylcholinesterase, voltage-gated chloride channel, the acetylcholine receptor and the g-aminobutyric acid receptor, others act as growth regulators or endotoxins (US-EPA 2019k). These modes of action can also affect soil fauna, such as earthworms, which are highly susceptible to insecticides. Studies have found significant effects on biomass reduction, growth, and reproduction by disrupting various physiological activities leading to loss of earthworm populations and soil biodiversity (Wang et al. 2012; Miglani and Bisht 2019). Organophosphates such as dimethoate cause physiological abnormalities in earthworms. Pyrethroids such as imidacloprid can induce developmental effects, reduced fertility, and affect earthworm populations, while cypermethrin is lethal to earthworms (Miglani and Bisht 2019).

The application of insecticides chlorpyrifos, imidacloprid, cypermethrin, endosulfan and carbofuran can cause considerable variation in soil bacterial populations (Meena et al. 2020). Insecticides belonging to the organophosphates group (i.e., dimethoate, diazinon, chlorpyrifos, quinalphos, and malathion) can inhibit the growth and population of soil bacteria, fungi, and alter soil enzymatic activity (Pandey and Singh 2004; Singh and Singh 2005).

Bacteria may potentially be exposed to the Cry gene through uptake of free DNA or RNA (Lorenz and Wackernagel 1994). As concluded in APHIS' PPRA, horizontal gene transfer and expression of DNA from a plant species to bacterial, fungal or invertebrate species is unlikely to occur (USDA-APHIS 2019). Biota such as earthworms, nematodes, and arthropods may be exposed to Cry protein via ingestion. The potential impacts of the trait Cry gene and gene product on soil biota are discussed following.

Cry Trait Genes and Gene Products

There is a substantial body of literature on the potential effects of Bt based Cry traits on soil microbial communities. Findings from these studies are somewhat mixed, although few or no significant adverse effects have been identified with the Cry traits commercialized to date. In general, Cry proteins released from root exudate and plant residues appear to have few or no significant long-term impacts on the diversity and function of soil communities (e.g., see (Ahmad et al. 2006; Icoz and Stotzky 2008; Naranjo 2009; Liu et al. 2015; Turrini et al. 2015)). Some minor differences in total numbers and community structure of soil microorganisms in Bt and non-Bt crops have been observed. However, many of these observations were not statistically significant, were transient, were not related to the transgene, or were the result of altered plant characteristics (e.g., lignin content) (Icoz and Stotzky 2008). Literature reviews conducted to date suggest that GE Cry based crop plants currently cultivated have had few or no significant adverse effects on soil biota (Icoz and Stotzky 2008; Carpenter 2011; Turrini et al. 2015).

mCry51Aa2 protein

For soil-dwelling organisms the most ecologically relevant route of exposure would be primarily from decomposing plant tissue; this would include root, and above-ground plant material deposited on or tilled into the soil. Soil-dwelling organisms would be exposed via feeding on living or dead crop material or ingesting or absorbing the mCry51Aa2 protein after release into the soil (e.g., via root exudates or degrading plant material). Cotton is commonly defoliated prior to harvest, to optimize yield and cotton fiber quality (PhytoGen 2020), and while a low residue crop (Claassen et al. 2018), defoliated plant matter would serve as a route of transgene exposure for soil organisms. Soil organisms may also be exposed to the mCry51Aa2 protein in MON 88702 cotton by feeding on or contact with roots during the growing season.

The mCry51Aa2 protein, due to its MOA (discussed in 4.1–Scope of Analysis, and further in 4.3.3.2–Wildlife Communities) has biological activity within the order Coleoptera (beetles), family Chrysomelidae (leaf beetles); Hemiptera (plant bugs); and Thysanoptera (thrips). Based on studies by (Bachman et al. 2017), and mCry51Aa2 spectra data presented by Monsanto (Monsanto 2019), impacts on other soil organisms (e.g., protozoa, nematodes, mites, springtails, earthworms) would not be expected.

The estimated environmental concentrations (EECs) were calculated for different MON 88702 cotton tissues as conservative estimates designed to capture the high-end of expression levels (95th percentile) from field samples taken in 2015 and 2018. When establishing the EEC for NTO assessment, the mean mCry51Aa2 expression level reported on a dry weight basis was used, and from these data, the 95th percentile expression values were calculated (Monsanto 2019). The 95th percentile expression levels for MON 88702 cotton mCry51Aa2 protein in leaf is around 494.4 µg/g fwt, root 83.1 µg/g fwt, square 770.7 µg/g fwt, and pollen 2.4 µg/g fwt. Thus, the expected environmental concentrations (EECs) derived from living and/or decaying plant material would be at or below these values. The effects of mCry51Aa2

protein on two species of soil biota were examined in laboratory toxicity studies. Earthworms were tested with 500 and 2500 µg mCry51Aa2 protein/g in soil to assess survival and biomass at 7 and 14 days, and springtails (*Collembola*) juveniles were tested over 28 days at 500 and 2500 µg/g mCry51Aa2 protein in diet to assess survival and reproduction. No adverse effects on either species were observed (US-EPA 2018b; Monsanto 2019).

The estimated time to 50% degradation (DT50) of mCry51Aa2 in three different soils ranges from 3.0 - 4.7 days, and time to 90% degradation (DT90) ranges from 23.7 - 74.5 days (US-EPA 2018b; Monsanto 2019). The degradation studies used root and shoot tissues of cotton expressing mCry51Aa2 protein and were spiked with additional mCry51Aa2 protein to improve accuracy of the analytical quantification. Thus, mCry51Aa2 is not expected to accumulate in soils, and exposure of biota to mCry51Aa2 in soil is expected to be limited on a temporal scale.

Based on these and other data, EPA concluded that exposure of biota to mCry51Aa2 in soil is expected to be of low concentration; around 9.3 µg mCry51Aa2/g soil is estimated in the top 3 inches of soil. Soil incorporation would occur after harvest when plants are in or past senescence, which is when concentration of the protein in plant material is expected to be lower. Even in a worst case scenario, the mCry51Aa2 concentration in soil is not expected to exceed 40 µg mCry51Aa2/g (US-EPA 2018b). The level of mCry51Aa2 exposure tested with earthworm and *Collembola* is approximately 63-times the worst case exposure level for soil biota (US-EPA 2018b).

Considering these factors and that discussed in 4.1–Scope of Analysis, the mCry51Aa2 protein is unlikely to present a significant risk to populations of soil biota or their ecological interactions.

One of the more common themes that has emerged from literature reviews addressing current GE Bt crop plants is that crop and soil management practices in association with environmental variables are the primary factors affecting the biotic composition and function of soils, as these practices can contribute to, or detract from, sustaining soil quality (Sanvido et al. 2007; Naranjo 2009; Kolseth et al. 2015; Turrini et al. 2015).

4.3.3.2 Wildlife Communities

There are no hazards to vertebrate taxa associated with exposure to the mCry51Aa2 protein in MON 88702 cotton (US-EPA 2018b). Numerous animal safety studies conducted over the past 40 years have found that Bt-derived insecticidal toxins present negligible risk to vertebrate taxa (McClintock et al. 1995; Bravo et al. 2007; Adel-Patient et al. 2011; Koch et al. 2015; Andreassen et al. 2016). Bt based Cry proteins primarily have activity among invertebrate taxa; thus their extensive use as insecticides—in conventional, organic, and GE cropping systems. Consistent with other Cry proteins, the results from acute toxicity studies conducted with the representative vertebrate species, northern bobwhite quail (*Colinus virginianus*) and mice (*Mus musculus*), demonstrated a lack of mCry51Aa2 toxicity at doses 2,500 mg/kg and 5,000 mg/kg, respectively, well above the maximum exposure levels anticipated from MON 88702 cotton (Monsanto 2019). While studies with vertebrate taxa used purified microbially-produced mCry51Aa2 protein, a comparison of the molecular characteristics of the microbially-produced mCry51Aa2 with the plant-produced protein, including the molecular weight, immunoreactivity, functional activity, and glycosylation status, demonstrated their equivalency (US-EPA 2018b).

The mCry51Aa2 protein, and the parent Cry51Aa2 protein, are β -pore forming proteins (β -PFPs) that belong to the ETX_MTX2 family of proteins. While ETX_MTX2 family members, and the broader β -PFPs, are found in a broad range of plant, animal and bacterial species. The mCry51Aa2 protein binds to specific receptors on the membranes of cells lining the insect midgut, receptors that are not present in humans and other mammals, nor in the majority of non-target insects. Because Cry toxins must be able to bind to cells to induce a toxic effect, this limits the potential hazards related to exposure in humans, animals, and the majority of non-target insects (Jerga et al. 2016; Farmer et al. 2017). Numerous reports demonstrate that many proteins from this β -PFP group have a lengthy history of safe use and differ significantly from mammalian toxins within the same protein family in sequence, structure, and most importantly, in target organism specificity (Moar et al. 2017).

4.3.3.2.1 Non-Target Organisms

When Bt based insecticides are used as a spray or powder, which is done in organic and conventional cropping systems, the opportunity for non-target organisms (NTO) to ingest Cry toxins is low due to the limited persistence of foliar applied Bt insecticides; Bt toxins degrade under UV light within a few days, and are removed from plants by rain and dew (Behle et al. 1997; Sanahuja et al. 2011). When planting fields with GE Bt based crop plants, the potential exposure of insects to Cry toxins involves a much longer period of time (the duration of the crop), and consequently a potentially broader range of non-target organisms. Thus, because the potential for exposure to Cry proteins in GE IR crop plants is chronic, relative to short-lived foliar applied Bt insecticides, the risk of potential adverse effects on NTO populations, in particular beneficial insects (parasitoids, predators, pollinators), and species of conservation concern, can be greater (Shelton et al. 2009; Gatehouse et al. 2011; Hilbeck and Otto 2015).

As discussed in 4.1–Scope of Analysis, while Bt toxins are generally recognized as having biological activity within specific orders of insects (e.g., for Lepidoptera (Cry1), Coleoptera (Cry3), Diptera (Cry4) and Lepidoptera and Diptera (Cry2)), some Cry proteins can also affect organisms outside their primary order of specificity (van Frankenhuyzen 2013; Hilbeck and Otto 2015). For example, Cry1Ac, Cry1Ba, Cry3Aa, Cry51Aa have been observed to affect species in three orders, Cry2Aa species in four orders, and Cry1Ab affect species in six orders (van Frankenhuyzen 2013). Thus, the characterization of Cry toxins by “order-specificity” is relatively accurate, but should be regarded as a general functional concept.

The reported cross-order effects of certain Cry toxins on NTOs include a range of lethal, and sub-lethal effects such as on behavior, development, growth, reproduction, sex ratio, feeding preference, prey consumption, and proportion of prey eaten (Shelton et al. 2009; Gatehouse et al. 2011; Hilbeck and Otto 2015). Lethality would lead a reduction in a NTO population with subsequent trophic effects on species composition at the community level, predator-prey relationships, and food webs. Sublethal NTO effects in the form of developmental delays or behavioral changes in host or prey preferences, for example, can likewise alter predator-prey relationships or/and food webs. Shifts in arthropod community structures resulting from lethal and sublethal effects on NTOs could also give rise to secondary pests (Hilbeck and Otto 2015).

Evaluation of potential effects on NTOs were based on (1) the potential consumption of MON 88702 cotton leaf, square, pollen, and root material, and (2) consumption of prey (herbivores) that have fed on MON 88702 cotton plant material. Exposure of NTOs to mCry51Aa2 in MON 88702 cotton can occur directly or indirectly. Direct exposure could occur by feeding on pollen or leaf material (e.g., a scavenger

or detritivore feeding directly on the plant or sloughed-off material). Predator species that feed on plants may do so to obtain moisture, to sustain themselves in periods of prey scarcity, or to supplement their diet when insufficient prey are present. Predator Heteroptera, a suborder of Hemiptera, in particular, are known to feed on green plant tissues and to derive nutritional benefit supplemental to a diet with optimal prey (e.g., (Kiman and Yeagan 1985; Gillespie and McGregor 2000)). Indirect exposure is generally understood to constitute trophic exposure, whereby a NTO is exposed to the plant-produced toxin via consumption of prey or host that has fed on the plant. Use of prey species that are not susceptible to the toxin excludes any confounding effects of intoxicated or suboptimal prey (Shelton et al. 2009; Gatehouse et al. 2011). Finally, any community-level effects due to a plant-incorporated toxin would not be a direct result of exposure to any toxin, but could be considered an indirect effect of a plant-produced toxin through removal of some target species, for example (González and Wilson 1982).

Surrogate beneficial species used in NTO assessments were selected based on the results of the activity spectrum exhibited by the mCry51Aa2 protein, and to ensure representation of different taxonomic and ecological functional groups (Monsanto 2019). The testing of potential impacts of mCry51Aa2 on NTOs was done according to U.S. regulatory guidelines for NTO testing and risk assessment of insect-protected crops (crops expressing PIPs) (USDA-EPA 2007). These were developed by USDA and EPA and suggest that testing and assessment be conducted based on a tier-based system (USDA-EPA 2007). Using this approach, risk is evaluated within different levels or “tiers” that progress from lab based studies to increasingly more realistic exposure scenarios, if the early tiered tests indicate a possible hazard to NTOs.

Tier 1 testing includes laboratory toxicity testing against selected sensitive or representative taxa. Several additional studies may be conducted, such as tri-trophic feeding studies using prey species (tier 2), leaf disk assays to model different feeding scenarios representing different exposure and feeding ecology (tier 3), and field studies to assess the most realistic exposure conditions (tier 4). NTOs assessed in Tier 1 and Tier 2 studies are those listed in Table 4-5. Testing to assess the hazard of MON 88702 cotton included a representative pollinator (honey bee larvae and adults (*Apis mellifera*)), eight beneficial insect species that represent biocontrol species: a parasitic wasp (*Pediobius foveolatus*), the predatory insects lady beetle (*Coccinella septempunctata*), rove beetle (*Aleochara bilineata*), lacewing (*Chrysoperla carnea*), insidious flower bug (*Orius insidiosus*), big-eyed bug (*Geocoris punctipes*), Western damsel bug (*Nabis alternatus*), and leafhopper assassin bug, (*Zelus renardii*), and two representative soil biota [earthworm (*Eisenia andrei*) and Collembola (*Folsomia candida*)].

Pollinators

Honey bee larvae (*A. mellifera*), 2 days old, were exposed to mCry51Aa2 protein at a single dose administered to the brood cell using a 500 µg/mL solution. Survival was 100% in the mCry51Aa2 protein treatment at a concentration up to 2 mg/mL diet solution. No effects on average development time were observed (Monsanto 2019). The NOEC for the mCry51Aa2 protein for honey bee larvae was found to be ≥ 5.6 µg/larvae, and the expected environmental concentration 0.0048 µg/g fwt pollen (Monsanto 2019).

Table 4-5. Expected Environmental Concentrations (EECs), No Observed Effect Concentrations (NOECs) from NTO Studies with Terrestrial Beneficial Invertebrate Species and Margins of Exposure (MOE) for mCry51Aa2 Protein

Test Organism	Common Name	Order	Function	EEC ¹	NOEC ²	MOE ³
<i>Coccinella septempunctata</i>	Lady Beetle	Coleoptera	Predator	2.4 µg/g fwt pollen	≥2500 µg/g	≥1041.7
<i>Aleochara bilineata</i>	Rove Beetle	Coleoptera	Predator	494.4 µg/g fwt leaf ⁴	≥2500 µg/g	≥5.1
<i>Apis mellifera</i> larvae	Honey Bee	Hymenoptera	Pollinator	0.0048 µg/g fwt pollen ⁵	≥5.6 µg/larvae ⁶	≥1166.7
<i>Apis mellifera</i> adult	Honey Bee	Hymenoptera	Pollinator	2.4 µg/g fwt pollen	≥500 µg/g	≥208.3
<i>Chrysoperla carnea</i>	Lacewing	Neuroptera	Predator	2.4 µg/g fwt pollen	≥2500 µg/g	≥1041.7
<i>Pediobius foveolatus</i>	Parasitic Wasp	Hymenoptera	Parasitoid	2.4 µg/g fwt pollen	≥2500 µg/mL	≥1041.7
<i>Orius insidiosus</i>	Insidious Flower Bug	Hemiptera	Predator	2.4 µg/g fwt pollen	13 µg/g	5.4
<i>Orius insidiosus</i>	Insidious Flower Bug	Hemiptera	Predator	1.58 µg/g fwt leaf ⁷	6.47 µg/g FAW	4.1
<i>Geocoris punctipes</i>	Big-eyed Bug	Hemiptera	Predator	770.7 µg/g fwt square	≥4000 µg/g	≥5.2
<i>Nabis alternatus</i>	Damsel Bug	Hemiptera	Predator	770.7 µg/g fwt square	≥4000 µg/g	≥5.2
<i>Zelus renardii</i>	Assassin Bug	Hemiptera	Predator	770.7 µg/g fwt square	≥4000 µg/g	≥5.2
<i>Eisenia andrei</i>	Earthworm	Haplotaxida	Decomposer	83.1 µg/g fwt root ⁸	≥2500 µg/g dry	≥30.1
<i>Folsomia candida</i>	Springtail	Collembola	Decomposer	83.1 µg/g fwt root ⁸	≥2500 µg/g	≥30.1

For a conservative tier 1 assessment, an MOE that is ≥10x the EEC, using a median lethal concentration (LC50), is indicative of negligible risk. EPA guidance states that only adverse effects to NTOs at ≤ 1x the realistic field exposure are viewed as an environmental risk (USDA-EPA 2007).

