

Journal of Environmental and Sustainability Law

Missouri Environmental Law and Policy Review
Volume 17
Issue 1 *Fall 2009*

Article 4

2009

Genetically Modified Insects: Why Do We Need Them and How Will They Be Regulated?

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Genetically Modified Insects: Why Do We Need Them and How Will They be Regulated?

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INTRODUCTION

The biotechnology¹ age began in 1973 with the publication of a research paper by Cohen and Boyer detailing their experiments in which they created a functional bacterial plasmid *in vitro*.² This initial report explained how to splice two different DNA strands together and create an entirely new and functional DNA molecule. This development, although ground-breaking, immediately raised questions about the risks involved with the application of this technology. In a letter to *Science* the following year, several Nobel prize-winning scientists voiced their concerns over recombinant DNA (hereinafter “rDNA”) technology.³ The group, including James Watson, proposed a moratorium on research using rDNA technology until a general meeting of scientists could be held.⁴ This proposed meeting was held in Asilomar, California in 1975. The output of the Asilomar conference was a set of conclusions about the potential uses of rDNA and recommendations for its regulation and safe use.⁵

The regulation of rDNA technology evolved from its beginnings in Asilomar. The Asilomar conference’s non-binding recommendations were later used as the basis for the National Institutes of Health’s (hereinafter “NIH”) rDNA mandatory safety requirements.⁶ The NIH’s mandatory guidelines, however, applied only to research groups using

¹ Biotechnology, broadly defined as “the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services,” ALAN T. BULL ET AL., ORG. FOR ECON. CO-OPERATION & DEV., BIOTECHNOLOGY: INTERNATIONAL TRENDS AND PERSPECTIVES 18 (1982) (internal quotation marks omitted), available at <http://www.oecd.org/dataoecd/34/9/2097562.pdf>, has technically been around for centuries. The use of yeast to make beer and wine is technically a use of biotechnology. The advent of recombinant DNA technology has allowed scientists to manipulate organisms used in providing goods and services, leading to what many have come to think of as modern-day biotechnology.

² See Stanley N. Cohen et al., *Construction of Biologically Functional Bacterial Plasmids In Vitro*, 70 PROC. NAT’L ACAD. SCI. 3240 (1973).

³ See Paul Berg et al., *Potential Biohazards of Recombinant DNA Molecules*, 185 SCI. 303 (1974).

⁴ *Id.*

⁵ See Paul Berg et al., *Summary Statement of the Asilomar Conference on Recombinant DNA Molecules*, 72 PROC. NAT’L ACAD. SCI. 1981, 1981-83 (1975).

⁶ Recombinant DNA Research, 41 Fed. Reg. 27,902, 27,902 (July 7, 1976).

federal funds.⁷ Any groups with independent means were free to take these rules under advisement but were not required to comply. Then, in 1986, the United States federal government published its own regulations in the Federal Register. These regulations, the *Coordinated Framework for Regulation of Biotechnology* (hereinafter "Coordinated Framework"), have remained the basis of biotechnology regulation.⁸ The Coordinated Framework uses the joint efforts of three federal agencies, the Food and Drug Administration (hereinafter "FDA"), the Environmental Protection Agency (hereinafter "EPA"), and the United States Department of Agriculture (hereinafter "USDA"), to regulate biotechnology.

Since the 1980s, the use of biotechnology has been both successful and controversial. Early on, many developments were not controversial as researchers were able to create plants that were resistant to a variety of chemicals.⁹ In 1987, five applications for field trials of genetically modified (hereinafter "GM") plants were approved, and since that date, more than 12,000 field trials have been approved by government agencies.¹⁰

More controversial, the 1980s also saw the creation of GM microorganisms for biotechnology uses.¹¹ Researchers in California created a strain of *Pseudomonas fluorescens* that incorporated a gene, which when expressed, produced an anti-freeze protein that delayed ice crystal formation.¹² This organism was named the "ice-minus" strain.¹³ The creators of this organism were interested in its potential agricultural applications for use in preventing frost damage to plants during the fall growing season.¹⁴ To test its potential viability as a biotechnology product, field tests were necessary. The creators applied for regulatory

⁷ See *id.*

⁸ See Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302 (June 26, 1986).

⁹ Alan McHughen & Stuart Smyth, *US Regulatory System for Genetically Modified [Genetically Modified Organism (GMO), rDNA or Transgenic] Crop Cultivars*, 6 PLANT BIOTECHNOLOGY J. 2, 4 (2008).

¹⁰ *Id.* at 5.

¹¹ See Jean L. Marx, *Assessing the Risks of Microbial Release*, 237 SCI. 1413 (1987).

¹² *Id.* at 1413-14.

¹³ *Id.* at 1413.

¹⁴ *Id.*

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approval of field tests; and after two years of delay, their applications were approved.¹⁵ Unfortunately, public sentiment was not on their side.¹⁶ Opposition to the field trials was strong enough to further delay the testing.¹⁷ Eventually, the field tests were moved to a new location, approved, and completed, although the product eventually proved not to be commercially viable.¹⁸

Applications of biotechnology have evolved over the last thirty years. In early 2009, the FDA approved the first pharmaceutical produced by livestock; an anti-clotting factor produced in goat milk.¹⁹ This was the first such approval of a pharmaceutical produced in a GM animal; however, humans have long taken pharmaceuticals from animals, such as insulin from pigs and cows. This regulatory approval shows the world that pharmaceutical-producing GM animals are not inherently dangerous and should reassure some critics of GM animals' safety. Also, hopefully this will lead to the approval of more pharmaceutical-producing GM animals.

In terms of molecular complexity, GM insects lie between pharmaceutical-producing livestock and GM crops. The first of these organisms, created before the rDNA revolution, set precedence for effectiveness. In the 1950s and 1960s, to cope with costly screwworm infestations, scientists used the Sterile Insect Technique (hereinafter "SIT")²⁰ to drastically reduce the worm burden in the southern United

¹⁵ Marjorie Sun, *Local Opposition Halts Biotechnology Test*, 231 SCI. 667, 667 (1986).