1 95th percentile expression levels determined from MON 88702 tissues across five and four sites in 2015 and 2018, respectively Table V-3.

2 NOECs reflect nominal test substance concentrations.

3 MOE values were calculated based on the ratio of the NOEC to EEC. The MOE was determined based on the 95th percentile expression level of the mCry51Aa2 protein in the tissue from MON 88702 deemed most relevant to the NTO exposure.

4 The 95th percentile expression value from the leaf development stage (OSL3) with the highest expression level was used to represent worst-case-scenario for a predator consuming a herbivorous prey.

5 EEC based upon mean quantity of mCry51Aa2 protein expressed in 2 mg of MON 88702 pollen fresh weight (fwt). The average consumption of pollen by honey bee larvae is 2 mg during development (Babendreier et al., 2004). The EEC was calculated as follows: (2 mg pollen × (2.4 µg mCry51Aa2 protein /1000 mg pollen).

6 The NOEC represents a single dose of 10 µl of 500 µg/mL solution added to each larval cell. The total mass added and consumed in each larval cell was 5.6 µg mCry51Aa2 protein/cell. The concentration of 500 µg/g mCry51Aa2 protein in the diet solution is calculated based on the density of the 30% sucrose/water (w/v) solution of 1.127 g/mL.

7 In the tri-trophic study (tier 2), the *S. frugiperda* (Fall armyworm – FAW) were fed artificial diet containing 1999 µg/mL mCry51Aa2 protein, resulting in 6.47 µg/g mCry51Aa2 protein concentration (0.32%) in the prey used as food source for *O. insidiosus* nymphs. The EEC was determined as 0.32% of 494 µg/g fwt leaf to represent worst-case-scenario of biotransfer of mCry51Aa2 protein between trophic levels.

8 The 95th percentile expression value from the root development stage (peak bloom) was used to represent worst-case-scenario for a soil dwelling invertebrate.

Source: (Monsanto 2019)

A. mellifera adults were exposed in a 14-day continuous feeding study. There were no significant differences in mean survival between the mCry51Aa2 protein and the control treatments. No abnormal behavior was observed in either the mCry51Aa2 protein treatment or the control treatment. The NOEC for the mCry51Aa2 protein for adult honeybees was ≥ 500 $\mu\text{g/g}$, and the expected environmental concentration 2.4 $\mu\text{g/g}$ fwt pollen (Monsanto 2019).

Beneficial Predator Species: Hemiptera, Hymenoptera, Coleoptera, Neuroptera

While mCry51Aa2 is primarily effective in *Lygus* spp. and *Frankliniella* spp, it has also been shown to have activity in the NTO *Orius insidiosus*, a beneficial predator species (Monsanto 2019). Because both *Lygus* and *Orius* belong to the order Hemiptera, testing was performed to assess the risk to several other predatory Hemiptera; the big-eyed bug (*Geocoris punctipes*), Western damsel bug (*Nabis alternatus*), and assassin bug (*Zelus renardii*), which are related to *Orius* spp. and likely be present in U.S. cotton fields (Monsanto 2019). *Zelus renardii* (Reduviidae) was also included because, although it tends to not engage in supplemental herbivory, it can be an important natural enemy in some cotton cropping systems. Protein amounts used in bioassays were either similar to or greater than what was quantified in the plant, in order to support a conclusion that these groups would not be negatively impacted by protein exposure expected in the environment.

In diet bioassays, one-day old nymphs of *Geocoris punctipes*, *Nabis alternatus*, and *Zelus renardii* were initially exposed to 4000 μg mCry51Aa2 protein/g diet, concentrations several-fold higher than the concentrations of mCry51Aa2 found in MON 88702 cotton plant tissues to allow for conservatism in dietary exposure to the protein. The mCry51Aa2 protein concentration used in the diet assays to estimate a 10-fold exposure was based on the mean, fresh weight mCry51Aa2 expression levels in MON 88702 cotton plant tissues. There were no differences in survival compared to a buffer control, and all surviving nymphs developed to adulthood under this chronic and conservative high exposure scenario. However, sublethal effects were observed at this concentration, including a longer development time for all three taxa and a significant decrease in adult biomass observed for *N. alternatus* and *Z. renardii*, when feeding on test compared to control diets (Table V-12 in Monsanto (2019)). When the study was conducted using a 400 μg mCry51Aa2 protein/g diet dose, the studies found that *N. alternatus* and *G. punctipes* nymphs took approximately one day longer to develop into adults as compared to the control diet. This difference was statistically significant, although it is unlikely that a one day developmental delay would result in an ecologically relevant effect on populations of *N. alternatus* and *G. punctipes* in the field. No difference in adult biomass was observed for either *N. alternatus* or *G. punctipes* at this dose. However, a statistically significant difference between the mCry51Aa2 and control diet for both adult biomass and development time was observed for *Z. renardii*. The biomass of the surviving adults feeding on diet containing 400 μg mCry51Aa2 protein/g was significantly reduced compared to the control diet. Although all nymphs were able to develop into adults, it took approximately 12.7 days longer when feeding on the test diet (Table V-12 in Monsanto (2019)). This exposure scenario of 400 μg mCry51Aa2 protein/g assumes worst-case, chronic, and obligate feeding on MON 88702 cotton plant tissue by these predators. Under more realistic field conditions the exposure to the mCry51Aa2 protein would primarily happen through consumption of a variety of prey that contain orders of magnitude less mCry51Aa2 protein.

In diet bioassay studies there were no effects observed for the predator species *Chrysoperla carnea* (Neuroptera; lacewing). Regarding Coleoptera, no mortality was observed in three species of predatory beetles representing two families; Coccinellidae and Staphylinidae. These were: rove beetle (*Aleochara*

bilineata: Coleoptera, Staphylinidae), seven-spotted lady beetle (*Coccinella septempunctata*: Coleoptera, Coccinellidae), and pink-spotted lady bug (*Coleomegilla maculata*, Coleoptera, Coccinellidae) (Table 4-5).

For beetles within Chrysomelidae (also known as leaf beetles, which are herbivores), one species exhibited no mortality (western corn rootworm, *Diabrotica virgifera virgifera*), and two species exhibited some mortality. For Colorado potato beetle (*Leptinotarsa decemlineata*) and southern corn rootworm, also known as the spotted cucumber beetle (*Diabrotica undecimpunctata howardi*), some mortality was observed, but in both cases 100% mortality was not achieved with increasing concentrations. Accurate LC50 values could not be obtained for either species. *L. decemlineata* appeared to be more sensitive with mortality estimates of up to 50% at 50 – 200 µg mCry51Aa2/ml of diet, or 65% in some assays as high as 800 µg mCry51Aa2/ml of diet. While for *D. undecimpunctata*, the estimated mortality rates were <36% when tested at doses from 200 – 800 µg mCry51Aa2/ml of diet, and weight gain was reduced by half even at 200 µg mCry51Aa2/ml of diet. Because high levels of mortality were never reached for any beetles that were tested, any negative effect that might be possible is expected to be minor. Testing of other closely related Coleoptera, as well as those that are relevant to the risk assessment of a cotton product showed no effect of mCry51Aa2 on these insects (Table 4-5), indicating that MON 88702 cotton does not pose a significant risk to coleopteran species (Monsanto 2019).

In the case of herbivores that feed on Bt crop plants, and which tend to accumulate relatively high levels of Cry proteins, like spider mites, the levels are typically an order of magnitude below those measured in plant tissue. In tier 2 studies completed with *Orius* spp., it was demonstrated that spider mites accumulated at most 85 µg mCry51Aa2 protein/g fwt. Calculated mCry51Aa2 protein expression levels in MON 88702 cotton tissues used to determine expected environmental concentrations (EEC) were 494.4 µg/g FWT in the leaf and 770.7 µg/g FWT in the square. Considering *Geocoris* spp. and *Nabis* spp. will spend the majority of their time feeding on herbivores present in cotton fields, exposure to the mCry51Aa2 protein would be several-fold lower than the tested concentration of 400 µg mCry51Aa2 protein/g diet. Even if these predator species were to exclusively consume spider mites, the exposure to mCry51Aa2 would be more than 5-fold less than the lowest mCry51Aa2 concentration tested. In the case of *Zelus* spp., exposure to the protein is expected to be even lower than for *Orius* spp., *Geocoris* spp. and *Nabis* spp., as *Zelus* tend to do less direct plant feeding than *Geocoris*, *Nabis*, or *Orius*.

Parasitic Wasps and Soil Macrofauna

Adults of *P. foveolatus* (Hymenoptera) were exposed to mCry51Aa2 protein incorporated into a diet at concentrations of 200 µg/mL and 400 µg/mL for a period of 20 days. 100% and 94.2% of the test wasps survived in the mCry51Aa2 protein treatment at 200 µg/mL and 400 µg/mL, respectively. The survival in both mCry51Aa2 treatments was similar to or greater than the buffer control and the untreated control. These results indicate no adverse effect of 400 µg mCry51Aa2 protein/mL diet on the survival of wasp adults after 20 days of continuous dietary exposure.

Juvenile *Folsomia candida* (Collembola, springtails) were exposed to mCry51Aa2 protein, buffer control, untreated control, or toxic reference treatment via a diet medium for 28 days. Results indicate that 400 µg mCry51Aa2 protein/g inactive-yeast diet had no significant effects on the survival or reproductive capacity of the springtails (Monsanto 2019). Adult earthworms (*Eisenia Andrei*; Haplotaxida) were exposed to mCry51Aa2 for 14 days at 400 µg protein/g soil dry weight. Mortality was assessed over a 14-

day testing period and the change in fresh weight of the worms was assessed for survivors at 14 days after treatment. These results from these studies indicated no adverse effect of 400 µg mCry51Aa2 protein/g soil dry weight on earthworm survival after 14 days of continuous exposure (Monsanto 2019).

Field Tests on NTOs

Monsanto also conducted field testing to ascertain whether MON 88702 cotton could have impacts on non-target organisms in areas where MON 88702 cotton is cultivated. Sampling was conducted during three field seasons, at 5-6 sites, in various locations in cotton growing regions of the United States. Field tests included MON 88702 cotton, its untreated parental control line (DP393 cotton), and treatments that included broad-spectrum (acephate) and selective insecticides (flonicamid, imidacloprid, sulfoxaflor) for comparison. Results were presented both by site and across sites. The number of acephate applications ranged from 1-3 across sites for treatment 1. Acephate is a broad spectrum organophosphate that is frequently used across the U.S. Cotton Belt as an effective option for *Lygus* spp. control, and known to adversely impact beneficial arthropods. Treatment 2 used flonicamid, imidacloprid, and sulfoxaflor, which are known to provide effective control against *Lygus* spp. but have minimal to no effect on beneficial arthropods (Monsanto 2019). The number of selective insecticide applications ranged from 1-2 across the season at most sites.

Orius spp. (minute pirate bugs) are considered beneficial as they feed on plant-eating mites and their eggs, various insect eggs, and other soft-bodied arthropods such as thrips and small caterpillars. As a beneficial insect, *Orius* spp. are mass-reared for use in the biological control of thrips. As discussed above, a tiered approach was utilized to evaluate the risk MON 88702 cotton may present to *Orius* spp. This assessment included a tier 1 study with 5-day old nymphs over a concentration range from 13 to 500 µg/g diet of mCry51Aa2 that established a NOEC at > 13 µg/g diet. This resulted in a MOE of 5.4 when considering exposure to MON 88702 pollen as main source of direct exposure to mCry51Aa2, given that its EEC in pollen is 2.4 µg mCry51Aa2/g fwt. Because a tier 1 diet feeding assay demonstrated significantly reduced survival of five-day old *O. insidiosus* nymphs at mCry51Aa2 protein concentrations > 13 µg/g diet (NOEC), this prompted tier 2 assays to assess risk under feeding scenarios representative of predatory insects.

In tier 2 studies, tri-trophic feeding assays with different prey items were used to characterize risk. In the first assay, five-day old *O. insidiosus* nymphs were exposed to mCry51Aa2 fed *S. frugiperda*. No adverse effects were observed, which was likely because the protein concentration in *S. frugiperda* was below the NOEC established for five-day old *O. insidiosus* nymphs. In a second tier 2 study, one-day old *Orius* spp. nymphs were exposed to MON 88702 fed *T. urticae* and significant effects on nymph survival and development were observed. This was presumed to be due to the higher mCry51Aa2 protein concentration in *T. urticae*. This feeding assay was repeated with five-day old *O. majusculus* nymphs and survival was not significantly different between MON 88702 fed *T. urticae* exposed nymphs, and those not exposed to mCry51Aa2. Thus, one-day old nymphs were more sensitive to the mCry51Aa2 protein than the five-day old nymphs.

Based on tier 2 study findings, tier 3 leaf disk assays, and a field study (tier 4) were conducted to determine the potential risks to *O. insidiosus*. The tier 3 study was a tri-trophic feeding study that provided one-day old *O. insidiosus* nymphs with two prey items in a leaf disk assay (MON 88702 fed *T. urticae* and *E. kuehniella* eggs). This refinement reflected more realistic exposure scenarios for a

generalist predator such as *Orius* spp. No adverse effects of MON 88702 on one-day old *O. insidiosus* nymphs were observed.

The tier 4 field study represented a range of environmental and agronomic conditions under which MON 88702 could be cultivated. Hemipteran predators, including *Orius* spp., were present and abundant at multiple sites, and were able to feed on any available food source (prey or plant tissue). The combined-site analysis showed no differences in abundance for *Orius* spp. (nymphs or adults, sampled throughout the entire growing season) between MON 88702 and DP393 (control) cotton (Monsanto 2019). Findings from these studies indicate and there is a low risk for adverse effects to *Orius* populations under realistic exposure conditions to the mCry51Aa2 protein expressed in MON 88702 cotton (Monsanto 2019).

Predatory Hemiptera closely related to *Orius* spp.—*Geocoris punctipes*, *Nabis alternatus*, and *Zelus renardii*—were also monitored in a tier 4 field study. No impacts on survival of these three genera from exposure to the mCry51Aa2 protein were observed. The results of the tier 4 field study found that there was no adverse effect of MON 88702 cotton on the abundance of *Geocoris* spp., *Nabis* spp. or *Zelus* spp. (US-EPA 2018b; Monsanto 2019).

Aquatic Invertebrates

Exposure of aquatic organisms to mCry51Aa2 is unlikely; movement of MON 88702 cotton plant material beyond the field in which it is planted into nearby water bodies is not expected to be significant. Considering mCry51Aa2 has a DT50 of 4.7 days in soils, and a maximum estimated DT90 of 74.5 days (US-EPA 2018b; Monsanto 2019), risks to aquatic insects via runoff, both freshwater and marine/estuarine, are not anticipated.

Summary

Susceptibility testing indicates that the introduced mCry51Aa2 protein in MON 88702 cotton primarily affects target insect pests among the orders Hemiptera (*Lygus* spp.; lygus bugs), Thysanoptera (*Frankliniella* spp., thrips), and limited non-target pest species of within the order Coleoptera (*Leptinotarsa* spp., *Diabrotica* spp.; beetles), family Chrysomelidae (leaf beetles). Across all NTOs assessed, no significant hazards to NTO populations were identified. Studies indicate that there is a low risk for adverse effects to *Orius* spp., or other predatory Hemiptera (*Geocoris* spp., *Nabis* spp. and *Zelus* spp.) under realistic exposure conditions to the mCry51Aa2 protein expressed in MON 88702 cotton (Monsanto 2019). Adverse effects of mCry51Aa2 protein on non-target ladybird beetles, rove beetles, parasitic wasps, and bees were not observed in bioassays with artificial diet, and are not expected (US-EPA 2018b; Monsanto 2019). The EPA concluded that, based on an ecological risk assessment, the weight of evidence supports low risk for *Zelus* spp. upon commercial cultivation of MON 88702 cotton (US-EPA 2020b). The EPA also found that the risk to predatory Hemiptera to be low upon commercial cultivation of MON 88702 cotton (US-EPA 2020b).