¹⁶ *Id.*

¹⁷ *Id.*

¹⁸ Gary E. Marchant, *Modified Rules for Modified Bugs: Balancing Safety and Efficacy in the Regulation of Deliberate Release of Genetically Engineered Microorganisms*, 1 HARV. J.L. & TECH. 163, 165 (1988).

¹⁹ Andrew Pollack, *F.D.A. Approves Drug from Gene Altered Goats*, N.Y. TIMES, Feb. 7, 2009, at B1, available at <http://www.nytimes.com/2009/02/07/business/07goatdrug.html>.

²⁰ The Sterile Insect Technique, is still a GM technique, though it does not involve rDNA technology. See R.C. Bushland et al., *Eradication of Screw-Worms Through Release of Sterilized Males*, 122 SCI. 287, 287 (1955).

SIT generally uses male insects, sterilized through exposure to radiation or a chemical, released at the proper proportion into the wild to mate with wild type females who only mate one time. *Id.*

States.²¹ Since those early efforts to protect agricultural investments using modified insects, many more experiments have been done with hopes of eliminating vectors of disease and other agricultural pests, as well as genetically “enhancing” some insect species.

In the United States, only two GM insects have been approved for a field test. The first, a predatory mite, was released into a controlled environment in 1996.²² These mites, though genetically modified, contained only the *lacZ* gene. This gene was used solely for testing gene migration from the GM mites to the native population.²³ The second test insect, the pink bollworm, is a pest whose larvae cost cotton farmers several million dollars a year.²⁴ The GM bollworms contained a green fluorescent protein gene which allowed investigators to more easily gauge mating of GM insects with the natural population.²⁵ The GM bollworms were released in contained field trials in Phoenix in 2001, but the trials were largely unsuccessful.²⁶ Currently, although outside of the purview of the United State’s Coordinated Framework, Malaysia is considering the release of a GM version of *Aedes aegypti*, an important disease vector.²⁷ This release is the latest attempt to curb dengue fever transmission.²⁸

Although there have only been two approved applications for controlled release of GM insects, many more may soon be applying for regulatory approval. Between the advances in molecular techniques, increased understanding of insect behavior and the ever-growing demand to combat morbidity and mortality associated with vector-borne diseases,

²¹ G. DAVIDSON, GENETIC CONTROL OF INSECT PESTS 32-35 (1974).

²² Marjorie A. Hoy, *Transgenic Arthropods for Pest Management Programs: Risks and Realities*, 24 EXPERIMENTAL & APPLIED ACAROLOGY 463, 478 (2000).

²³ *Id.*

²⁴ Aaron Bouchie, *First GM Insect Field Trial Planned in US*, NATURE BIOTECHNOLOGY, April 2001, at 297.

²⁵ *Id.*

²⁶ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, BUGS IN THE SYSTEM? ISSUES IN THE SCIENCE AND REGULATION OF GENETICALLY MODIFIED INSECTS 6 (2004), available at http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/Food_and_Biotechnology/pifb_bugs_012204.pdf.

²⁷ Susan Aldridge, *Genetically Modified Mosquitoes*, NATURE BIOTECHNOLOGY, July 2008, at 725.

²⁸ *Id.*

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research on GM insects is booming. In light of these promising advances and the likely corresponding increase in GM insects seeking regulatory approval, an examination of the Coordinated Framework and the path GM insects' creators must travel for regulatory approval is needed.

This paper is divided into two major sections. The first is the introductory section that investigates the motivations for the creation of GM insects and the techniques used by scientists. The section also will report on the successes and failures of GM insects, and the public's response to these organisms. The second section will analyze the regulatory framework. This section will first focus on the broader Coordinated Framework and how it generally applies to biotechnology and then on the regulatory path for GM insects.

I. THE SCIENCE OF AND PUBLIC RESPONSE TO GM INSECTS

A. *Motivations for GM Insects*

There are several reasons why scientists wish to alter the genes of insects. Important motivations like human health and agricultural prosperity have driven this research. This section will first address motivations associated with human health, focusing on vectors-borne diseases. The second section will focus on agricultural motivations, including pests of crops and livestock.

1. Human Health

The preservation of human health is a major driving force behind the push for GM insects. Recent World Health Organization data indicates that between seven diseases (malaria,²⁹ dengue fever,³⁰ lymphatic

²⁹ World Health Organization, Malaria, <http://www.who.int/mediacentre/factsheets/fs094/en/print.html> (last visited Nov. 11, 2009) (stating there were 247 million infections in 2006).

³⁰ World Health Organization, Dengue and Dengue Hemorrhagic Fever, <http://www.who.int/mediacentre/factsheets/fs117/en/print.html> (last visited Nov. 11, 2009) (stating there were fifty million yearly infections).

filariasis,³¹ yellow fever,³² leishmaniasis,³³ Chagas' disease,³⁴ and African sleeping sickness³⁵) account for close to one-half billion infections each year. The common thread among these seven infectious diseases is that each is transmitted by insects. Although there is growing attention paid to these diseases through efforts such as the Gates' Foundation's partnership with the World Health Organization in the "Roll Back Malaria" effort,³⁶ funding for combating many of these diseases is still drastically inadequate. Amazingly, only one percent of the fourteen hundred drugs approved between 1975 and 1999 were for tropical diseases.³⁷

Even when chemotherapies are developed for these diseases, troubles still arise. There are a variety of issues that can arise; most important to Western pharmaceutical companies is that these diseases largely occur in the developing world. With the costs of gaining regulatory approval for a drug or biologic nearing one billion dollars, there would be little opportunity for these companies to profit on investment if the new drug is aimed toward low income nations. Another potential problem with the

³¹ World Health Organization, Lymphatic Filariasis, <http://www.who.int/mediacentre/factsheets/fs102/en/print.html> (last visited Nov. 11, 2009) (stating there were approximately 120 million infections affected by this disease).