Based on the data evaluated, APHIS concluded that exposure to and/or consumption of the mCry51Aa2 protein in MON 88702 cotton is unlikely to have a significant adverse impact on non-target organisms beneficial to agriculture. Impacts on non-target organisms are expected to be restricted to groups of species related to the target hemipteran and thysanoperan pests. Effects on predator coleopteran species (beetles) are possible, but not highly likely. Effects on predator *Orius* spp. are possible, namely juveniles,

although, based on Tier 1-3 feeding assay and Tier 4 field studies presented by Monsanto (Bachman et al. 2017; Monsanto 2019), a negative impact at the population level is considered unlikely.

Because MON 88702 cotton production may require fewer foliar insecticide applications, this would—relative to non-IR crops—be considered of benefit to non-target organisms. However, if adoption of MON 8702 causes resurgence of any secondary pests, due to reduced competition by target pests, by a reduced efficacy of the natural enemy community, or even reduced opportunistic predation by thrips (Trichilo and Leigh 1986; D'Ambrosio et al. 2020b) or *Lygus* (Rosenheim et al. 2004), then insecticide sprays may not decrease as expected.

Although no significant differences in arthropod abundance were found, a few caveats with the data are noted. First, a power analysis is provided that calculates the ability to detect a 50% difference, but when reductions in the target pest are approximately 40-60%, then perhaps a lower percentage should be used for examining effects to non-target species (USDA-APHIS 2019). Second, there are some inherent difficulties in drawing definitive conclusions from field sampling data. An example is that seasonality effects are not included in the analyses. Another example is time of day for collecting samples; some arthropods are more active at different times of day, or even nocturnal. Similarly, as to what time of the day/night sampling occurs can affect the conclusions drawn (i.e., diurnal bias). Further, if there were low-level lethal effects or sublethal effects on predator/parasitoid species, with potential cumulative effects on populations and community structures, it would be difficult to conduct a study to detect these effects. APHIS acknowledges that field studies examining potential impacts on non-target insect populations, communities, and trophic interactions can be complex, and data should be interpreted bearing the inherent limitations of field studies, as well as laboratory based bioassays (e.g., lack of real world feeding behaviors in the field, predator-prey interactions, trophic effects), in mind.

The EPA has evaluated and registered the mCry51Aa2 protein in MON 88702 cotton under FIFRA section 3(c)(5). On January 11, 2017, EPA issued an Experimental Use Permit (EUP) to Monsanto under FIFRA section 5, to allow for field trials of the cotton plant-incorporated protectant (PIP), and issued a temporary tolerance exemption for mCry51Aa2 for the duration of the EUP (40 CFR §174.536) (US-EPA 2018b). The registration was time limited for two years and have a cumulative annual planting cap of 40,000 acres in the continental United States and Puerto Rico, as well as a cumulative annual planting cap of 2,000 acres per county. After reviewing data and information provided by Monsanto, and publicly available sources, EPA concluded that, for limited EUP issued, MON 88702 cotton would not cause any unreasonable adverse effects to human health or the environment, and that there is reasonable certainty that no harm to the U.S. population would result from aggregate exposure to the mCry51Aa2 protein (US-EPA 2018b). The EPA registered MON 88702 x MON 15985 x COT 102, for breeding purposes/seed production, in April, 2020 (US-EPA 2020a).

4.3.3.3 Plant Communities

The agronomic practices and inputs that will be used for MON 88702 cotton/progeny production are the same as those for other GE and non-GE cotton varieties (apart from minor reduced insecticide use). Thus, the potential impacts on vegetation proximate to fields of MON 88702 cotton/progeny would not substantially differ. As with all conventional and GE cotton crop production, relative to the particular herbicides used and application practices, herbicide spray drift/volatilization may inadvertently impact non-target plants proximate to MON 88702 cotton/progeny fields. In addition, based on the activity

spectrum studies for the mCry51Aa2 in MON 88702 cotton, no effects are expected on pollinators such as honey bees based on tier 1 assays with honey bee larvae and adults. Likewise, mCry51Aa2 is unlikely to have activity against pollinators that are caterpillars or moths as there was no activity detected in larvae of four species from three families of lepidopteran pests (reviewed above in 4.3.3.2.1–Non-Target Organisms). Therefore pollinator services in vegetation adjacent to MON 88702 cotton/progeny fields are unlikely to be impacted.

4.3.3.4 Gene Flow and Weediness

MON 88702 cotton is agronomically and phenotypically (apart from the IR trait) comparable to currently cultivated upland cotton varieties and would present the same potential risk for gene flow, specifically the propensity and frequency of gene flow. Accordingly, MON 88702 cotton and its progeny would not be expected to present more or less risk for gene flow to wild relative species as do current cotton varieties. Based on data summarized below, that there is low potential for introgression of transgenes from MON 88702 cotton into wild relative species (USDA-APHIS 2019). While outcrossing is possible, significant impacts on wild cotton populations are unlikely to occur based on the following factors.

Gene Flow

Upland cotton, *G. hirsutum* L., is known to have sexually compatible wild relative species in the form of indigenous and feral populations of *G. hirsutum* and *G. barbadense* L. in the Florida Keys, Puerto Rico, Hawaii, and the U.S. Virgin Islands (Wozniak and Martinez 2011; Coppens d'Eeckenbrugge and Lacape 2014). Both species are capable of interbreeding with each other (Brubaker and Wendel 1994; Wozniak and Martinez 2011). Therefore, outcrossing and gene introgression in areas where these species are co-located is possible. In Puerto Rico, Hawaii, and the U.S. Virgin Islands, there is no commercial cultivation of cotton, thus, there is no risk for outcrossing in these areas. In Florida, the naturalized populations of *G. hirsutum* are far removed from the panhandle area—northwest Florida— where cotton is commercially grown (Dehart 2013; Wunderlin et al. 2019).

G. tomentosum (Hawaiian cotton) is endemic to the Hawaiian archipelago; present on all of the main Hawaiian Islands except Hawaii and Kauai. Upland (*G. hirsutum*) and Hawaiian (*G. tomentosum*) cotton can crossbreed—interspecific hybrids are easily formed and are fully fertile however, genetic breakdown occurs in second generation hybrids (F2) giving rise to hybrids of low viability. No information was found to indicate that hybrids of *G. tomentosum* and *G. hirsutum* are considered weedy or invasive (US-EPA 2001; Wozniak and Martinez 2011; Coppens d'Eeckenbrugge and Lacape 2014). Because there is no commercial cotton cultivation in Hawaii, and APHIS has no record showing that seed companies use the Hawaiian Islands as a cotton winter nursery (USDA-APHIS 2019), gene introgression from MON 88702 cotton to Hawaiian populations of *G. tomentosum* is considered highly improbable. As discussed in Chapter 3, hybrids of *G. hirsutum* and *G. thurberi* (Arizona cotton) would be sterile and unable to reproduce.

Outcrossing rates reported for upland cotton are relatively low, even at short distances from neighboring fields in commercial settings (Van Deynze et al. 2011). Generally, gene flow is less than 1% at distances beyond 10 m, although can be detected at very low levels (<0.05%) at distances up to 1625 m (1 mile) (Llewellyn et al. 2007; Van Deynze et al. 2011). In general, buffers of 20 m of conventional cotton surrounding GE fields, if needed, prove to be highly effective in isolating GE cotton crops, unless bee or other pollinator numbers are unusually high (Llewellyn et al. 2007).

The current FIFRA registration for mCry51Aa2, which expires January 31, 2021, prescribes the following restrictions (US-EPA 2019o):

- a) No planting of MON 88702 (mCry51Aa2) × MON 15985 × COT102 cotton is permitted south of Route 60 (near Tampa) in Florida.
- b) Experimental plots and breeding nurseries of MON 88702 × MON 15985 × COT102 cotton are prohibited on the U.S. Virgin Islands and Hawaii.
- c) Test plots or breeding nurseries, regardless of plot size, established on the island of Puerto Rico may only be established without restriction if insecticide applications are used to effectively mitigate gene flow. Otherwise, established test plots or breeding nurseries, regardless of plot size, established on the island of Puerto Rico must not be planted within three miles of feral cotton and must be surrounded by 24 border rows of a suitable pollinator trap crop, and
- d) Harvested seed are not allowed for sale as commercial seed in the U.S. under the current terms of this registration, but any seed containing MON 88702 × MON 15985 × COT102 may be handled in accordance with legal and regulatory requirements.

It is anticipated the future FIFRA registrations for mCry51Aa2 would impose similar restrictions.

Considering all these factors, and that EPA imposes strict geographical restrictions on the sale and distribution of Bt cotton in order to mitigate the potential for gene flow to wild populations of *Gossypium* species (US-EPA 2019m), gene flow from MON 88702 cotton to wild relative species is not likely to occur.

Weediness

As reviewed in Chapter 3, in suitable areas, such as southern Florida, Hawaii, and Puerto Rico, upland cotton can become locally feral or naturalize. However, *G. hirsutum* does not possess any of the attributes commonly associated with weeds, such as the production of highly persistent seeds, the ability to readily spread and invade habitats, or become a dominant competitive species in areas outside of cultivation (USDA-APHIS 2019). Cotton has been grown throughout the world without any reports that it occurs as a problematic weedy plant. The occurrence of feral or naturalized cotton populations in the United States appears to be extremely rare. The expression of the mCry51Aa2 protein and resulting insect resistance in MON 88702 cotton is unlikely to have a meaningful impact on weediness potential (USDA-APHIS 2019).

4.3.3.5 Biodiversity

There are no risk to vertebrate taxa presented by the mCry51Aa2 protein (US-EPA 2018b, e). As discussed in 4.3.3.2.1–Non-Target Organisms, the mCry51Aa2 trait protein is unlikely to present significant risks to communities of non-target species, or plant, fungal, or bacterial communities (US-EPA 2018b; Monsanto 2019). Bt based crop plants, while insecticidal, are still considered more environmentally benign than broad-spectrum synthetic chemical insecticides commonly used in on non-IR cotton crops (Storer et al. 2008; Koch et al. 2015). For cotton, the most common foliar applied chemical insecticides are broad-spectrum organophosphates, neonicotinoids, and pyrethroids (see Table

3-6). While synthetic chemical insecticides are used on all Bt crops, as discussed in 3.1.2.4–Pest and Pest Resistance Management, the average applications per crop cycle are typically reduced. Any reduction in broad-spectrum chemical insecticide applications will help conserve populations of beneficial insects, and avoid impacts on non-pest insect populations. Other benefits include potential reductions in insecticides in runoff and emissions of NAAQS air pollutants.

The EPA registered a MON 88702 x MON15985 x COT102 stacked-trait product in 2020 (US-EPA 2020a). COT102 produces the Bt Vip3Aa19 protein and MON15985 produces the Cry1Ac and Cry2Ab2 proteins. Vip3Aa19 protein targets the lepidopteran pests tobacco budworm (*Heliothis virescens*), cotton bollworm (*Helicoverpa zea*), and pink bollworm (*Pectinophora gossypiella*) (Liu et al. 2007). Cry1Ac targets the lepidopteran pest tobacco budworm (*Heliothis virescens*) and pink bollworm (*Pectinophora gossypiella*), and Cry2Ab2 the lepidopteran pest beet armyworm (*Spodoptera exigua*) and fall armyworm (*Spodoptera frugiperda*) (Sivasupramaniam et al. 2008). Thus, MON 88702 progeny (MON 88702 x MON15985 x COT102 stacked-trait product) would potentially provide protection against thrips, lygus bugs (tarnished plant bugs), bollworms, tobacco budworm, and armyworm.

Bt delta-endotoxins have largely proven to have a spectrum of activity to a limited number of species within certain orders of insects (Ahmad et al. 2006; Bravo et al. 2007; Sivasupramaniam et al. 2008; Hilbeck and Otto 2015; Bachman et al. 2017). Cry1Ac type proteins primarily affect Lepidoptera, and to a much lesser extent some species of Coleoptera (7 species), Hemiptera (8 species), Hymenoptera (8 species), and Diptera (2 species); Cry2Ab2 type proteins primarily affect Lepidoptera, and a limited number species of Coleoptera (1 species), Hemiptera (1 species), Neuroptera (1 species), and Diptera (3 species) (van Frankenhuyzen 2013). Species outside of these insect orders are not directly affected. By contrast, the spectrum of activity of most conventional insecticides is considerably broader (see Table 3-6). Growers will commonly use a single insecticide that will control multiple pest species so that they will not need multiple applications of different insecticides to achieve the same insect control (Storer et al. 2008).

Considering these factors, production of MON 88702 cotton/progeny would likely, to some degree, present fewer risks to biodiversity in areas proximate to MON 88702 cotton/progeny fields relative to non-IR cotton crop production systems utilizing broad-spectrum synthetic chemical insecticides. The production of MON 88702 cotton/progeny would be expected to affect biodiversity in and around MON 88702 cotton hybrid crops similar to other IR cotton cropping systems, with minor transient differences in the targeted insect populations affected (thrips, lygus bugs (tarnished plant bugs), bollworms, tobacco budworm, and armyworm), and predator-prey relationships.

4.3.4 Human Health and Worker Safety

There are no risks to public health that would derive from approval of the petition for MON 88702 cotton. Numerous safety studies on mammals and other animals conducted over the past 40 years have found that Bt-derived insecticidal toxins are non-hazardous to vertebrate taxa (McClintock et al. 1995; Bravo et al. 2007; Adel-Patient et al. 2011; Koch et al. 2015; Andreassen et al. 2016; Farmer et al. 2017). Monsanto consulted with FDA on MON 88702 cotton (BNF 000160) in September 2018. The FDA found that MON 88702 cotton does not raise any safety or regulatory issues with respect to its uses in human or animal food (US-FDA 2019). The EPA concluded that there is a reasonable certainty no harm to the U.S. population will result from aggregate exposure to the mCry51Aa2 protein, including infants and children

(US-EPA 2018b). The mCry51Aa2 protein was registered under FIFRA section 3(c)(5)(US-EPA 2018b). The EPA issued an exemption from the requirement of a tolerance for residues of Cry51Aa2.834_16 protein in or on cotton (US-EPA 2018e). All pesticides used with MON 88702 cotton would need to comply with EPA requirements (Section 1.3 – Coordinated Framework for the Regulation of Biotechnology). Reductions in insecticide use with MON 88702 cotton would be of benefit to worker safety.

The National Bioengineered Food Disclosure Law, passed by Congress in July of 2016, directed USDA to establish this national mandatory standard for disclosing foods that are or may be bioengineered. The implementation date of the Standard is January 1, 2020, except for small food manufacturers, whose implementation date is January 1, 2021. The mandatory compliance date is January 1, 2022. Regulated entities may voluntarily comply with the Standard until December 31, 2021. The Standard requires food manufacturers, importers, and certain retailers to ensure bioengineered foods are appropriately disclosed. It is expected that any food products derived from MON 88702 cotton would require labeling, and consumers would choose to consume such foods based on preference.

It is noted that Cry proteins are generally not detected in refined cottonseed oil—the only part of cotton seed consumed by humans. For example, quantitative expression data for Cry proteins in transgenic cotton plants and processed products have been previously evaluated. Expression data for Cry1F and Cry1Ac protein were evaluated in young leaves, squares, flowers, boll, whole plant, pollen, nectar, root, seed, and cottonseed process fractions consisting of kernel, hulls, meal, and oil. The Cry1Ac and Cry1F proteins were detected in all matrices except nectar, meal, oil, and hulls (Health-Canada 2005; US-EPA 2005b).

4.3.5 Animal Health and Welfare

Processing of cottonseed provides cottonseed meal, cottonseed hulls, and whole cottonseed that can be utilized in the animal feed industry as sources of protein and fiber. Cottonseed meal can be fed to ruminant animals such as cattle, goats, and sheep, as well as poultry. Many cattle producers also use whole cottonseed as a supplement for beef and dairy cattle. The hulls are used in feeds for cattle, sheep, and goats. As discussed for human health, based on Monsanto's FDA consultation, and EPA registration and tolerance exemption for the mCry51Aa2 protein, there is not risk to animal health and welfare that would derive from approval of the petition.

Monsanto provided data on compositional assessments comparing MON 88702 cotton with non-GE cotton. Thirty components, including major nutrients of cottonseed (protein, amino acids, total fat, carbohydrates, linoleic acid, acid detergent fiber (ADF), neutral detergent fiber (NDF) and ash), as well as the anti-nutrients included here were assessed (Monsanto 2019). Apart from the modified Cry trait, there are no compositional or nutritional differences between MON 88702 and non-GE cotton varieties. The FDA agreed with Monsanto's conclusion that MON 88702 cotton does not raise any safety or nutritional issues with respect to its uses in human or animal food (US-FDA 2019).

4.3.6 Socioeconomics

4.3.6.1 Domestic Economy

Approval of the petition and eventual production of MON 88702 cotton/progeny would have no effect on cotton commodities markets, or trade of U.S. cotton commodities. Hybrid stacked-trait IR progeny derived from MON 88702 would be used by growers for production and trade of standard cotton commodities—fiber, linters, hulls, cottonseed oil, and meal.

Monsanto registered a MON 88702 x MON 15985 x COT 102 stacked-trait product with EPA in 2020, which is intended to provide protection against thrips, lygus bugs (tarnished plant bugs), bollworms, tobacco budworm, and armyworm. Yield losses and economic impacts from these pests can be substantial. In 2018, yield losses to insects amounted to costs totaling \$567,047,283; around \$42.45/acre (Williams 2019). The highest yield losses were associated with a bollworm/budworm complex (1.16%), lygus bugs (0.66%), stink bugs (0.27% + 0.37%), spider mites (0.27%), thrips (0.24%), and cotton fleahoppers (0.21%) (Williams 2019). MON 88702 cotton progeny, were it adopted, would be expected to replace GE IR cotton varieties currently cultivated, commensurate with benefits MON 88702 cotton progeny provided growers in pest management. The expected efficacy provided by MON 88702 cotton hybrids in the management of thrips and tarnished plant bugs, in addition to bollworms, tobacco budworm, and armyworm, achievement of optimal yields, and reduced reliance on synthetic chemical insecticides (Graham and Stewart 2018) would collectively be expected to have positive effects on grower net returns and cotton commodities market prices. As discussed in Chapter 3, due to efficacies in pest control and achievement of optimal yields GE IR cotton has been found to provide, in general, average farm income benefits around \$111/hectare (\$45/acre) (Brookes and Barfoot 2018).

Thrips have historically been controlled through a combination of seed treatment and foliar insecticides, however, development of resistance in some populations to both pyrethroid and organophosphate insecticides (Bielza 2008), as well as neonicotinoids, has made these pests more difficult to control (Huseth et al. 2016; Hesler et al. 2018). Historically, lygus bugs have been controlled by broad spectrum insecticides such as organophosphates, carbamates, and pyrethroids; however, development of resistance to these insecticides has been steadily increasing in lygus populations since the mid-1990s (Snodgrass 1996; Parys et al. 2015). Resistance to pyrethroids among lygus was first observed in 1993 in the Mississippi Delta (Snodgrass 1996). Resistance to pyrethroids and organophosphates is now widespread in many areas of the mid-south (Gore et al. 2012). Additionally, some lygus populations exhibit cross-resistance to organophosphate and carbamate insecticides.

Increased resistance to pyrethroids and organophosphates resulted in an increased use of neonicotinoid insecticides for lygus insect control in cotton during pre-flowering and flowering stages. However, neonicotinoid usage may be associated with declines in honey bee (*Aphis mellifera* Linnaeus) and other insect pollinator populations (Woodcock et al. 2017). Pollinator population decline and the potential causes are of great concern (Stewart et al. 2014; Luttrell et al. 2015), prompting a ban of neonicotinoid use in several countries (Woodcock et al. 2017; North et al. 2019). In the United States, EPA announced in May of 2019 that the registrations for 12 of the total of 59 neonicotinoid-based insecticide products (e.g., those containing the active ingredients clothianidin, imidacloprid, thiamethoxam) would be canceled (US-EPA 2019a).

Studies by Graham and Stewart (2018) found there was a 181 kg/hectare (73.3 kg/acre) increase in cotton yield with Bt Cry51Aa2 cotton due to thrips protection. This type of increase is consistent with a meta-analysis by North (2016) who reported a 127 kg/ha (51.4 kg/acre) increase in yield when a neonicotinoid seed treatment was used in cotton. This yield increase demonstrates the potential importance of mCry51Aa2 for management of thrips, particularly when considering the documented occurrence of thrips resistance to neonicotinoid insecticides (Darnell et al. 2015; Huseeth et al. 2016).

Of consideration: Pest control provided by natural predator and parasitoid insects is an essential ecosystem service. For croplands, biological control of pests is valued at around \$24 billion per year worldwide (Costanza et al. 1997). In addition to functioning as biological controls for crop pests, insects provide pollination for more than two-thirds of the world's cultivated plant species (Costanza et al. 1997). The value of the pollination services has been estimated to be between \$5 billion and \$14 billion per year in the United States alone (Southwick and Southwick Jr 1992; Morse and Calderone 2000), from which a large proportion is attributed to native insect pollinators (Losey and Vaughan 2006; González et al. 2016). As discussed in 4.3.3—Biological Resources, insect biodiversity can be impacted by agronomic practices and inputs; by pesticide use, PIPs in GE crops, and mono-cropping.

While MON 88702 cotton would reduce populations of certain species of Hemiptera and Thysanoptera, and progeny populations of Hemiptera, Thysanoptera, and Lepidoptera, which could have some cascading/trophic effects on predator/parasitoid populations (Chaplin-Kramer et al. 2011; Letourneau et al. 2011; González et al. 2016), this would not be expected to have long-term deleterious effects on beneficial insect populations in areas adjacent to MON 88702 cotton/progeny fields. As to the new mCry51Aa2 trait, there are no obligate lygus or thrips predators. For example, minute pirate bugs feed on thrips, as well as aphids, spider mites, psyllids, whiteflies, small caterpillars, and insect eggs (UMD 2020). Adult and nymph damsel bugs will eat lygus bugs, aphids, mites, caterpillars, other insect nymphs, larvae and eggs, and occasionally feed on other predators (Ramirez and Patterson 2011). Bigeyed bugs feed on a wide variety of prey smaller than themselves. They are among the most important natural enemies in cotton. They feed on eggs and small larvae of most lepidopteran pests (bollworm, pink bollworm, tobacco budworm), on the eggs and nymphs of plant bugs (e.g., lygus), and on all life stages of whiteflies, mites, and aphids (Hagler 2020). Adult green lacewing feed mostly on nectar, pollen, and honeydew but some species the adults will feed on insects. Green lacewing larvae feed on thrips, and a variety of soft-bodied insects like aphids, insect eggs, mealybugs, immature whiteflies, psyllids, small caterpillars, and some beetles (UC-IPM 2015a; Bessin 2019). Spiders eat a wide variety of insects. Although the combined lethal and sublethal effects of the mCry51Aa2 protein on target organisms may lead to shifts in species composition at the community level, predator-prey relationships, and/or food webs, these types of effects on insect communities are expected to result in adaptive responses, as opposed to leading to detrimental outcomes on insect community structures and populations. As previously discussed, GE Bt crop varieties tend to result in higher insect biodiversity, when compared to crops lacking a Bt trait that are treated with synthetic chemical insecticides (Carpenter 2011; NAS 2016).

Secondary pest outbreaks can potentially occur when the use of a pesticide (to include PIPs such as Cry proteins) to reduce densities of an unwanted target pest species triggers subsequent outbreaks of other pest species. With Bt crops, it may be possible that once the primary pest is brought under control, secondary pests have a chance to emerge due to the lower pesticide applications in Bt cotton cultivars (Zhao et al. 2011). Pests not controlled by the Bt traits can emerge as problems, especially the sucking

bug complex (e.g., thrips) (Trapero et al. 2016). Control of increased sucking bug populations with pesticides can in turn cause a reduction in beneficial invertebrate populations, allowing other secondary pests to increase and require control (Naranjo 2011; Wilson et al. 2013; Trapero et al. 2016). Control of both the sucking bug complex and secondary pests is problematic due to the cost of pesticides and/or high risk of selecting for pesticide resistance (Trapero et al. 2016). While the emergence of secondary pest populations are reported, field studies/data on the development of such populations are scarce (Gross and Rosenheim 2011; Trapero et al. 2016). Of the few studies available, Gross and Rosenheim (2011) estimated the cost of these late-season pesticide applications caused by early-season pesticide treatment for *Lygus* to be around \$6.00 per acre (SE = \$1.30 per acre).

If adoption of MON 88702 cotton/progeny causes resurgence of any secondary pests (Gross and Rosenheim 2011; Zhao et al. 2011), either due to reduced competition by targeted pests or reduced efficacy of the natural enemy community, or even reduced opportunistic predation by thrips (Trichilo and Leigh 1986; D'Ambrosio et al. 2020a) or lygus bugs (Cleveland 1997; Rosenheim et al. 2004), then insecticide sprays may not decrease as much as expected. However, there is no reason to expect that insecticide sprays will increase above what is currently applied (USDA-APHIS 2019). It is expected that the introduction on MON 88702 cotton, as well IR progeny, will likely result in at least some reduction in insecticide use, although due to incomplete control of lygus bugs and thrips, in addition to the other cotton pests not affected by mCry51Aa2, insecticide usage will not be eliminated from cotton production practices.

4.3.6.2 International Trade

Approval of the petition is not expected to have any effect on the trade of cotton based fiber, food, feed, or industrial products. Primary cotton exports include the fiber, whole seeds, oil, and meal/cake. The degree of foreign acceptance of GE cotton can affect international trade and may create the need to segregate and identify GE cotton products. As with the trade of most all GE crop commodities, there exist the potential for low level presence (LLP) occurring in countries importing U.S. agricultural commodities. The issue of asynchronous approval (AA), and resulting LLP situations, can lead to trade delays, shipment rejection, and costs to traders (FAO 2014). International trade is facilitated by the World Trade Organization (WTO) and the Organization for Economic Cooperation and Development (OECD) (FAO 2019; OECD 2019). Standards and guidelines for the safety evaluation and trade of GE crop commodities are established under international policy and agreements such as the Codex Alimentarius (FAO/WHO 2019), the WTO International Plant Protection Convention (FAO 2019), WTO Sanitary and Phytosanitary Measures (WTO 2019b), WTO Technical Barriers to Trade Agreement (WTO 2019a), and the Cartagena Protocol on Biosafety (CBD 2019a).

Commodities derived from MON 88702 cotton progeny would be subject to the same international regulatory requirements, discussed above, as currently traded cotton commodities. Food based commodities would be subject to Codex standards, and perhaps other safety standards, relative to importing country requirements. GE cotton products that are not used for food or feed are not subject to safety approval, labeling requirements, or GE free private standards in major importing countries. For example, neither Japan nor the European Union directly regulate textile products derived from GE cotton. As far as imports of cotton products into the EU are concerned, official statistics do not distinguish between imports of GE and non-GE raw cotton, intermediate products such as cotton fiber and fabrics, or GE and non-GE finished products, e.g., garments and household linen (EU 2008). On the other hand,

organic cotton is subject to organic standards requirements (e.g., USDA National Organic Program), and may be subject to identity preservation (IP), dependent on the commodity.

In general, developers have various legal, quality control, and marketing motivations to implement rigorous stewardship measures to ensure IP, prevent commingling, and avoid AP and LLP. By necessity, all international regulatory and industry standards and requirements must be met for marketing of MON 88702 cotton commodities. Monsanto implements a product stewardship program through participation in Excellence Through Stewardship® (ETS). Monsanto's stewardship principles are also implemented through Monsanto Technology Stewardship Agreements that are signed by growers who utilize Monsanto branded traits to ensure stewardship compliance (Monsanto 2019). As an integral action of fulfilling this stewardship commitment, Monsanto states they will seek biotechnology regulatory approvals for MON 88702 cotton in all cotton import countries to assure global compliance, and support the flow of international trade in cotton and cotton by-products (Monsanto 2019).

5 CUMULATIVE IMPACTS

CEQ NEPA implementing regulations (40 CFR 1508.7) define a cumulative impact as an “impact on the environment which results from the incremental impact of the action when added to other past, present, and reasonably foreseeable future actions regardless of what agency [federal or non-federal] or person undertakes such other actions”. Emissions of air pollutants from a multitude of individual sources is an example of a cumulative environmental impact.

5.1 Assumptions and Uncertainties

If there are no direct or indirect impacts associated with those aspects of the human environment discussed in Chapter 4, APHIS assumes there can be no cumulative impacts. Further assumptions and uncertainties that are part of evaluation of potential cumulative impacts are summarized as follows.

MON 88702 cotton will not be used for production of cotton commodities, directly; its purpose is for breeding of IR cotton hybrids and seed production. As previously discussed in Chapter 4, Monsanto registered a MON 88702 x MON 15985 (expressing Cry1Ac & Cry2Ab2) x COT 102 (expressing Vip3Aa19) stacked-trait variety in 2020. This variety is intended to provide protection against the insect pests: tobacco budworm, pink bollworm, beet armyworm, and cotton bollworm, as well as thrips and lygus bugs. MON 88702 cotton and any progeny derived from it could also be combined with other nonregulated GE varieties through traditional breeding techniques. For example, MON 88702 cotton/progeny could be crossed with other nonregulated herbicide resistant cotton varieties, insect resistant, and/or disease resistant varieties.

It is assumed that these types of conventionally crossed stacked-trait varieties would be produced only as a result of their potential utility; to expand grower choice and production efficiencies in the management of plant pests, pathogens, and agricultural weeds. To date, in commercial agriculture, up to 3 Bt (Cry, VIP) toxins have been combined in a single cultivar, with in combination with up to 3 HR traits (see Table 4-4).

The adoption level of crossbred progeny of MON 88702 cotton would depend on the extent to which producers valued the traits offered by such stacked-trait cotton varieties, and the pricing and production efficiencies, as well as the availability of such stacked-trait/pyramided cotton, relative to other GE IR and GE IR/HR cotton varieties.

5.2 Acreage and Areas of Cotton Production

The commercial availability of MON 88702 cotton stacked-trait, or “pyramided” hybrid cotton varieties, would have no effect on the acreage or area devoted to cotton production in the United States, thus there are no reasonably foreseeable cumulative impacts on corn acreage, or the areas of corn production, that would derive from approval of the petition.

5.3 Agronomic Practices and Inputs Used in Cotton Production

As discussed in Chapter 3 and Chapter 4, Bt crops have provided agronomic benefits via effective, targeted pest control, reduced insecticide use, and area-wide suppression of targeted plant pest (NAS 2016; Dively et al. 2018). MON 88702 x MON 15985 x COT 102 hybrids would be expected to provide similar benefits to growers in the potential suppression of cotton bollworm (*Helicoverpa zea*), tobacco

budworm (*Heliothis virescens*), pink bollworm (*Pectinophora gossypiella*), beet armyworm (*Spodoptera exigua*), and fall armyworm (*Spodoptera frugiperda*), relative to non-IR cotton varieties. The potential for area-wide suppression of thrips (*Frankliniella* spp.) and plant bugs (*Lygus hesperus* and *Lygus lineolaris*) is less certain. It was found that mCry51Aa2 protein does not cause a high level of mortality in tarnished plant bugs, and that some tarnished plant bug nymphs survived to larger nymph stages (Graham and Stewart 2018). For larger nymphs and adults, mortality at field-relevant mCry51Aa2 exposure levels required about 6 days (Baum et al. 2012). The mCry51Aa2 trait primarily appears to have an anti-feedant effect on thrips, as opposed to lethality; these insects tend to avoid MON 88702 cotton after first feeding, as well as avoid oviposition (D'Ambrosio et al. 2020a; Huseh and DA 2020). Similarly, adult tarnished plant bug exhibited a non-preference for a diet containing lyophilized mCry51Aa2 leaves and for excised mCry51Aa2 squares in choice tests with non-Bt squares.

As with synthetic chemical pesticides, insects are capable of developing resistance to Bt based insecticidal proteins, which are used in organic and conventional crops, as well GE crops, for control of insect pests. Currently registered Cry PIPs for cotton include Cry1Ab, Cry1Ac, Cry1F, Cry2Ab2, Cry2Ae, Cry51Aa2.834_16 (the PIP in MON 88702 cotton), FLCry1Ab, and Vip3Aa19 (US-EPA 2018c). Some populations of cotton bollworm (*Helicoverpa armigera*) have exhibited resistance to Cry1Ac, Cry2Ab2, and Cry1F (Few and Kerns 2019). Field-evolved resistance by corn rootworm to GE Cry3Bb1 corn, GE mCry3A corn, and GE eCry3.1Ab corn has been documented in multiple Midwestern states (Gassmann et al. 2016; Jakka et al. 2016), and cross-resistance among Cry3Bb1, mCry3A, and eCry3.1Ab has also been reported (Jakka et al. 2016). However, instances of insect resistance to the Vip3A Bt toxin have not been reported.

Sustaining the efficacy of transgenic Cry based crops—as well Bt preparations (powder, sprays), which are used in organic and conventional crops—is a primary concern among growers, industry, and the federal government. The EPA places a high value on the efficacy of IR crops (the PIPs, such as Cry proteins) and preserving their agricultural and environmental benefits (US-EPA 2019i). To counter the development of insect resistance EPA has mandated the implementation of an Insect Resistance Management (IRM) plan for each commercially registered PIP that provides insect resistance. The goal of IRM is to prevent the onset of resistance, while acknowledging that it may not be possible to entirely prevent resistance from evolving. Insect resistance management requirements for MON 88702 cotton/progeny would be the same as those for other Bt crops (US-EPA 2019i). Registrants of Bt PIPs are required to annually monitor pest populations for indications that resistance may be developing among the key target pests (US-EPA 2019i). The specific monitoring strategies employed for Bt PIPs are described in EPA's Biopesticide Registration Action Documents (BRADs). Bt registrants are required to submit an annual report describing their resistance monitoring activities, including reports of unexpected damage, pest sampling, and bioassay results.