³² World Health Organization, Yellow Fever, <http://www.who.int/mediacentre/factsheets/fs100/en/print.html> (last visited Nov. 11, 2009) (stating there are 200,000 yellow fever infections each year).

³³ World Health Organization, Magnitude of the Problem, http://www.who.int/leishmaniasis/burden/magnitude/burden_magnitude/en/print.html (last visited Nov. 11, 2009) (stating approximately two million new cases are seen each year).

³⁴ Centers for Disease Control and Prevention, Chagas Disease – Detailed Fact Sheet, <http://www.cdc.gov/print.do?url=http%3A//www.cdc.gov/chagas/factsheets/detailed.html> (last visited Nov. 11, 2009) (stating that there are between eight and eleven million infections of Chagas' disease).

³⁵ World Health Organization, African Trypanosomiasis (Sleeping Sickness), <http://www.who.int/mediacentre/factsheets/fs259/en/print.html> (last visited Nov. 11, 2009) (stating there are between fifty and seventy thousand infections each year).

³⁶ See generally Roll Back Malaria (RBM) Partnership, <http://www.rollbackmalaria.org/> (last visited Nov. 11, 2009).

³⁷ World Health Organization, 10 Facts on Neglected Tropical Diseases, http://www.who.int/features/factfiles/neglected_tropical_diseases/en/index.html (last visited Nov. 11, 2009).

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deployment of a treatment or vaccination regimen is the break down in the “cold chain.” The “cold chain” is the supply chain in which a product requiring refrigeration is maintained at a low temperature during transit to ensure potency and prevent spoilage.³⁸ The problem here arises, once again, because of the populations for which these products are intended. These are some of the poorest communities in the world. Often times, treatment sites may not have electricity to maintain the cold chain, leading to likely spoilage of any pharmaceuticals that make it to that locale.

Another problem that arises in the development of chemotherapeutics is drug resistance. Even when pharmaceutical companies work to produce chemotherapeutic agents, the targeted organisms are quickly adapting. An organism illustrative of this disturbing phenomenon is *Plasmodium falciparum*, the etiological agent of malaria, which is one of the most devastating vector-borne diseases. Traditionally, this parasite was controlled with quinine;³⁹ a drug initially derived from the bark of the chinchona tree several centuries ago. In the early 20th Century, a more effective derivative agent was created: chloroquine.⁴⁰ Thereafter, resistance to anti-malarial compounds soon began to surface in Southeast Asia.⁴¹ Other agents were developed, and in the case of each drug, resistance began to appear.⁴² Significantly, resistance was recently discovered for the latest “miracle drug,” a traditional Chinese anti-malarial, artemisinin.⁴³ Malaria is not the only vector-borne disease to develop drug resistance; similar phenomena have been seen in leishmaniasis⁴⁴ and sleeping sickness,⁴⁵ among other tropic diseases.

³⁸ See DEP’T OF VACCINES & BIOLOGICALS, WORLD HEALTH ORG., ADOPTING GLOBAL VACCINE MANAGEMENT POLICIES FOR NATIONAL USE annex A, at 29 (2002), available at <http://www.who.int/vaccines-documents/DocsPDF02/www713.pdf>.

³⁹ Karen Hayton & Xin-zhuan Su, *Drug Resistance and Genetic Mapping in Plasmodium falciparum*, 54 CURRENT GENETICS 223, 226 (2008).

⁴⁰ *Id.* at 224.

⁴¹ *Id.*

⁴² *See id.*

⁴³ See Harald Noedl et al., *Evidence of Artemisinin-Resistant Malaria in Western Cambodia*, 359 NEW ENG. J. MED. 2619 (2008).

⁴⁴ See Simon L. Croft et al., *Drug Resistance in Leishmaniasis*, 19 CLINICAL MICROBIOLOGY REV. 111 (2006).

These organisms' ability to rapidly reproduce, together with strong drug pressures on the microorganism population, will continue to lead to the spread of drug resistance.

Additionally, hardships have also been seen when nations attempt to combat the disease vectors. The major method of combating disease vectors is through the use of insecticides. Two modes of delivery are generally preferred: direct spraying on vector habitats or through the use of insecticide-impregnated bed nets. The more widely used method, direct spraying on vector habitats, leads to two major problems: environmental or human effects and insecticide resistance.

The impact on humans is a major concern with the spraying of insecticides. One report gathered data from smaller cohort studies and concluded that exposure to certain chemicals, including dichlorodiphenyl trichloroethane (hereinafter "DDT"), correlates with delays in cognitive and neuromuscular development in children.⁴⁶ Another study concluded that DDT can have a serious impact on a child's endocrine system.⁴⁷ In addition to DDT, other pesticides have been severely limited from once-broad applications because of concerns over potential impacts to human health.⁴⁸

Environmental concerns also arise from the spraying of insecticides. In Egypt, the spraying of insecticides has led to major problems with farm animal poisonings, death of beneficial insects, as well as pollution of the food and water supply.⁴⁹ Additionally, the EPA published a report stating

⁴⁵ See Pascal Maser et al., *Drug Transport and Drug Resistance in African Trypanosomes*, 6 DRUG RESISTANCE UPDATES 281 (2006).

⁴⁶ Susan A. Korrick & Sharon K. Sagiv, *Polychlorinated Biphenyls, Organochlorine Pesticides and Neurodevelopment*, 20 CURRENT OPINION PEDIATRICS 198, 202-03 (2008).

⁴⁷ See Walter J. Rogan & N. Beth Ragan, *Some Evidence of Effects of Environmental Chemicals on the Endocrine System in Children*, 210 INT'L J. OF HYGIENE & ENVTL. HEALTH 659 (2007).