5.4 Physical Environment

Production of cotton entails the use of pesticides, fertilizers, and tillage, which can contribute to cumulative impacts on water, soil, and air quality. The agronomic practices and inputs that would be used in the cultivation of MON 88702 cotton/progeny, and the contribution to the cumulative impacts of these practices and inputs on water, soil, and air quality, would be similar to that of currently cultivated cotton varieties. Any contribution to beneficial cumulative impacts are expected to be marginal, possibly negligible improvements soil and water quality since estimates were only to reduce insecticide treatments

by 1.25 application per crop cycle (Graham and Stewart 2018), in part due to the relatively low efficacy in control of lygus bugs. In general, other GE IR cotton varieties have, at least initially, performed better, due to greater lethality of the Cry traits. If secondary pest outbreaks occur it could actually result in a no gain situation or worse, if additional insecticides are used to control those pests.

5.4.1 Soils

Any contribution to cumulative impacts on soil quality resulting from cultivation of MON 88702 cotton and progeny would be the same as or similar to that of other IR cotton varieties currently cultivated. Relative to non-IR cotton cropping systems, reductions in insecticide use would contribute in a cumulative manner to reducing potential impacts on soils, such as compaction and soil fertility.

5.4.2 Water Quality

Cumulative impacts on water resources derive from point source and non-point source (NPS) pollutants. NPS contaminants in runoff originate from sources such as construction sites (e.g., residential and commercial development, construction of roads/highways), impervious surfaces (parking lots, roads/highways, rooftops), and crop fields and livestock rearing facilities. NPS pollutants include pesticides applied to residential, commercial, and agricultural sites, and sediments from the built environment as well as unmanaged landscapes. As discussed in 3.2.2–Water Resources, the most common NPS contaminants in agricultural run-off are sediment, nutrients such as nitrogen and phosphorus, and pesticides, all of which can adversely affect aquatic ecosystems.

Point source pollutants are discharged from any identifiable, singular source, such as a pipe, drain, conduit, or vessel. Factories and sewage treatment plants are examples of point sources. Factories, including oil refineries, pulp/paper mills, and chemical, electronics, and automobile manufacturers typically discharge one or more pollutants in EPA regulated effluents. Some factories discharge effluents directly into a waterbody, others treat it themselves before it is released, and some send their wastes to sewage treatment plants. Livestock rearing facilities (e.g., dairy and beef cows, pigs, chickens) are another source of point source pollution. These types of operations are identified as concentrated animal feeding operations (CAFOs). Waste from agricultural livestock operations has been a long-standing concern with respect to contamination of water resources, particularly in terms of nutrient pollution, microbial pathogens, and pharmaceuticals present in the waste (Burkholder et al. 2007).

To control point source discharges, the Clean Water Act established the National Pollutant Discharge Elimination System (NPDES). Under the NPDES program, factories, CAFOs, sewage treatment plants, and other point sources must obtain a permit from the state and EPA before they can discharge their waste or effluents into any body of water. Prior to discharge, the point source must use the latest technologies available to treat its effluents and reduce the level of pollutants. If necessary, a second, more stringent set of controls can be placed on a point source to protect a specific waterbody.

As discussed in 3.2.2–Water Resource, tillage and agronomic inputs, on a regional scale, can and do contribute to the impairment of surface waters through soil erosion and runoff of pesticides and fertilizers (nutrients). Agricultural inputs can also impact groundwater through leaching. Agricultural runoff, to include from cotton fields, is a primary contributor to NPS pollutants that impact streams, rivers, lakes, and estuaries (US-EPA 2019b). Cultivation of MON 88702 cotton and progeny would potentially contribute to cumulative impacts on water quality as do other IR cropping systems. In general, MON

88702 x MON 15985 x COT 102 progeny production—targeting control of cotton bollworm (*Helicoverpa zea*), tobacco budworm (*Heliothis virescens*), pink bollworm (*Pectinophora gossypiella*), beet armyworm (*Spodoptera exigua*), and fall armyworm (*Spodoptera frugiperda*), thrips (*Frankliniella* spp.), and plant bugs (*Lygus hesperus* and *Lygus lineolaris*)—would likely contribute to reductions in insecticide use, to some extent, in areas where cotton is grown, which could be of benefit to surface and groundwater resources.

Currently, approximately 92% of cotton acreage is comprised of GE IR varieties. MON 88702 cotton hybrids are expected to replace other GE IR cotton varieties in the event of adoption (no increase in acreage); thus, increased contribution to sediment, pesticides, and nutrients in run-off in areas where MON 88702 cotton progeny is grown is not expected.

Cotton growers in the southeast impacted by development of HR weed populations are by necessity having to diversify their weed management strategies (Smith 2010). Many growers who adopted no-till production are now resorting to increased tillage in their weed management programs. Growers in Arkansas, California, Georgia, Louisiana, Mississippi, Missouri, and Texas, have been using more tillage to manage HR weeds (e.g., see (Smith 2010)). Increased tillage may have the potential to impact soil erosional capacity, and thereby water quality. If MON 88702 cotton/progeny were used to develop IR/HR hybrids, such hybrids would not be expected to present any greater or lesser risk for development of HR weed populations than current GE and non-GE conventional crops. Successful management of development of HR weeds, and extant HR weed populations, are relative to the IWM strategies employed in cultivation of crops, principally the integration of diversified non-chemical control strategies. As discussed in 3.1.2.3—Weed and Herbicide Resistant Weed Management, development of HR weed populations is not a recent concern, nor is it unique to GE crops. Herbicide resistant weed populations have been occurring since the advent and wide-spread use of chemical herbicides in the 1950s.

To mitigate the cumulative impacts of agriculture on water resources various national and regional efforts have been instituted to reduce NPS contaminants in agricultural run-off, and run-off itself (US-EPA 2019e; USDA-NRCS 2019c). For example, the Mississippi River/Gulf of Mexico Watershed Nutrient Task Force seeks to reduce nutrients in runoff from agricultural sites by coordinating and supporting nutrient management activities (US-EPA 2019e). In 2012, the USDA Natural Resources Conservation Service (NRCS) launched the National Water Quality Initiative (NWQI), in collaboration with EPA and state water quality agencies, to reduce nonpoint sources of nutrients, sediment, and pathogens related to agriculture in high-priority watersheds in each state (USDA-NRCS 2019c).

5.4.3 Air Quality

Air pollution is inherently a problem resulting from the cumulative emissions of various sources. The EPA has categorized primary emissions sources into: point, mobile, biogenic, and area. Point sources include major industrial facilities such as chemical plants, oil refineries, and power plants. Mobile sources include cars, trucks and buses and off-road equipment such as ships, airplanes, and agricultural and construction equipment. Area sources are defined as smaller operations such as dry cleaners and gas stations. Biogenic sources are comprised of vegetation, soils, and animals.

The Clean Air Act (CAA) establishes a number of permitting programs designed to carry out the goals of the Act. Some of these programs are directly implemented by EPA through its Regional Offices but most

are carried out by states, local agencies, and approved tribes. As discussed in 3.2.3–Air Quality, EPA establishes NAAQS pursuant to the CAA that are intended to protect public health and the environment. The EPA has also identified over 187 HAPs, including substances that cause cancer, neurological, respiratory, and reproductive effects. While EPA establishes NAAQS, the standards do not set emission control requirements for any particular industry, including agriculture. The USDA and EPA provide guidance for regional, state, and local regulatory agencies, and farmers, on how to best manage agricultural emissions sources. Agricultural emission sources include: PM from tillage and agricultural burning; CO₂, NO₂, SO₂ from fossil fuel consumption associated with equipment used in tillage, pesticide application, and harvest; and soil nitrous oxide (N₂O) emissions from the use of fertilizers/manure. Volatilization of pesticides can also be a concern.

Because there would be no increase in acreage resulting from MON 88702 cotton hybrid production, nor changes to emission sources (i.e., tillage, fossil fuel burning equipment, the application of fertilizers and pesticides), cumulative effects on emissions of NAAQS pollutants would be similar to what currently occurs. If MON 88702 cotton/progeny were produced, air quality would continue to be affected along current trends by emission sources such as tillage (PM), pesticide application (aerosols, spray drift), and use of farm equipment that combusts fossil fuels (NAAQS pollutants). The EPA and USDA efforts to reduce emissions, along with state and local efforts would likewise continue (USDA-EPA 2012). As with water quality, relative to non-IR cotton varieties, as a result of reduced insecticide use, MON 88702 cotton would contribute to reducing emissions from U.S. cropping systems.

5.5 Biological Resources

Considering that discussed in Chapter 4, EPA registration review data (US-EPA 2018b), that provided by Monsanto (Monsanto 2019), and that mCry51Aa2 is exempt from the requirement for a tolerance in or on cotton (US-EPA 2018e), MON 88702 cotton nor its progeny (MON 88702 x MON 15985 x COT 102) would be expected to present any risk to vertebrate taxa. There are no contributions to cumulative impacts on biological resources, beyond those already known to occur with cotton and other crop production (discussed in Chapter 3 and 4), that would derive from cultivation of MON 88702 cotton and progeny. Neither MON 88702 cotton nor progeny would result in any change in agronomic practices or inputs used to cultivate cotton, with exception of possibly reduced reliance on chemical insecticides as compared to non-IR cotton varieties.

There are some minor concerns in regard to the effect of stacked-trait and pyramided GE IR crop varieties on insect populations/community dynamics. However, as discussed below, it is unlikely that cultivation of MON 88702 cotton based IR stacked-trait/pyramided hybrids would contribute in a cumulative manner to adversely affecting local or regional insect ecology.

5.5.1 Stacked-Trait and Pyramided Bt Crop Varieties: Ecological Considerations

Developers commonly combine crop varieties with traits for resistance to different pests, such as among the orders Lepidoptera and Coleoptera. A pyramided variety could include two or more traits targeting the same pest. For example, the Cry1Ac and Vip3Aa19 traits, which will be introduced into MON 88702 cotton progeny via traditional breeding, both target pink bollworm (*Pectinophora gossypiella*). The spectrum of activity for the Cry1A (tobacco budworm (*Heliothis virescens*) and pink bollworm (*Pectinophora gossypiella*)) and Cry2Ab2 (beet armyworm (*Spodoptera exigua*) and fall armyworm (*Spodoptera frugiperda*)) proteins are specific for certain Lepidoptera species, although the combined

activity of the Cry1Ac and Cry2Ab2 proteins has previously been shown to be additive (see review by (Levine et al. 2016)). GE crop varieties with pyramided traits producing two or more Bt toxins that target the same insect pest have been widely used to delay/prevent the development of insect resistance (US-EPA 2018c, 2019i). This is because pyramided traits are considered more durable and less at risk for insects developing resistance, as compared to varieties that contain only one Bt toxin (US-EPA 2019i). MON 88702 cotton hybrids could be generated comprised of pyramided or/and stacked Cry/Vip trait genes (as well as herbicide resistant traits).

While the bulk of studies have not identified any significant ecological risks associated with introduced Cry and Vip traits (e.g., see Koch et al. (2015) and Yu et al. (2011), and EPA Biopesticides Registration Action Documents (US-EPA 2018c)), there has been some concern as to the potential ecological impacts of increased use of stacked-trait and pyramided Bt crop varieties on non-target organisms (Brévault et al. 2013; Hilbeck and Otto 2015; Latham et al. 2017). This derives from the spatiotemporal scale on which stacked-trait and pyramided Bt crops are increasingly cultivated, the increasing number and diversity of insecticidal traits in Bt crops (e.g., up to 3 IR PIPs in cotton, currently), and prolonged exposure of non-target insects to combinations of these traits (as compared to Bt foliar applied sprays). Ecological concerns include cumulative lethal effects, sublethal effects on development and fitness, and perhaps behavioral changes (Hilbeck and Otto 2015; Latham et al. 2017). Combined effects could comprise synergistic, antagonistic, and additive effects among introduced PIPs. Potential combined effects could also include interactions of PIP toxins with naturally occurring plant-, bacteria-, or insect-compounds that are encountered by non-target organisms feeding on stacked-trait GE IR plants.

5.5.1.1 Commercialization and Safety Assessment of MON 88702 cotton Hybrids

When MON 88702 cotton (mCry51Aa2) is used to create stacked-trait/pyramided hybrids via breeding with other GE IR cottons (e.g., with 3, 4, or 5 insecticidal proteins), it is theoretically possible that additive or synergistic effects could occur, potentially increasing the range of insects affected. Some uncertainty exists in this area due to data gaps, mainly in relation to potential adverse effects on non-target genera, and the activity and specificity of modified Cry proteins (Brévault et al. 2013; Hilbeck and Otto 2015; Latham et al. 2017). The insect populations that occur in cotton fields, and most likely affected by the introduced Cry1Ac, Cry2Ab2, Vip3Aa19, and mCry51Aa2 traits, would be among the orders Hemiptera, Lepidoptera, and Thysanoptera (US-EPA 2007, 2008, 2018b).

The EPA has previously reviewed and registered Cry1Ac, Cry2Ab2, and Vip3Aa19 as PIPs in cotton (US-EPA 2003, 2005a, 2008). In 2003 EPA registered Bollgard II cotton (MON15985), comprised of Cry1Ac and Cry2Ab (US-EPA 2003). In 2008, EPA issued a conditional registration for COT102 (Vip3Aa19)(US-EPA 2008). In 2018, EPA registered Bollgard III cotton (COT102 × MON 15985), comprised of Cry1Ac, Cry2Ab2, and Vip3Aa19 (US-EPA 2018a).

Relative to potential synergistic/additive effects among PIPs, based on its registration review EPA found no evidence of either a synergistic or antagonistic interaction between Vip3Aa19 and modified Cry1Ab (US-EPA 2008). Whitehouse et al. (2005) found only a subtle shift in arthropod communities between Bollgard II (Cry1Ac and Cry2Ab) and conventional cotton, which was concluded to likely derive from a reduction in *Helicoverpa* and other lepidopteran species. Evaluations of Bollgard II (Cry1Ac, Cry2A) and Bollgard III (Cry1Ac, Cry2Ab2, Vip3Aa19) found no overall significant difference in invertebrate communities between these cotton crops (Whitehouse et al. 2007; Levine et al. 2016). In individual

qualitative site assessments of arthropods, no differences were observed between Bollgard III and the conventional control for all arthropod species examined; these included aphids, boll weevils, fleahoppers, white flies, grasshoppers, spider mites, stink bugs, and thrips (Levine et al. 2016).

Any future stacked-trait/pyramided hybrids of MON 88702 cotton, comprised of newly developed Bt toxins, would likewise be reviewed and registered under FIFRA provided they meet EPA’s criteria. It is expected that the potential combinatorial effects of stacked-trait/pyramided hybrids would be evaluated by EPA on a case-by-case basis.

These factors considered, hemipteran, lepidopteran, thysanopteran, and other orders of insect pests targeted by Cry/Vip proteins are currently controlled in non-IR crops by the use of synthetic chemical insecticides that have less specificity, impacting a much broader range of insect genera. In this respect, considering current data discussed above, it is unlikely that the spectrum of insecticidal activity of mCry51Aa2 protein in combination with Cry1Ac, Cry2Ab2, and Vip3Aa19 proteins would exceed that of synthetic chemical insecticides. For example, in 2017, there were around 17 different insecticides applied to cotton, at a total of 4,469,000 lbs a.i./year. Among these were pyrethroids, organophosphates, neonicotinoids, hormone mimics/growth regulators, and nicotinic acetylcholine receptor (nAChR) modulators (prior Table 3-6). Broad-spectrum insecticides include most neonicotinoids, organophosphates, pyrethroids, and carbamates. Common insecticides and use rates for control of lygus bugs and thrips are in Table 5-1.

Insecticide	Chemical Class	Use Rate (lbs a.i./year)	Rate (lbs a.i./acre)	Percentage of Total Use	Target Pests
Imidacloprid	Neonicotinoid	204,000	0.17	11%	lygus bug, aphids
Bifenthrin	Pyrethroid	267,000	0.16	15%	lygus bug, whiteflies, beet armyworm, looper
Diclotophos	Organophosphate	525,000	0.53	9%	aphids, thrips, stink bugs and plantbugs
Acephate	Organophosphate	3,101,000	1.08	25%	thrips, lygus bug, loopers, whiteflies

* This is an approximation of total insecticide use. Not all use data is reported for each year, and each insecticide. Source: (USDA-NASS 2019d)

Based on current threshold recommendations for tarnished plant bug, one to seven insecticide applications are needed to manage tarnished plant bug depending on the year and test location (Graham and Stewart 2018). On average, based on field trials, Bt Cr51Aa2 cotton required 1.25 fewer insecticide applications for tarnished plant bug than non-Bt cotton (Graham and Stewart 2018). The use of the m Cry51Aa2 trait, particularly in areas with high tarnished plant bug pressure, may reduce the total number of insecticide applications made during the growing season (Graham and Stewart 2018). However, proper scouting and timely applications of insecticides are still needed to manage tarnished plant bug (Graham and Stewart 2018).