⁴⁸ See L. RITTER ET AL., INT'L PROGRAMME ON CHEM. SAFETY, A REVIEW OF SELECTED PERSISTENT ORGANIC POLLUTANTS (1995), available at http://www.who.int/ipcs/assessment/en/pes_95_39_2004_05_13.pdf.

⁴⁹ Sameeh A. Mansour, *Environmental Impact of Pesticides in Egypt*, 196 REV. ENVTL. CONTAMINATION & TOXICOLOGY 1 (2008).

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that a major concern associated with DDT was its environmental impact.⁵⁰ To help ensure that both human health and environmental concerns are minimized, the World Health Organization has created the WHO Pesticides Evaluation Scheme.⁵¹ This program evaluates and makes recommendations concerning the regulations of these potentially deadly chemicals.⁵²

In addition to human and environmental concerns, incidents of insecticide resistance have been observed. According to one review of the scientific literature, more than 500 insect species have acquired some type of resistance to insecticides.⁵³ These resistances often develop to more than one class of insecticide, making control efforts more difficult.⁵⁴ To attempt to monitor and keep abreast of resistance developing in the field, the World Health Organization publishes a manual with insecticide-resistance detection techniques.⁵⁵

Public health concerns are a major motivation for the development of GM insects. There are serious issues involved in the development and implementation of chemotherapeutics to treat infectious diseases transmitted by insects. Additionally, direct attacks on insects can prove costly to human health and the environment, and lead to the development of insecticide resistance. Thus, major human health concerns are a driving force in the push for GM insects.

⁵⁰ U.S. ENVTL. PROT. AGENCY, DDT: A REVIEW OF SCIENTIFIC AND ECONOMIC ASPECTS OF THE DECISION TO BAN ITS USE AS A PESTICIDE (1975), available at <http://www.epa.gov/history/topics/ddt/DDT.pdf>.

⁵¹ See World Health Organization, WHO Pesticides Evaluation Scheme: "WHOPES," <http://www.who.int/whopes/en/> (last visited Nov. 20, 2009).

⁵² *Id.*

⁵³ Marjorie A. Hoy, *Myths, Models, and Mitigation of Resistance to Pesticides*, 353 PHIL. TRANSACTIONS ROYAL SOC'Y LONDON 1787, 1787 (1998).

⁵⁴ *See id.*

⁵⁵ See JANET HEMINGWAY & WILLIAM BROGDON, DEPARTMENT OF DISEASE PREVENTION AND CONTROL, WORLD HEALTH ORG., TECHNIQUES TO DETECT INSECTICIDE RESISTANCE MECHANISMS (1998), available at http://whqlibdoc.who.int/hq/1998/WHO_CDS_CPC_MAL_98.6.pdf.

2. Agricultural Concerns

Agricultural concerns were the original motivation for modifying insects to alter the native population. The original use of GM insects was implemented to deal with the burden of the New World screwworm.⁵⁶ The screwworm was a major agricultural pest in the southern United States.⁵⁷ The screwworm, a parasitic fly that lays its eggs in farm animals' skin, was a 120 million dollar per year problem (1958 US dollars).⁵⁸ The development and emergence of larvae from the animals' skin leads to problems such as carcass damage and secondary infections.⁵⁹ Additionally, a heavy larvae burden could kill younger animals.⁶⁰ To combat the economic problem associated with screwworm infestations, "altered" insects were used.⁶¹ Although not GM, these insects were the beginnings of the GM insect movement.

In addition to alleviating concerns regarding farm animals, other agricultural motivations, such as crop and plant pests, have pushed the development of GM insects. One of the most important plant and crop pests, in terms of economic impact, is the Mediterranean fruit fly. Not only does this insect attack more than 250 different types of fruits, nuts, and vegetables; it also leads to a constraint on trade.⁶² These trade restrictions stem from an importing country's fear that the fruit fly may be harbored in imported agricultural products. Once released, the fruit fly will operate as an invasive species, wreaking havoc on local flora.⁶³ This huge economic concern is a strong motivator for development of GM insects that can control this pest.

The Mediterranean fruit fly is not the only crop and plant pest that has

⁵⁶ See DAVIDSON, *supra* note 21, at 32.

⁵⁷ *Id.*

⁵⁸ *Id.*

⁵⁹ *Id.*

⁶⁰ *Id.*

⁶¹ See Bushland et al., *supra* note 20.

⁶² Peng Gong et al., *A Dominant Lethal Genetic System for Autocidal Control of the Mediterranean Fruit Fly*, 23 NATURE BIOTECHNOLOGY 453, 453 (2005).

⁶³ *Id.*

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strengthened the call for GM insects. Additionally, pests of corn,⁶⁴ cotton,⁶⁵ cowpea,⁶⁶ potatoes,⁶⁷ and others⁶⁸ are all important agricultural pests with strong economic impacts that will further the call for GM insects.

In addition to pests, there are other agricultural concerns that could motivate the creation of GM insects. One major example is the honeybee. Although not an agricultural pest, the honeybee and its recent disappearance is a major concern.⁶⁹ Currently, the underlying mechanism or pathogen associated with the honeybees' disappearance is unknown.⁷⁰ Further research could identify areas for potential genetic modification that could alleviate this significant problem.

Finally, there is also a potential social impact of agricultural pests. The destruction of agricultural outputs by pests leads to increased consumer costs. Agricultural pests can lead to costs in the hundreds of millions of dollars to the farmer, which will be passed on to the consumer. Although in Western countries this increased cost could be absorbed by the consumer, in developing countries this increase could put some foods out of reach for import and purchase. These social costs, stemming from the economic toll of pests, could be just as important as the economic ones.

Overall, the huge economic and social impact of agricultural pests is a strong motivator for the development of GM insects.

⁶⁴ See generally J.D. DeVault et al., *Gene Transfer into Corn Earworm*, 6 GENOME RESEARCH 571 (1996).

⁶⁵ See generally J.J. Pelloquin et al., *Genetic Transformation of the Pink Bollworm, Pectinophora gossypiella with the piggybac Element*, 9 INSECT MOLECULAR BIOLOGY 323 (2000).

⁶⁶ See generally Andre M. Murad et al., *Proteomic Analysis of Metarhizium anisopliae Secretion in the Presence of the Insect Pest Callosobruchus maculatus*, 154 MICROBIOLOGY 3766 (2008).

⁶⁷ See generally N.T Mbungu & G. Boiteau, *Flight Take-Off Performance of Colorado Potato Beetle in Relation to Potato Phylogeny*, 101 J. ECON. ENTOMOLOGY 56 (2008).

⁶⁸ See generally Peter W. Atkinson, *Genetic Engineering in Insects of Agricultural Importance*, 32 INSECT BIOCHEMISTRY & MOLECULAR BIOLOGY 1237 (2002).

⁶⁹ Benjamin P. Oldroyd, *What's Killing American Honey Bees?*, 6 PUB. LIBR. SCI. & BIOLOGY 1195, 1195 (2007).

⁷⁰ *Id.*

3. Other Potential Motivators for the Development of GM Insects

In addition to public health and agricultural concerns, other miscellaneous motivators exist for the development of GM insects. One paradigm for this group is the silk worm, *Bombyx mori*. Silk worms are quickly reproducing organisms that have the capability to produce massive amounts of protein, most commonly silk.⁷¹ Recent developments in scientific techniques have allowed researchers to create GM silk worms, harnessing the strong protein production of the worm for production of other proteins. One group recently created a GM strain of silkworms that produce human antibodies.⁷² This application could be expanded into other innovations. Silkworms could be used as bioreactors, similar to plants in the "Pharming" movement. This application, plus many other potential uses, serves as further motivation for the creation of GM insects.

In conclusion, there are several motivating factors for the creation of GM insects. These factors range from improving public health to alleviating agricultural burdens due to insect infestations. Additionally, insects can be genetically modified to produce beneficial products, similar to procedures used in the Pharming movement. Overall, there is a strong need for the development of these insects.

B. *How to Make a GM Insect*

There are several methods available to create GM insects, and two broad categories of modifications. First, the modification can be directed at the genome of the insect. This is the method usually associated with GM insects. This method involves altering the insect's genome to result in a chosen outcome, be it pathogen-resistance, sterility, or some other desired trait. The second category, paratransgenesis, involves modification of the gut flora of the insect. For instance, using this technique, scientists are able to modify the insect's commensal organisms

⁷¹ Marian R. Goldsmith et al., *The Genetics and Genomics of the Silkworm, Bombyx mori*, 50 ANN. REV. ENTOMOLOGY 71, 72 (2005).

⁷² See Enoch Y. Park et al., *Human IgG1 Expression in Silkworm Larval Hemolymph Using BmNPV Bacmids and Its N-Linked Glycan Structure*, 139 J. BIOTECHNOLOGY 108, 111-12 (2009).

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to interrupt the disease transmission cycle. This section will provide an overview of these two processes.

1. Direct Genome Modification

Under the heading of direct genome modification, two subcategories exist. The first is sterile insect technique (hereinafter "SIT"). The second is genetic manipulation using rDNA technology. This section will highlight both of these techniques

a. SIT

SIT, the oldest form of human-mediated direct genome modification, has been largely successful.⁷³ Pioneered by Knipling, SIT uses an insect species against itself.⁷⁴ Non-viable offspring is the goal of SIT; the sterile males inseminate the females, producing non-viable eggs, thus reducing the population.⁷⁵ The technique uses factory-bred, mass-reared male insects that have been exposed to massive amounts of radiation or a chemical mutagen.⁷⁶ This exposure to radiation or other mutagens damages the males' gametes.⁷⁷ Gamete damage does not later prevent insemination of wild females; however, it does lead to non-viable offspring.⁷⁸

The next steps involve release. Prior to release of these sterilized males, a population study must be performed.⁷⁹ These males must be released in numbers approximately ten to 100 times more than the natural population of males.⁸⁰ The release of these excess sterile males aids in competing with the wild type males.⁸¹ Finally, once the proper numbers

⁷³ See generally DAVIDSON, *supra* note 21, ch. 2.

⁷⁴ See Bushland, *supra* note 20, at 287.

⁷⁵ DAVIDSON, *supra* note 21, at 14-17.

⁷⁶ *Id.*

⁷⁷ *Id.*

⁷⁸ *Id.*

⁷⁹ See *id.* at 17.

⁸⁰ See *id.* at 23, 28-29.

⁸¹ *Id.* at 17.

are determined, the males are released and monitored to determine the success of the effort.

In spite of SIT's success, there are drawbacks to this technique. The major drawbacks are the irradiation procedure and the limitations naturally inherent in the technique. First, the irradiation process, in addition to sterilizing the males, reduces the fitness of the males relative to the wild population.⁸² The weaker sterile males are at a disadvantage in the wild and may not be selected by a female for mating.⁸³ The excess of released males partially compensates for this weakness, but does not completely alleviate it. The second drawback is the naturally inherent limitations in the process. This process can only work for insects that can be mass-reared at facilities.⁸⁴ Also, prior to implementation, much must be known about the insects, including population dynamics and ecology. Finally, the insects at the facility are in-bred, making the altered insects less fit than their natural relatives, further making implementation difficult. In spite of these complications, SIT has been successful.

b. Genetic Manipulation

Many of the recent advances in the field of genetically modifying insects have come due to the rDNA revolution. This section is an overview of this process.

Prior to the advent of the rDNA age, genetic manipulation was possible, but limited to only the natural variations present in a species. Modern techniques have expanded the realm of possible genetic alterations.⁸⁵ The initial step in genetic modification is the identification of a desirable trait researchers wish to "drive" into a population.⁸⁶ This trait, ideally expressed from one gene, could lead to pathogen resistance or

⁸² See Alan S. Robinson & Gerald Franz, *The Application of Transgenic Insect Technology in the Sterile Insect Technique*, in INSECT TRANSGENESIS 315 (2000).