5.5.2 Gene Flow and Weediness

The risk of gene flow and weediness with MON 88702 cotton, as well as hybrids developed from MON 88702 cotton, is no more or less than that of conventional cotton varieties (USDA-APHIS 2019). Future MON 88702 cotton hybrids could be comprised of 2 or more trait genes, and if produced commercially, add in a cumulative manner to the diversity of stacked-trait/pyramided genes in U.S. cotton fields. Theoretically, an increase in the diversity and number of trait genes in U.S. cotton fields that could be

transferred to wild relatives could increase the risk for gene flow, the risk for occurrence. However, this theoretical increase in risk is unlikely to arise. MON 88702 cotton progeny, stacked-trait/pyramided hybrids, would be expected to replace currently cultivated varieties, as opposed to increasing acreage. Thus, given that around 98% of cotton acres are already comprised of GE cotton varieties, increases in the diversity and number of GE trait genes extant in U.S. cotton fields, as a result of adoption of MON 88702 cotton progeny in the coming years, would be expected to be minor. Generally, the most efficacious Cry and Vip traits would likely be utilized in lieu of those with less specificity/insecticidal activity, as well as traits with which insect resistance issues have arisen. Thus, it is expected that some of the extant Cry/Vip traits will be substituted with newer modified Cry/Vip varieties introduced in the future (currently, there no Cyt toxins that target cotton pests). Considering these factors, and that MON 88702 cotton/progeny present no more or less risk for risk of gene flow than that of conventional and other GE cotton varieties, cumulative impacts on the risk of gene flow from cultivated to wild/feral *Gossypium* spp. is considered unlikely.

5.6 Human and Animal Health

There were no risks to public health or worker safety identified in Chapter 4 that differ from the production of other cotton crops. Consequently, there are no potential cumulative effects on human or animal health that would derive from approval of the petition, and subsequent commercial use of MON 88702 cotton.

Any MON 88702 cotton hybrids that were intended for use in food and feed commodities would need to comply with FDA food and feed safety requirements. It is expected that FDA would be consulted in regard to any MON 88702 cotton hybrids with newly introduced traits as to the food/feed safety, prior to introduction to commercial markets.

5.7 Socioeconomics

The efficacy provided by MON 88702 cotton hybrids in the management of thrips, plant bugs, and lepidopteran plant pests, achievement of optimal yields, and reduced reliance on synthetic chemical insecticides would be expected to have positive effects on grower net returns and cotton commodities market prices. MON 88702 cotton varieties, in combination with current and future IR crops utilizing differing PIP MOAs (e.g., RNAi) could potentially contribute to keeping the cost of cotton production limited via effective insect pest control (discussed below) and sustaining of optimal yields. The EPA recently banned 12 products containing neonicotinoid insecticides, and future uses of neonicotinoids may be further restricted due adverse impacts bee populations (Blacquiere et al. 2012; Morfin et al. 2019). It follows, Cry/ /Vip PIPs, and RNAi based PIPs, are of increasing value in controlling problematic cotton pests. Considering the costs of insect pest control in cotton crop production, and potential impacts of pests on yield (Section 3.1.2.4—Pest and Pest Resistance Management), the cost of cotton crop commodities to consumers could, as a consequence, remain competitively priced.

In general, the average farm income benefit from GE IR cotton is reported to be around \$107/hectare (\$43/acre) (Brookes and Barfoot 2018). In 2016, at the aggregate level, the global gross farm income gains from using GE IR cotton was \$3.7 billion. Cumulatively, since 1996, the gains are reported to be \$54 billion for GE IR cotton cropping systems (Brookes and Barfoot 2018).

5.7.1 Insect and Insect Resistance Management Costs

One of the economic benefits derived from IR cotton varieties is the area-wide suppression of insect pest populations (NAS 2016; Dively et al. 2018). As discussed in 3.1.2.4–Pest and Pest Resistance Management, in 2018, yield to insects amounted to costs totaling \$567 million; around \$42.45/acre (Williams 2019). The highest yield losses were associated with a bollworm/budworm complex (1.16%), lygus bugs (0.66%), stink bugs (0.27% + 0.37%), spider mites (0.27%), thrips (0.24%), and cotton fleahoppers (0.21%). Foliar insecticide costs, nationwide, amounted to \$361,856,425, or \$27.09/acre (Williams 2019). In areas where cultivation of IR corn and IR cotton is high, the use of IR crop varieties has been associated with reduced insecticide use in adjacent cropping systems cultivating non-IR varieties, a result of the area-wide suppression of insect pest populations (NAS 2016). For example, a 10-year study in 15 regions across Arizona shows that Bt cotton suppressed pink bollworm (*Pectinophora gossypiella*) independent of demographic effects of weather and variation among regions. Pink bollworm population density declined only in regions where Bt cotton was abundant. Such long-term suppression has not been observed with insecticide sprays, showing that transgenic crops open new avenues for pest control (Carrière et al. 2003). Adoption of Bt cotton in China suppressed pink bollworm [*Pectinophora gossypiella* (Saunders)] and cotton bollworm [*Helicoverpa armigera* (Hübner)] populations in non-Bt cotton (Wu et al. 2008; Wan et al. 2012). Bt cotton adoption also suppressed cotton bollworm larval density in other host crops (Wu et al. 2008). Using data spanning 1976–2016, (Dively et al. 2018) demonstrated that vegetable growers benefited via decreased crop damage and insecticide applications in relation to pest suppression in the Mid-Atlantic United States. The authors provided evidence for the regional suppression of European corn borer (*Ostrinia nubilalis* (Hübner)) and corn earworm (*Helicoverpa zea* (Boddie)) populations in association with widespread Bt corn adoption (1996–2016).

Thus, cultivation of MON 88702 cotton progeny could potentially contribute in a cumulative manner to reducing, to some extent, pest management costs in nearby crops, as have other GE IR cotton varieties. This would be primarily for Lepidoptera pests, as suppression of thrips and lygus bugs would be less likely due to the non-lethal, primarily avoidance type effects on thrips and lygus, of the mCry51Aa2 trait on these species (Graham et al. 2019; D'Ambrosio et al. 2020b; D'Ambrosio et al. 2020a).

As discussed in Section 5.3 above, MON 88702 cotton progeny could, to some extent, potentially help preserve the efficacy of certain foliar applied synthetic chemical insecticides by limiting their use (Table 3-6), and thereby the risk of insect pests developing resistance. While this is conceptually a potential beneficial outcome of utilizing MON 88702 cotton hybrids (in combination with other stacked-trait/pyramided IR hybrids), reductions in insecticide use would likely be minimal.

6 THREATENED AND ENDANGERED SPECIES

The Endangered Species Act (ESA) of 1973, as amended, is a far-reaching wildlife conservation law. Congress passed the ESA to prevent extinctions facing many species of fish, wildlife and plants. The purpose of the ESA is to conserve endangered and threatened species and the ecosystems on which they depend as key components of America's heritage. The U.S. Fish & Wildlife Service (USFWS) and the National Marine Fisheries Service (NMFS) together comprise "the Services" and implement the ESA by working with other federal, state, and local agencies, Tribes, non-governmental organizations, and private citizens.

Before a plant or animal species can receive the protection provided by the ESA, it must be added to the federal list of threatened and endangered wildlife and plants. Threatened and endangered (T&E) species are those plants and animals at risk of becoming extinct throughout all or part of their geographic ranges (endangered species) or species likely to become endangered in the foreseeable future throughout all or a significant portion of their ranges (threatened species).

The Services add a species to the list when they determine the species to be endangered or threatened because of any of the following factors:

- The present or threatened destruction, modification, or curtailment of its habitat or range;
- Overutilization for commercial, recreational, scientific, or educational purposes;
- Disease or predation;
- The inadequacy of existing regulatory mechanisms; and
- The natural or manmade factors affecting its survival.

Once a species is added to the list, in accordance with the ESA, protective measures apply to the species and its habitat. These measures include protection from adverse effects of federal activities.

6.1 Requirements for Federal Agencies

Section 7(a)(2) of the ESA requires that federal agencies, in consultation with USFWS and/or the NMFS, ensure that any action they authorize, fund, or carry out is "not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat." It is the responsibility of the federal agency taking the action to assess the effects of their action and to consult with the USFWS and NMFS if it is determined that the action "may affect" listed species or designated critical habitat (a process is known as a Section 7 Consultation).

To facilitate the development of its ESA consultation requirements, APHIS met with the USFWS from 1999 to 2003 to discuss factors relevant to APHIS' regulatory authority and effects analysis for petitions for nonregulated status of GE crop lines. By working with USFWS, APHIS developed a process for conducting an effects determination consistent with the Plant Protection Act (PPA) of 2000 (Title IV of Public Law 106-224). APHIS uses this process to help fulfill its obligations and responsibilities under Section 7 of the ESA for biotechnology regulatory actions.

As discussed in Chapters 1 and 2, APHIS regulatory authority over GE organisms under the PPA is limited to those instances when there are reasons to believe a GE organism could pose a plant pest risk, or

when the Agency does not have sufficient information to determine that a GE organism is unlikely to pose a plant pest risk. Monsanto has requested that APHIS determine that MON 88702 cotton is not a plant pest as defined in 7 CFR part 340. If APHIS concludes from its PPRA that MON 88702 cotton does not pose a plant pest risk, then it is not subject to the plant pest provisions of the PPA, the regulations at 7 CFR part 340, and the Agency would have no authority to regulate MON 88702 cotton.

As discussed in Chapter 4, Monsanto MON 88702 cotton will be used to generate stacked-trait IR cotton varieties. Monsanto registered a MON 88702 x MON 15985 x COT 102 stacked-trait product with EPA in 2020. MON 15985 and COT 102 cotton have been previously reviewed by APHIS for potential effects on TES (USDA-APHIS 2020). For this EA, APHIS analyzed the potential effects of MON 88702 cotton on listed T&E species, those proposed for designation as threatened or endangered, and critical habitats of listed or proposed T&E species. For the analysis, APHIS thoroughly reviewed data related to the transgene/transgenic plant, and supporting data related to the organism for possible ESA effects.

For each transgene/transgenic plant petition, APHIS considers the following:

- A review of the biology, taxonomy, and weediness potential of the crop plant and its sexually compatible relatives;
- Characterization of each transgene with respect to its structure and function and the nature of the organism from which it was obtained;
- A determination of where the new transgene and its products (if any) are produced in the plant and their quantity;
- A review of the agronomic performance of the plant including disease and pest susceptibilities, weediness potential, and agronomic and environmental impact;
- Determination of the concentrations of known plant toxicants (if any are known in the plant); and
- Analysis to determine if the transgenic plant is sexually compatible with any T&E species or a host of any T&E species.
- Any other information that may inform the potential for an organism to pose a plant pest risk.

APHIS met with USFWS officials on June 15, 2011, to discuss and clarify whether APHIS has any obligations under the ESA regarding analyzing the effects on T&E species that may occur from the use of pesticides associated with GE crops. As a result of these joint discussions, USFWS and APHIS have agreed that it is not necessary for APHIS to perform an ESA effects analysis on pesticide use associated with GE crops because EPA has both regulatory authority over the labeling of pesticides under FIFRA, and the necessary technical expertise to assess pesticide effects on the environment. APHIS has no statutory authority to authorize or regulate the use of pesticides by corn growers. Genetically engineered plant produced pesticides are termed plant incorporated protectants (PIPs) and regulated by EPA pursuant to the FIFRA. Under APHIS' 7 CFR part 340 regulations, APHIS has the authority to regulate a GE organism if the GE organism poses a plant pest risk. APHIS has no regulatory jurisdiction over any other risks associated with GE organisms, including risks resulting from the use of pesticides on those organisms.

6.2 Potential Effects of MON 88702 cotton on T&E Species and Critical Habitat

APHIS evaluated the potential effects that a determination of nonregulated status for MON 88702 cotton may have, if any, on federally listed TES and species proposed for listing, as well as designated critical habitat and habitat proposed for designation. As described in further detail elsewhere in this EA, in the petition (Monsanto 2019), Monsanto engineered MON 88702 cotton for resistance to certain insect pests among the order Hemiptera and Thysanoptera.

Based on the information submitted by the applicant and reviewed by APHIS, MON 88702 cotton, with the exception of insect resistance, is agronomically and compositionally comparable to conventional cotton (Monsanto 2019). The common agricultural practices that would be carried out in the cultivation of MON 88702 cotton are not expected to deviate from current practices, including the use of EPA-registered pesticides, with the possible exception that a slight reduction may occur in the number of insecticide applications to control the target lygus bugs and thrips.

The issues discussed herein focus on the potential environmental consequences of approving the request for nonregulated status of MON 88702 cotton on T&E species and critical habitat in the areas where cotton is currently cultivated. APHIS has determined that the agronomic characteristics and cultivation practices required for MON 88702 cotton are essentially indistinguishable from practices used to grow other cotton varieties. Although MON 88702 cotton may replace certain other varieties of cotton that are cultivated currently, APHIS does not expect the introduction of MON 88702 cotton to result in new cotton acres, or for this variety to be planted in areas that are not already devoted to cotton production. Accordingly, the issues discussed herein focus on the potential environmental consequences that a determination of nonregulated status for MON 88702 cotton would have on T&E species in the areas where cotton is currently grown. APHIS obtained and reviewed the USFWS list of T&E species (listed and proposed) for all states and U.S. territories where cotton is produced from the USFWS Environmental Conservation Online System (USFWS 2020a).

For its analysis on T&E plants and critical habitat, APHIS focused on: the agronomic differences between the regulated article and cotton varieties currently grown; the potential for increased weediness; and the potential for gene movement to native plants, listed species, and species proposed for listing.

For its analysis of potential effects on T&E animals, APHIS focused on the implications of exposure to the Bt derived Cry protein expressed in MON 88702 cotton, and the ability of the GE plants to serve as a host for a T&E species. The novel Cry protein produced by MON 88702 cotton is summarized in Table 6-1.

Table 6-1. Protein Produced by MON 88702 cotton that is Novel in Cotton

Regulated Article	Protein	Desired Phenotypic Effects	Additional Phenotypic Effects
<p>MON 88702 cotton</p>	<p>Modified Bt-derived Cry51Aa2 (assigned the unique name Cry51Aa2.834_16 and referred to as mCry51Aa2)</p>	<p>Protects against feeding damage caused by targeted hemipteran (<i>Lygus hesperus</i> and <i>Lygus lineolaris</i>) and thysanopteran (<i>Frankliniella</i> spp.) insect pests.</p>	<p>Exhibits insecticidal activity against two coleopteran insect pests, Colorado potato beetle (<i>Leptinotarsa decemlineata</i>) and corn rootworm (<i>Diabrotica undecimpunctata howardi</i>). Activity was observed against the hemipteran pest <i>Pseudatomoscelis seriatus</i>, although observed effects inconsistent and below commercial efficacy levels. Activity was also observed in one hemipteran predator species (<i>Orius insidiosus</i>), although this species was not adversely affected in Tier 3 and 4 studies at more relevant field level exposure scenarios, and two coleopteran species (<i>Leptinotarsa decemlineata</i> and <i>Diabrotica undecimpunctata howardi</i>).</p>

Source: (Monsanto 2019)

6.2.1 Threatened and Endangered Plant Species and Critical Habitat

The agronomic data provided by Monsanto were used in the APHIS analysis of the weediness potential for MON 88702 cotton (Monsanto 2019), and evaluated for the potential to impact T&E species and critical habitat. No substantive differences were detected between MON 88702 cotton and non-GE cotton in hardiness, persistence, seed dormancy, germination, or susceptibility to pests and diseases, other than the intended effect of resistance to insect pests (Subsection 4.3.1.2.1 – Pest and Pest Resistance Management). As discussed in Section 3.3.4–Gene Flow and Weediness of Cotton, and APHIS’ PPRA (USDA-APHIS 2019), due to domestication, there are no weed risks associated with cotton, although cotton can occur as volunteers or feral plants (USDA-APHIS 2015). The Global Invasive Species database has no *Gossypium* species listed as invasive weeds (ISSG 2019). Cotton has been cultivated around the globe without any report that it occurs as a serious weed or that it forms persistent feral populations. Volunteer or feral cotton plants can be easily controlled if needed, either with herbicides or manual removal.

APHIS evaluated the potential of MON 88702 cotton to cross with sexually compatible wild relative species, to include listed species. As discussed in Gene Flow and Weediness (Subsections 3.3.4 and 4.3.3.4), and summarized below, gene introgression from MON 88702 cotton to indigenous and feral populations of *Gossypium* species is considered highly improbable.

Upland cotton, *G. hirsutum* L., is known to have sexually compatible wild relative species in the form of indigenous and feral populations of *G. hirsutum* and *G. barbadense* L. in the Florida Keys, Puerto Rico, Hawaii, and the U.S. Virgin Islands (Wozniak and Martinez 2011; Coppens d'Eeckenbrugge and Lacape 2014). There is limited, restricted cultivation of cotton in Puerto Rico and Hawaii. APHIS is unaware of any cultivation of cotton in southern Florida or Virgin Islands. In Florida, the naturalized populations of *G. hirsutum* are far removed from the panhandle area—northwest Florida— where cotton is commercially grown (Dehart 2013; Wunderlin et al. 2019). *G. tomentosum* (Hawaiian cotton) is endemic to the Hawaiian archipelago; present on all of the main Hawaiian Islands except Hawaii and Kauai. Upland (*G. hirsutum*) and Hawaiian (*G. tomentosum*) cotton can crossbreed, however, genetic breakdown occurs in second generation hybrids (F₂) giving rise to hybrids of low viability. (Llewellyn et al. 2007). The EPA imposes geographical restrictions on the sale and distribution of Bt cotton in order to mitigate the potential for gene flow to wild populations of *Gossypium* species. For example, experimental plots and breeding nurseries of MON 88702 cotton are prohibited on the U.S. Virgin Islands and Hawaii (US-EPA 2018b). Test plots or breeding nurseries, regardless of plot size, established on the island of Puerto Rico may be established without restriction if insecticide applications are used to effectively mitigate gene flow. Otherwise, established test plots or breeding nurseries, regardless of plot size, established on the island of Puerto Rico must not be planted within three miles of feral cotton and must be surrounded by 24 border rows of a suitable pollinator trap crop (US-EPA 2018b). In general, buffers of 20 m of conventional cotton surrounding GE cotton fields, if needed, prove to be highly effective in isolating GE cotton crops, unless bee or other pollinator numbers are unusually high (US-EPA 2018d). As discussed in Chapter 3, hybrids of *G. hirsutum* and *G. thurberi* (Arizona cotton) would be sterile and unable to reproduce.

Based on all of these factors, APHIS determined that MON 88702 cotton will have no effect on T&E plant species or on critical habitat in the United States.

6.2.2 Threatened and Endangered Animal Species

T&E animal species that may be exposed to the GE components of MON 88702 cotton would include those that inhabit cotton fields and potentially feed on MON 88702 cotton. To identify potential effects on T&E animal species, APHIS evaluated the risks to them from consuming MON 88702 cotton.

Monsanto carried out a compositional assessment of MON 88702 cotton by comparing MON 88702 cottonseed to seed from conventional control varieties, and provided data on compositional assessments comparing MON 88702 cotton with non-GE cotton. Apart from the modified Cry trait, there are no compositional or nutritional differences between MON 88702 cotton and non-GE cotton varieties (Monsanto 2019). There is no evidence of allergenicity with MON 88702 cotton, and no evidence of an increased toxicity (Monsanto 2019). Therefore, APHIS concluded there is no increased risk of toxicity or allergenicity, either through direct consumption, or indirectly through biological food chains. The FDA agreed with Monsanto's conclusion that MON 88702 cotton does not raise any safety or nutritional issues with respect to its uses in human or animal food (Monsanto 2019; US-FDA 2019).

APHIS considered the potential for the production of mCry51Aa2 protein in MON 88702 cotton to impact invertebrate organisms. The *mCry51Aa2* gene was derived from the bacterium *Bacillus thuringiensis* (Bt), a bacterium that occurs naturally in soil. Cry proteins, such as mCry51Aa2, disrupt the lining of the midgut of certain insects causing leakage and death. Multiple structural categories of Cry

proteins exist. Each determines the mechanism by which the protein acts as an insecticide, and limits the insecticidal activity to certain taxa (Bravo et al. 2007; Pardo-López et al. 2013; van Frankenhuyzen 2013). Bt Cry proteins are typically toxic to only a limited range of insect orders (e.g., Cry 1, Lepidoptera; Cry 2, Lepidoptera and Diptera; Cry 3, Coleoptera; Cry4, Diptera). The toxicity of Bt crystalline proteins to susceptible insect larvae, but not to non-susceptible insects and other organisms (e.g., birds and mammals), results from the presence of receptors in the midgut that are highly specific for these proteins (Bravo et al. 2007; Pardo-López et al. 2013). Once activated by insect-specific proteases in the insect midgut, Cry proteins bind to cell surface receptors in the midgut. Such binding leads to the formation of pores in the cell membrane, osmotic disruption, cell lysis and insect death. The specific binding of Bt Cry proteins to midgut membrane receptors is a key determinant of pest specificity (Bravo et al. 2007; van Frankenhuyzen 2013).

As discussed in Chapter 4, feeding assay studies of the insecticidal activity of mCry51Aa2 protein on a spectrum of taxa showed that this protein demonstrated activity to select insect species in the orders Hemiptera (Miridae: *Lygus* spp., as well as *Pseudatomoscelis seriatus*), Thysanoptera (Thripidae: *Frankliniella* spp.) and two species in the order Coleoptera (Chrysomelidae: *Leptinotarsa decemlineata* and *Diabrotica undecimpunctata howardi*). Thus, susceptibility testing indicates that the introduced mCry51Aa2 protein in MON 88702 cotton primarily affects a limited number of target insect pests within the orders Hemiptera (which includes cicadas, aphids, planthoppers, leafhoppers, plant bugs, among others), Thysanoptera (thrips), and Coleoptera (family, Chrysomelidae, more commonly known as leaf beetles).

Accordingly, APHIS focused its review of the potential impacts of mCry51Aa2 on federally listed threatened and endangered hemipterans, thysanopterans, and coleopterans in the cotton growing regions of the United States. As one cannot quantify the sensitivity of newly expressed proteins directly on T&E species, APHIS' evaluation focused on the likelihood of exposure of T&E species to the Bt-endotoxin expressed in MON 88702 cotton. Exposure of T&E species to the Bt-based Cry protein in MON 88702 cotton plants is only likely if the species occurs in the areas where cotton is grown since cotton plant parts (seeds, pollen, and crop debris) are not readily transported long distances without human involvement. In addition, Bt crystals generally have low persistence (e.g. half-lives ranging from 0.5 to 4 days) in the environment, particularly in the presence of sunlight or high temperatures (Ujváry 2001). Laboratory studies of degradation of the mCry51Aa2 protein in multiple agricultural soil types showed a maximum estimated time of 4.7 days to 50% degradation and 74.5 days to 90% degradation (Monsanto 2019). The mCry51Aa2 protein would likely degrade, as any other protein, in the environment, which would reduce exposure to T&E species. While predatory T&E animal species located in cotton-growing areas could conceivably consume non-target prey organisms that might ingest MON 88702 cotton, data from laboratory experiments show that the concentrations of mCry51Aa2 protein in the prey organisms are far lower than observable effects levels (exposure through prey is expected to be about 25 – 50 micrograms/gram) and low in comparison to the amount in the cotton leaf or square tissue (Monsanto 2019; Section 4.3.3.2.1 – Non-Target Organisms). Therefore, any exposure to the mCry51Aa2 protein through predation on NTOs would be very low and would therefore not likely harm a T&E predator. T&E species Hemiptera, Thysanoptera, and Coleoptera species in the United States are listed in Table 6-2.

Table 6-2. Federally Listed and Proposed Hemipteran, Thysanopteran, and Coleopteran Species			
Scientific Name	Common Name	Family	Federal Listing
<i>Cicindelidia floridana</i>	Miami tiger beetle	Carabidae	E
<i>Elaphrus viridis</i>	Delta green ground beetle	Carabidae	T
<i>Rhadine exilis</i>	[no common name] Beetle	Carabidae	E
<i>Rhadine infernalis</i>	[no common name] Beetle	Carabidae	E
<i>Rhadine persephone</i>	Tooth Cave ground beetle	Carabidae	E
<i>Desmocerus californicus dimorphus</i>	Valley elderberry longhorn beetle	Cerambycidae	T
<i>Cicindela dorsalis</i>	Northeastern beach tiger beetle	Cicindelidae	T
<i>Cicindela nevadica lincolniana</i>	Salt Creek Tiger beetle	Cicindelidae	E
<i>Cicindela ohlone</i>	Ohlone tiger beetle	Cicindelidae	E
<i>Cicindela puritana</i>	Puritan tiger beetle	Cicindelidae	T
<i>Stygoparnus comalensis</i>	Comal Springs dryopid beetle	Dryopidae	E
<i>Heterelmis comalensis</i>	Comal Springs riffle beetle	Elmidae	E
<i>Brychius hungerfordi</i>	Hungerford's crawling water Beetle	Halipilidae	E
<i>Ambrysus amargosus</i>	Ash Meadows naucorid	Naucoridae	T
<i>Batrisodes venyivi</i>	Helotes mold beetle	Pselaphidae	E
<i>Texamaurops reddelli</i>	Kretschmarr Cave mold beetle	Pselaphidae	E
<i>Batrisodes texanus</i>	Coffin Cave mold beetle	Pselaphidae	E
<i>Dinacoma caseyi</i>	Casey's June Beetle	Scarabaeidae	E
<i>Polyphylla barbata</i>	Mount Hermon June beetle	Scarabaeidae	E
<i>Nicrophorus americanus</i>	American burying beetle	Silphidae	E

E = Endangered; T = Threatened

Source: (USFWS 2020a)

The sole known location of extant *Cicindelidia floridana* (Miami tiger beetle) exists in Miami-Dade County (USFWS 2016). Since GE cotton may not be grown in South Florida, this protected species will not be exposed to MON 88702 cotton or to the mCry51Aa2 protein.

To date, *Elaphrus viridis* (delta green ground beetle), of the Carabidae family, has only been found in the Jepson Prairie area in south-central Solano County, California, though there have been unconfirmed reports of the species in a wildlife preserve in the Sacramento Valley near Sutter Buttes. While the delta green ground beetle occurs throughout agricultural lands in the area, it appears to feed only on other insects, including springtails, chironomid midges, and larvae of other beetles (USFWS 2005). Upland cotton is not grown in Solano county or adjacent counties where known or suspected populations of this species exist (USDA-NASS 2019b).

Multiple federally protected beetles inhabit the caves and mesocaverns of the karst limestone landscape exclusively in Bexar County, Texas. This includes two from the Carabidae family (neither have a common name); *Rhadine exilis* is known from 51 caves and *Rhadine infernalis*, which is known from 39 caves. *Batrisodes venyivi* (Helotes mold beetle), from the Pselaphidae family, is known from 8 caves. These three species are small, essentially eyeless beetles (USFWS 2011b). Given that these three species are highly limited to the karst geomorphic areas, they would not likely

exist in or wander into proximity of cotton fields and would therefore not likely be exposed to MON 88702 cotton or the mCry51Aa2 protein. Cotton is not produced in Bexar County (USDA-NASS 2019b).

Three endangered beetle species of the Pselaphidae family, *Rhadine persephone* (Tooth Cave ground beetle), *Texamaurops reddelli* (Kretschmarr Cave mold beetle), and *Batrisodes texanus* (Coffin Cave mold beetle), are endemic to karst formations in Travis and Williamson counties, Texas. They spend their entire lives underground in the dark zones of caves, sinkholes, and other subterranean voids. They are presumably predators on other insects or other small arthropods (USFWS 1994b). Given their limitations to karst geomorphological areas, cave-dwelling life histories, and predatory nature, they would not be likely to encounter MON 88702 cotton or prey that would have fed on it, so would not be expected to directly or indirectly ingest it (or the mCry51Aa2 protein).

Desmocerus californicus dimorphus (Valley elderberry longhorn beetle) is nearly always found on or close to its host plant, red or blue elderberry (*Sambucus* spp.), along rivers and streams (USFWS 2019). Suitable habitats for this beetle species occur below 500 feet [150 m] in elevation across a range that spans much of the Central Valley of California; Valley elderberry (*Sambucus* spp.) shrubs or small trees located in moist, riparian ecosystems serve as the host plant for the listed threatened beetle. While its elderberry host does occur in upland areas, the highest occupancy of Valley elderberry longhorn beetles occurs in metapopulations along riparian communities associated with its host plant (USFWS 2019). Assessments demonstrated that the mCry51Aa2 protein has biological activity on certain beetles in the Chrysomelidae family (Bachman et al. 2017; Monsanto 2019). The Valley elderberry longhorn beetle resides within the Cerambycidae family, which is closely related to the Chrysomelidae family. However, Cerambycids feed on dry wood with low water content, while chrysomelids feed on leaves with high water content (Zachariassen et al. 2008). In California, upland cotton is grown in Merced, Kings, and Tulare Counties (USDA-NASS 2019b), which lie within the Central Valley. But the Valley elderberry longhorn beetle lives in close association with its obligate host, elderberry shrubs and trees, typically in riparian areas, and is therefore not likely to encounter cotton crops. In the event that it did, however, the mCry51Aa2 protein is primarily expressed in the leaves and squares of the MON 88702 cotton plant (Monsanto 2019), and as Cerambycids, the Valley elderberry longhorn beetle feeds on wood. Therefore, this beetle would not be expected to ingest the mCry51Aa2 protein in the unlikely event that it encountered cotton.

Cicindela dorsalis dorsalis (Northeastern beach tiger beetle), a member of the Cicindelidae family, historically ranged along the northeast Atlantic coast from Massachusetts to New Jersey and at sites along the Chesapeake Bay shoreline in Maryland and Virginia (USFWS 1994a). Northeastern beach tiger beetles spend their entire life in their beach habitat (USFWS 2011a) and scavenge on dead amphipods, crabs, and fish and prey on small amphipods, flies, or other beach arthropods (USFWS 1994). While populations of Northeastern beach tiger beetle are known to exist (USFWS 1994a) along the Chesapeake Bay shoreline, Virginia counties that also grow cotton (USDA-NASS 2017a), cotton is not grown on or typically adjacent to beach habitat. While the beetle can disperse tens of miles in search of habitat, and it could potentially alight in a cotton field, cotton is not a prominent crop in the region and any beetles encountering a cotton field would be expected to continue to seek out suitable beach habitat and would not likely remain in a cotton field. Further, as this beetle is a detritivore of sand-

dwelling invertebrates, it would not be expected to ingest the mCry51Aa2 protein in the unlikely event that it encountered MON 88702 cotton.

Cicindela nevadica lincolniana (Salt Creek tiger beetle) is limited to three (presumed) extant populations located within segments of the Little Salt Creek and adjacent remnants of saline wetlands in northern Lancaster County, Nebraska (Hogan 2016). Cotton is not produced in Nebraska (USDA-NASS 2019b).

Cicindela ohlone (Ohlone tiger beetle) is endemic to Santa Cruz County, California and only known from coastal terraces supporting patches of native grassland. Cotton is not produced in Santa Cruz County (USDA-NASS 2019b).

Cicindela puritana (Puritan tiger beetle) is a predatory beetle found on shoreline habitat, particularly sandy beaches, along the Connecticut River in New Hampshire, Massachusetts, and Connecticut, and along the eastern and western shores of Maryland in the Chesapeake Bay, within Calvert County and near the mouth of the Sassafras River in Kent and Cecil Counties (USFWS 1993). Cotton is not reported growing in any of the counties or states within which populations of this species are known to exist (USDA-NASS 2019b).

Stygoparnus comalensis (Comal Springs dryopid beetle), a member of the Dryopidae family, and *Heterelmis comalensis* (Comal Springs riffle beetle), a member of the Elmidae family of beetles, are both restricted to spring sites (and also the aquifer, in the case of Comal Springs dryopid beetle) within Comal and Hays County, Texas, where they spend their whole lifecycles within the spring and aquifer system. The diet of these beetles is not clearly known (USFWS 1997). Cotton is not produced in these counties (USDA-NASS 2019b).

Brychius hungerfordi (Hungerford's crawling water beetle), a member of the Halipilidae family, is known in the United States from five clean, clear streams in northern Lower Peninsular Michigan (USFWS 2006). No cotton is produced in Michigan (USDA-NASS 2019b).

Ambrysus amargosus (Ash Meadows naucorid), lives entirely in the flowing water associated with the Point of Rocks Springs located in Ash Meadows National Wildlife Refuge in Nye County, Nevada. This non-flying, aquatic insect clings to rocks in riffle habitat where it hunts its prey of aquatics and crustaceans (USFWS 1990, 2014a). There is no cotton grown in Nye County, Nevada (USDA-NASS 2019b).

Dinacoma caseyi (Casey's June beetle), a member of the Scarabaeidae family, is found only within an area of less than 800 acres (324 hectares (ha)) in southern Palm Springs, California (USFWS 2009a), which lies within Riverside County. Its preferred habitat consists of gravelly sand on disturbed, gently sloping depositional surfaces of alluvial fans, predominantly vegetated with native desert scrub vegetation, at the base of the Santa Rosa Mountains in the Coachella Valley Region (USFWS 2009a). The food source for its underground larvae is unknown, though other species of June beetles eat plant roots or detritus from plants or other organisms (USFWS 2009a). Some cotton is grown in Riverside County (USDA-NASS 2019b). In the Coachella Valley region, where all known and potential habitat for this species is located, agricultural production focuses on food crops such as grapes, dates, lemons, lettuce and corn, whereas cotton production occurs on the far eastern

reaches of the county near Blythe (Riverside-County 2019). Even if cotton were to be planted closer to Casey's June beetle habitat, crop land is not suitable for this species. Therefore, Casey's June beetle individuals are unlikely to enter a crop field or to encounter cotton and would therefore not be exposed to MON 88702 cotton or the mCry51Aa2 protein.