⁸³ See *id.*

⁸⁴ See DAVIDSON, *supra* note 21, at 6.

⁸⁵ See Paul Eggleston & Yuguang Zhao, *Targeted Transformation of the Insect Genome*, in INSECT TRANSGENESIS, *supra* note 82, at 29.

⁸⁶ The implications of selecting what traits to remove from a population, or conversely "drive" in to a population, are a difficult decision, with serious potential consequences.

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it could be a lethal mutation, which, when activated, kills the organism.⁸⁷ Ideally, the trait selected would be from a related organism. This makes integration and expression of the gene in the GM insect easier.⁸⁸ The sequencing of several vectors' genomes aids in the selection of genes for genetic modification.

After selection of a trait, researchers have two options for inserting the gene into the insect's genome. The first option, transposons or "jumping genes," have the ability to cut and paste themselves into and out of DNA. Researchers can put the desired gene within a transposons' molecular machinery and expose it to insect cells.⁸⁹ One of the drawbacks to this technique is that the area into which the transposon integrates is relatively random. There are certain sequences in DNA into which a transposon will preferentially insert itself, but other than that, insertion is random. The second option is through the use of viral vectors.⁹⁰ Similar to transposons, a desired gene can be spliced into a virus construct. Then, viral vectors can be used to integrate into the genome, also on a random basis.⁹¹

After attempting to integrate the gene into the insect's genome, researchers must ensure that the gene has been properly integrated and expressed. This can be done by including a selectable marker within the gene's vector or through checking for actual expression of the gene.⁹²

Although this technique appears straightforward, there are still concerns with its application. The issues regarding spread of the gene to non-intended population is a serious one, and will be discussed later. There are other concerns, including, similar to SIT, the fitness of the GM insects. GM insects, after receiving the new gene, are much less fit than the wild type, making mating selection difficult.⁹³ After integration using a transposon, it is possible that the gene will excise itself, and relocate to another, non-expressing part of the genome.⁹⁴ In spite of these concerns,

⁸⁷ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 15, 26.

⁸⁸ *See id.* at 9.

⁸⁹ Eggleston & Zhao, *supra* note 85, at 29-30.

⁹⁰ *Id.*

⁹¹ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 10.

⁹² Eggleston & Zhao, *supra* note 85, at 31-33.

⁹³ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 10.

⁹⁴ *Id.*

this type of genetic modification has promise for the future.

2. Paratransgenesis

In addition to direct genome modification, another tool available to alter insects is paratransgenesis.⁹⁵ This technique involves altering the flora (or adding completely new flora) in the gut of an insect, but not altering the insect's own genome.⁹⁶ Nearly all vectors transmit disease as an unintended consequence of a hemataphagous lifestyle. Researchers can use the interaction between the pathogen and the natural flora of the insect's gut to destroy the disease agent.⁹⁷

One real life example of paratransgenesis in use is the kissing bug. The kissing bug (*Rhodnius prolixus*) transmits Chagas' disease (*Trypanosoma cruzi*).⁹⁸ Researchers have been able to alter the bacteria commonly found in the gut of the kissing bug to produce an anti-trypanosome peptide, cecropin.⁹⁹ When expressed, this peptide does not harm the insect, but is deadly to the pathogen.¹⁰⁰

This technique has a major advantage over direct insect genetic modification; it does not involve modifying the insect's genome. Bacteria are much easier to add or remove DNA because bacteria lack a nucleus. Also, bacterial genetic techniques have been in use since 1973 and have been extensively refined, relative to insect genetics techniques.¹⁰¹ The major drawback associated with paratransgenesis is its real world application. Driving this modified bacterial strain into an insect population in a sustainable manner will prove daunting.¹⁰²

Overall, this section provided a cursory overview of techniques scientists have developed to modify insects. These techniques range from

⁹⁵ See generally Charles B. Beard et al., *Bacterial Symbiont Transformation in Chagas Disease Vectors*, in *INSECT TRANSGENESIS*, *supra* note 82, at 289-98.

⁹⁶ *Id.* at 289.

⁹⁷ *See id.*

⁹⁸ *Id.* at 289-90.

⁹⁹ *Id.* at 293.

¹⁰⁰ *See id.* at 294.

¹⁰¹ *See* Cohen et al., *supra* note 2.

¹⁰² Beard et al., *supra* note 95, at 298-300.

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directly modifying an insect's germ line, to destroying an insect's germ line, to altering the natural flora of an insect. Although some of these techniques have proven successful, much more work is needed before any are perfected.

C. The Possible Drawbacks to GM Insects

Although there are strong motivations for the creation of GM insects, there are still scientifically-valid concerns; many stemming from a lack of data on this topic. This section will analyze the possible direct human health and environmental impacts of GM insects. Please note that this section will only address drawbacks considered to be scientifically-valid. More common "mass-hysteria" concerns will be addressed below in "The Public's Views" section.

1. Direct Impacts on Human Health

Although impacts on human health are possible through the alteration of ecosystems due to GM insects, this section will cover potential direct impacts. Direct consumption of insects, while not usually practiced in the United States, could still be a problem globally.¹⁰³ As has been the case with GM crops, there are concerns that additionally expressed proteins in GM insects could lead to an allergic reaction.¹⁰⁴ To address this issue, allergenicity testing of these expressed proteins should be performed.

An additional concern is the consumption of insect products. For instance, humans consume honey. If a honeybee was genetically engineered to resist the plague that is currently decimating this population, allergenicity testing must be performed to ensure that the honey produced by such altered bees is a relatively safe product.¹⁰⁵

The final concern is the potential alteration of the insect itself. Although purely hypothetical, GM insects, no longer able to transmit disease X, could *now* be competent to transmit disease Y. Also, the trait

¹⁰³ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 43.

¹⁰⁴ *Id.*

¹⁰⁵ *See id.*

conferred on a GM insect could make it more fit and potentially expand its geographic reach, meaning more people could be exposed to the insect.

Overall, these concerns are serious, but are largely unsubstantiated. Little data exists and many of these concerns stem from a fear of the unknown.

2. Environmental Impacts

Environmental concerns are pervasive in the GM field. These issues vary by choice of GM technique. The concerns associated with the SIT differ from those stemming from direct genome modification.

The environmental concerns surrounding the use of the SIT to eliminate or control a native population stem from a permanent alteration of the ecosystem. If the SIT is a success, and a population is either eliminated or vastly reduced, the ecosystem is permanently altered.¹⁰⁶ It is difficult to predict all of the broader ecological impacts of these changes. It is possible that the elimination or vast reduction in numbers of this organism could have dire consequences for other non-targeted organisms.¹⁰⁷ A likely food source and predator will have been eliminated and this could have a serious impact. Scientists have emphasized that pre-release investigation of the targeted organism's ecology must be performed to plan for these environmental impacts.¹⁰⁸

Concerns with direct insect genome modification differ from those associated with the SIT. The goals of these two techniques differ; SIT's goal is population elimination or control, whereas direct genome modification's goal is population replacement, so there is unlikely to be the same impact on the population of the target species. The idea of horizontal gene flow is a concern with direct genome modification.¹⁰⁹ Critics of GM insects fear that genes inserted into an insect's genome via

¹⁰⁶ See *id.* at 31.

¹⁰⁷ See *id.*

¹⁰⁸ See Thomas W. Scott et al., *The Ecology of Genetically Modified Mosquitoes*, 298 SCI. 117, 119 (2002).

¹⁰⁹ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 36. Horizontal gene flow is the movement of genes from one species to another through means other than sexual reproduction. *Id.*

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transposons will have the ability to “jump” from the GM insect to other organisms.¹¹⁰ These fears are at least partially grounded in real science. The machinery used to originally insert genes into the insect’s genome is mobile by nature, and thus scientists are concerned that the genes will continue to “jump” once the GM insect is released into the environment.¹¹¹ Depending on what the gene is, this could impact other species’ fitness in their natural environment. No data, however, supports this concern.¹¹²

In conclusion, these concerns are valid (for now) because of the current lack of scientific literature and actual experience. Once more research is conducted, these concerns will either be confirmed or dispelled.

D. *The Public’s Views*

Similar to all GM organisms, there is a broad spectrum of public approval and disapproval of GM insects. Ideas range from positive, pro-GM insect views to the commonly found anti-GM sentiments. This section reports on the two different societal views of GM insects.

1. Pro GM Insects

Much of the public’s concern revolves around which end of the risk spectrum they find themselves. If one believes that the risk is minor and the benefits will out-weigh the risks, there is generally a positive sentiment; this is the pro-GM insect group. This group focuses on the beneficial financial (including agricultural) and human health impacts GM insects can provide.¹¹³

¹¹⁰ See *id.* at 34-37.

¹¹¹ See Ronald H.A. Plasterk, *Molecular Mechanisms of Transposition and Its Control*, 74 CELL 781, 781 (1993).

¹¹² PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 38.

¹¹³ See, e.g., Stephen Evans, *Worm Turns for US Cotton Farmers*, BBC NEWS, WORLD EDITION, June 20, 2002, <http://news.bbc.co.uk/2/hi/science/nature/2053884.stm>; Arlene Weintraub, *Much Ado Over “Lethal Genes,”* BUS. WEEK, Jan. 16, 2006, http://www.businessweek.com/magazine/content/06_03/b3967112.htm; Scientists Say

Currently, there is not much discussion regarding GM insects in public fora. Scientists have previously discussed GM insects and have generally advocated GM insects as an “eco-friendly” way of eliminating insect pests.¹¹⁴ Outside of the implementation of the SIT for screwworms and other organisms, no GM insects have been released in a non-field trial setting. Thus, there has yet to be a true “lightning rod” incident to test the public sentiment.¹¹⁵ Perhaps with the release of GM mosquitoes in Malaysia and a corresponding success of reducing dengue fever, more public sentiment will swing in favor of GM insects.¹¹⁶

2. Anti-GM Insects

All technologies have critics. One of the major driving forces behind criticism of GM insects is the main rationale for releasing GM insects: free release. A concern associated with biotechnological products is the lack of control over those organisms. With GM insects, especially those with direct genome modifications, the goal is free release and population replacement. As discussed in section C, potential problems could arise; however, there is limited data available to support any valid conclusions that GM insects will destroy ecosystems.¹¹⁷

The “anti-GM insects” position is based largely on fears of horizontal gene transfer, ecosystem collapse, and lack of regulation.¹¹⁸ These fears highlight the one true problem associated with GM insects: a lack of knowledge. The idea of an insect with a foreign gene inserted into its genome can be frightening; however, when the population is apprised of

Genetically Modified Insects Can Improve Health and Farming,
http://www.gmofoodforthought.com/2005/11/scientists_say_genetically_mod.htm (Nov. 12, 2005, 17:01 EST).

¹¹⁴ See, e.g., Ernst A. Wimmer, *Eco-Friendly Insect Management*, 23 NATURE BIOTECHNOLOGY 432 (2005).

¹¹⁵ There have been small, *very controlled* releases of genome modified insects in California and Florida, but no completely wild release has been achieved yet. See PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 18; Hoy, *supra* note 22, at 475.

¹¹⁶ See Aldridge, *supra* note 27.

¹¹⁷ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 38.

¹¹⁸ See *id.* at 34-37, 50.

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that gene's function(s) and the benefits associated with it, the public's opinions may change.