Polyphylla barbata (Mount Hermon June beetle), a member of the Scarabidae family, is currently known to live only in the Zayante sandhills of Santa Cruz County, California, in loose, sandy soil, preferably with widely spaced ponderosa pines and open sand surface, where it spends much of its life underground (USFWS 2009b). Cotton is not produced in Santa Cruz County (USDA-NASS 2019b).

Nicrophorus americanus (American burying beetle), a member of the Silphidae family, both larvae and adults, depend on carrion of dead animals for food and moisture (USFWS 2014b). This species had historically been found across much of the United States, but was only known at the time of listing in 1989 to exist in Block Island off the coast of Rhode Island and in eastern Oklahoma. Its range is now known to include nine states, as well as experimental populations in a tenth (USFWS 2020b). Its habitat requirements appear to vary but all require soil characteristics that allow the beetle to bury carrion, which excludes extremely xeric, saturated or loose sandy soils (USFWS 2014b). While the range of this species overlaps with cotton-production areas (USDA-NASS 2019b), it is not likely to coexist with agriculture and would not likely be found in cotton fields. Given its diet of animal tissue, it would not be expected to ingest cotton tissue in the event that it encountered it and would therefore not likely be exposed to MON 88702 cotton or the mCry51Aa2 protein.

APHIS also considered the possibility that MON 88702 cotton could serve as a host plant for a T&E species (i.e., a listed insect or other organism that may use the cotton plant to complete its lifecycle). A review of the T&E species list did not reveal any species that would be likely to use cotton as a host plant (USFWS 2020a). In summary, APHIS has determined that contact and ingestion of MON 88702 cotton plants or plant parts are unlikely to affect T&E species. There is no evidence of allergenicity with MON 88702 cotton, and no evidence of an increased toxicity. Therefore, APHIS concluded that there is no increased risk of toxicity or allergenicity impacts directly to animal species or indirectly through their biological food chains from contact with or feeding on MON 88702 cotton. Based on this analysis, APHIS concluded that contact with MON 88702 cotton plants or plant parts by T&E species is unlikely, and if it occurred, consumption would be unlikely and therefore would not have an effect on any listed T&E animal species or animal species proposed for listing.

6.2.3 Conclusion

After reviewing the possible effects of a determination of nonregulated status of MON 88702 cotton, APHIS has not identified any stressor that would or could affect the reproduction, numbers, or distribution of a listed T&E species or species proposed for listing. As a result, a detailed exposure analysis for individual species is not necessary. APHIS also considered the potential effect of a determination of nonregulated status of MON 88702 cotton on designated critical habitat or habitat proposed for designation. Compared to other cotton varieties that are currently in use, APHIS determined that MON 88702 cotton production would not differentially affect critical habitat. Like many crops, cotton has been selected for yield rather than its ability to compete and persist in the environment. MON 88702 cotton is not expected to outcompete other plants and persist outside of direct cultivation. Cotton is

not sexually compatible with, and does not serve as a host species for, any T&E species or species proposed for listing. There is no evidence that any T&E species or species proposed for listing will consume MON 88702 cotton, so APHIS concluded that they will not be subject to any allergic or toxic reactions.

Based on this evidence, APHIS has concluded that a determination of nonregulated status of MON 88702 cotton, and the corresponding environmental release of this cotton variety will have no effect on T&E listed species or species proposed for listing, and would not affect designated habitat or habitat proposed for designation. Because of this “no-effect” determination, consultation under Section 7(a)(2) of the ESA, or the concurrence of the USFWS or NMFS is not required.

7 CONSIDERATIONS OF FEDERAL AND STATE LAWS AND REGULATIONS, EXECUTIVE ORDERS, STANDARDS, AND TREATIES

7.1 Federal Laws and Regulations

The laws most relevant to APHIS determinations of regulatory status (7 CFR part 340) are the National Environmental Policy Act of 1969 (NEPA), the Clean Water Act of 1972 (CWA), the Safe Drinking Water Act of 1974 (SDWA), the Clean Air Act of 1970 (CAA), the Endangered Species Act of 1973 (ESA), and the National Historic Preservation Act of 1966 (NHPA). Compliance with the requirements of the ESA has been addressed in Chapter 6. Compliance with the requirements of NEPA, CWA, SDWA, CAA, and NHPA, are specifically addressed in the following subsections.

7.1.1 National Environmental Policy Act (NEPA)

NEPA (42 United States Code (U.S.C) 4321, *et seq.*) is designed to ensure transparency and communication of the possible environmental effects of federal actions prior to implementation. The Act and implementing regulations require federal agencies to document, in advance and in detail, the potential effects of their actions on the human environment, so as to ensure that there is a full understanding of the possible environmental outcomes of federal actions by both the decision-makers and the public. This EA documents the potential environmental outcomes of the alternatives considered, approval or denial of Monsanto's petition, consistent with the requirements of NEPA and Council on Environmental Quality implementing regulations at 40 CFR parts 1500-1508.

7.1.2 Clean Water Act, Safe Drinking Water Act, and Clean Air Act

The CAA, CWA, and SDWA authorize EPA to regulate air and water quality in the United States. Because MON 88702 cotton is agronomically equivalent to currently cultivated cotton varieties, the potential sources of impacts on water resources and air quality are the same under both the No Action and Preferred Alternatives. MON 88702 cotton production would entail the use of pesticides and fertilizers, and to some extent tillage, which will contribute to potential cumulative impacts on air quality, and potentially water quality. The sources and degree of potential impacts would generally be no different than that which occurs with current cotton production. As a GE IR crop there would be reductions in insecticide use, relative to non-Bt cotton, which would reduce use of fossil fuels in the machinery used for application, and thereby volume of fossil fuel based emissions. There would also be commensurate reductions in insecticide drift and volatilization from MON 88702 cotton crops. Runoff from MON 88702 cotton production fields would be comprised of lesser quantities of insecticides, reducing risks to surface waters and groundwater, as compared to non-IR cotton crops. APHIS assumes use of all pesticides on MON 88702 cotton will be compliant with EPA registration and label requirements. Considering these factors, approval of the petition would not lead to circumstances that resulted in non-compliance with the requirements of the CWA, CAA, and SDWA.

7.1.3 National Historic Preservation Act (NHPA) of 1966 as Amended

The National Historic Preservation Act of 1966 (NHPA; Public Law 89-665; 16 U.S.C. 470 *et seq.*) designates federal agencies that are proposing federally funded or permitted projects on historic properties (buildings, archaeological sites, etc.) to consider the impacts using the required Section 106 Review process. The NHPA and its implementing regulations (36 CFR 800) require federal agencies to: 1)

determine whether activities they propose constitute "undertakings" that have the potential to cause impacts on historic properties; and 2) if so, to evaluate the impacts of such undertakings on historic resources and consult with the Advisory Council on Historic Preservation (i.e., State Historic Preservation Office, Tribal Historic Preservation Officers), as appropriate.

Approval of the petition is not a decision that would directly or indirectly result in alteration of the character or use of historic properties protected under the NHPA, nor would it result in any loss or destruction of cultural or historical resources. Where MON 88702 cotton is cultivated there may be the potential for increased noise during the operation of machinery and other equipment, as with all cotton crop production, however, these activities would have only temporary effects on historic sites in the way of noise, with no consistent long-term effects on the enjoyment of a historical site.

7.2 Executive Orders Related to Domestic Considerations

The following executive orders (EO) require consideration of the potential impacts of federal actions on human health, cultural resources, wildlife, and the environment.

- **EO 12898 – Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations**

This EO requires federal agencies to conduct their programs, policies, and activities that substantially affect human health or the environment in a manner so as not to exclude persons and populations from participation in or benefiting from such programs. It also enforces existing statutes to prevent minority and low-income communities from being subjected to disproportionately high and adverse human health or environmental effects.

- **EO 13045 – Protection of Children from Environmental Health Risks and Safety Risks**

Children may suffer disproportionately from environmental health and safety risks due to their developmental stage, higher metabolic rates, and behavior patterns, as compared to adults. This EO requires each federal agency to identify, assess, and address the potential environmental health and safety risks that may disproportionately affect children.

- **EO 13175 – Consultation and Coordination with Indian Tribal Governments**

Executive departments and agencies are charged with engaging in consultation and collaboration with tribal governments; strengthening the government-to-government relationship between the United States and Indian tribes; and reducing the imposition of unfunded mandates upon Indian tribes. This EO emphasizes and pledges that federal agencies will communicate and collaborate with tribal officials when proposed federal policy or actions have potential tribal implications.

Neither alternative evaluated in this EA is expected to have disproportionate adverse impacts on minorities, low-income populations, or children, or adversely affect tribal entities. The trait *cry* gene and Cry gene product in MON 88702 cotton present no risks to human health, nor to food animal health and welfare. MON 88702 cotton would be cultivated as are all other cotton varieties, using the same agronomic practices and inputs, albeit with reduced insecticide use as compared to conventional cotton varieties.

Tribal entities are recognized as independent governments and agricultural activities on tribal lands would only be conducted if approved by the tribe. Tribes would have control over any potential conflict with cultural resources on tribal properties. Approval nor denial of the petition would have any effect on Indian tribal self-governance or sovereignty, tribal treaties, or other rights.

- **EO 13751 – Safeguarding the Nation from the Impacts of Invasive Species**

Invasive species are a significant issue in the United States, causing both adverse economic and environmental impacts. This EO directs actions to continue coordinated federal prevention and control efforts related to invasive species. This order maintains the National Invasive Species Council (Council) and the Invasive Species Advisory Committee; expands the membership of the Council; clarifies the operations of the Council; incorporates considerations of human and environmental health, climate change, technological innovation, and other emerging priorities into federal efforts to address invasive species; and strengthens coordinated, cost-efficient federal action.

In areas below 29° N latitude, such as southern Florida, Hawaii, and Puerto Rico, upland cotton can persist become locally feral, naturalize (Wozniak and Martinez 2011; Coppens d'Eeckenbrugge and Lacape 2014). There are native indigenous and feral populations of *G. hirsutum* in Puerto Rico and the U.S. Virgin Islands. The naturalized *G. hirsutum* growing in Puerto Rico appears to derive from primitive cultivars that naturalized centuries ago, at least some of which appear to have undergone substantial hybridization with *G. barbadense* (USDA-APHIS 2015).

G. hirsutum does not exist in the environment as a perennial in colder temperatures found above 29 ° N latitude. In these areas in the United States the risk of *G. hirsutum* being weedy is negligible as the plant is highly domesticated, and grown in the U.S for over 200 years without feral or self-sustaining populations recorded as escapes from that cultivation (USDA-APHIS 2015). As part of its PPRA, APHIS evaluated the potential weediness and invasiveness of MON 88702 cotton and concluded that it is unlikely that MON 88702 cotton will become weedy or invasive in areas where it is grown (USDA-APHIS 2019). Cotton has been grown throughout the world without any reports that it occurs as a problematic or invasive weed.

- **EO 13186 – Responsibilities of Federal Agencies to Protect Migratory Birds**

The United States has recognized the critical importance of migratory birds as a shared resource by ratifying international, bilateral conventions for the conservation of migratory birds. These conventions impose substantive obligations on the United States for the conservation of migratory birds and their habitats. Through the Migratory Bird Treaty Act (Act) the United States has implemented these conventions with respect to the United States. This Executive Order directs executive departments and agencies to take certain actions to further implement the Act.

Cotton crops can potentially provide habitat for migratory birds along migratory routes in North America. Migratory birds could potentially transit cotton fields and forage on cotton seed, although cotton seed is not considered a preferred food for avian species. APHIS is unaware of any bird species considered an animal pest in cotton; birds that preferentially forage on cottonseed or other plant parts. Birds may consume pest insects that have eaten plant material and ingested the mCry51Aa2 protein; this, however, would not be considered of any risk to birds. As discussed in Chapter 4, Cry proteins present negligible

risk to vertebrate taxa (Rubio-Infante and Moreno-Fierros 2016). Even if birds were exposed to mCry51Aa2 via ingestion of plant parts, or insects that have consumed MON 88702 cotton plant parts, results of a 28-day single dose acute study with mCry51Aa2 in mice (5,000 mg/kg) and a 14-day acute study in Northern bobwhite quail (2,500mg/kg) showed no adverse effects (US-EPA 2018b). Expression of mCry51Aa2 protein in the cotton square (flower bud) is around 770 µg/g fwt, and in leaf tissue, around 494 µg/g fwt. Considering these factors, there are no potential adverse effects on migratory birds that would derive from cultivation of MON 88702 cotton or hybrid progeny.

7.3 Executive Orders on International Issues

- **EO 12114 - Environmental Effects Abroad of Major Federal Actions**

This Order requires federal officials to take into consideration any potential environmental effects that may occur outside the United States, its territories, and possessions, that may result from actions being taken.

As discussed in Chapter 3 and 4, all crop production can potentially have adverse impacts on soils, and air and water quality. Any cultivation of MON 88702 cotton outside of the United States, its territories, or possessions would utilize the same (or similar) agronomic practices and inputs as those utilized in the United States. Consequently, the sources and degree of environmental impacts that derive from cotton crop production abroad would be similar to those described for United States, as discussed in this EA. In the event APHIS approves the petition for MON 88702 cotton, significant adverse environmental impacts outside the United States as a result of cultivation of this cotton variety are unlikely.

The United States is a member of the World Trade Organization (WTO), which facilitates harmonizing the global rules of trade between nations. The Agreement on the Application of Sanitary and Phytosanitary Measures (the "SPS Agreement"), entered into force with the establishment of the WTO on January 1, 1995, sets out the basic rules for food safety and animal and plant health standards (WTO 2019b). The SPS agreement recognizes three international organizations/frameworks that have established standards and guidelines related to SPS measures, these are; the Codex Alimentarius Commission (Codex), the World Organization for Animal Health (OIE), and the International Plant Protection Convention (IPPC). Any international trade of MON 88702 cotton or products derived from it following a determination of nonregulated status would be subject to national phytosanitary requirements and be in accordance with international SPS standards; Codex (food safety) international food standards, guidelines, and codes of practice that contribute to safety, quality, and fairness in the international trade of food; and the IPPC, the purpose of which is to protect the world's plant resources from the spread and introduction of pests, and promote safe trade.

7.4 State and Local Requirements

The PPA contains a preemption clause (7 U.S.C. § 7756) that prohibits state regulation of any, “plant, biological control organism, plant pest, noxious weed, or plant product” to protect against plant pests or noxious weeds if the Secretary (USDA) has issued regulations to prevent the dissemination of biological control organisms, plant pests, or noxious weeds within the United States. The PPA preemption clause does however allow states to impose additional prohibitions or restrictions based on special needs supported by sound scientific data or risk assessment. Consequently, while the PPA limits states' issuance

of laws and regulations governing GE organisms and bars conflicting state regulation, it does allow state oversight when there is a special need for additional prohibitions or restrictions.

States use a variety of requirements to regulate the movement or release of GE organisms within their jurisdiction. For example, South Dakota simply authorizes holders of a federal permit issued under 7 CFR part 340 to use it within the state (SD Stat § 38-12A-31 (2015)). Minnesota issues state permits for release of genetically engineered agriculturally related organisms only after federal applications or permits are on file (MN Stat § 18F.07 (2015)). Nebraska may rely on APHIS or other experts before they issue their permit (NE Code § 2-10,113 (2015)). These examples show the range of state approaches to regulating the movement and release of GE organisms within state boundaries.

States with an organic program generally adopt 7 CFR part 205 by reference and may codify provisions. For example, Iowa (Iowa Code 190C.1-190C.26), Puerto Rico (5 L.P.R.A. §§ 131 to 141 (2013)), Oklahoma (Okla. Admin. Code §§ 35:37-15-1 to 35:37-15-11), Texas (Texas Agric. Code Ann. § 18 (2015)), and Utah (Utah Admin. Code r. R68-20 (2016)). When a state adopts the prohibitions on methods excluded by the USDA National Organic Program, then organic producers cannot use GE seed unless an exception in 7 CFR § 205.204 applies.

Neither of the alternatives considered would affect APHIS partnerships with states in the oversight of GE organisms, specifically in regulation of interstate movement and environmental releases. Under both alternatives, APHIS would continue working with states. The range of state legislation addressing agricultural biotechnology, namely in the way of permitting, crop protection, seed regulation, and economic development, would be unaffected by denial or approval of the petition.

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