The lack of knowledge issue is highlighted by anti-GM insect propaganda spread by activist groups. The anti-GM insect side uses this lack of knowledge to scare the public. They use words like "frankenbugs,"¹¹⁹ "ecological dynamite,"¹²⁰ and phrases like "ill-conceived arrogance of industry scientists who are playing havoc with my world"¹²¹ to describe the GM insect initiative. Also, the anti-GM movement attempts to raise concerns about how transposons could make the move from GM insects to humans and other organisms.¹²² It is never mentioned, however, that these DNA elements are ubiquitous throughout nature, and that horizontal gene transfer outside of the laboratory rarely occurs.¹²³

This propaganda can change people's unbiased perceptions of the technology and lead to scary consequences. This phenomenon was seen in India when a newspaper article was able to destroy valuable research. In 1975, two days before the implementation of an SIT program to reduce the mosquito population in India, a newspaper reported that the program was actually a test of the United States' biological weapons.¹²⁴ This article led to mass hysteria among residents and the Indian government ending this potentially life-saving exercise.¹²⁵ This illustrates how misinformation can have a profound impact on social progress.

In conclusion, GM insects have not yet polarized the global population in the same way as GM crops. After more public tests and the possible commercial release of GM insects, however, these pro and anti-GM

¹¹⁹ Jeffrey Benner, *Frankenbugs in the Wings*, ORGANIC CONSUMERS ASS'N, Dec. 7, 2001, <http://www.organicconsumers.org/clothes/geinsects.cfm>.

¹²⁰ Rick Weiss, *Mutant Bugs: Genetically Altered Heroes or Spineless Menaces?*, WASH. POST, Dec. 18, 1996, at A03 (quoting Jeremy Rifkin).

¹²¹ Rima E. Laibow, Med. Dir., Natural Solutions Found., GM Files: Genetically Modified Insects (Oct. 23, 2008), <http://www.healthfreedomusa.org/?p=1252>.

¹²² Joe Cummins, Professor Emeritus of Genetics, Univ. of W. Ontario, Transgenic Pink Bollworms FONSI? (Dec. 14, 2001), <http://www.i-sis.org.uk/pinkbollworms.php>.

¹²³ Margaret G. Kidwell & Damon Lisch, *Transposable Elements as Sources of Variation in Animals and Plants*, 95 PROC. NAT'L ACAD. SCI. 7704, 7704-05 (1997).

¹²⁴ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 46.

¹²⁵ *See id.*

positions are likely to grow to be more entrenched and more vocal.

E. *The Potential Impacts – Surrogate Models*

There has yet to be a public, non-confined release of GM insects (not including SIT insects). Thus, there is yet to be a situation where GM insects have “over-stepped” their bounds and made an impact where one was not needed or wanted. This section will describe two occasions where non-GM insects were released and a negative impact resulted on the native populations. These occurrences can serve as a model for potential unintended consequences of the release of GM insects. The first case is the cactus moth and the second is the “Africanized” honeybee.

1. The Cactus moth

The cactus moth has been used as a biological control mechanism since the 1920s.¹²⁶ It is a pest of several species of *Opuntia* cactus and is imported with the goal of destroying these invasive cacti.¹²⁷ The cactus moth has been successful in destroying this invasive cactus species where it has been released, including its 1957 release in the Caribbean.¹²⁸ In the early 21st century, however, the cactus moth was discovered in Florida.¹²⁹ The moth has never been deliberately released in the continental United States.¹³⁰ More importantly, it was also discovered that the moth was attacking an endangered native species of cactus.¹³¹ This invasion of Florida is still being combated in an effort to save the endangered cacti.¹³²

The cactus moth serves as a lesson to those who wish to use GM insects to control agricultural pests and disease vectors, but have not looked at the invasiveness of the insect and the potential unintended

¹²⁶ H. G. Zimmermann et al., *The Renowned Cactus Moth, Cactoblastis cactorum: Its Natural History and Threat to Native Opuntia Floras in Mexico and the United States*, 84 FLA. ENTOMOLOGIST 543, 543 (2001).

¹²⁷ *Id.*

¹²⁸ *Id.* at 543-44.

¹²⁹ *Id.* at 544.

¹³⁰ *See id.*

¹³¹ *Id.*

¹³² *Id.*

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consequences. GM insects will not usually involve release of a new species into an ecosystem that previously lacked that species, which was the case with the cactus moth. These factors are difficult to determine ahead of time; close and careful monitoring will be needed when GM insects are released.

2. "Africanized" Honeybees

African honeybees were originally introduced to the Western Hemisphere in South America in 1956 to produce a population of bees which could adequately produce honey in tropical climates.¹³³ Initially, it was thought that the African and European (native species found in North and South America) bees would mate and produce a hybrid population, making the European population of bees "Africanized."¹³⁴ Unfortunately, these African bees were accidentally released from their confined environment.¹³⁵ The population of African bees began migrating north and in 1990 reached the United States.¹³⁶ In the last twenty years, the bees have colonized southern regions of Texas, New Mexico, Arizona, and California.¹³⁷ Interestingly, in those states, the European honeybee species have not been displaced, but rather the two populations have hybridized, forming a new, more aggressive subspecies.¹³⁸ Efforts to control this new species have been unsuccessful.¹³⁹

"Africanized" honeybees serve as an example of how quickly a population can spread throughout a region with negative consequences. Also, the entire African honeybee population explosion began as the result of a simple accident. An individual left a bee crate open, thus allowing for a few to escape.¹⁴⁰ This serves as a warning for testing GM insects: once

¹³³ Stanley Scott Schneider et al., *The African Honey Bee: Factors Contributing to a Successful Biological Invasion*, 49 ANN. REV. ENTOMOLOGY 351, 351 (2004).

¹³⁴ M. Alice Pinto et al., *Africanization in the United States: Replacement of Feral European Honeybees by an African Hybrid Swarm*, 170 GENETICS 1653, 1653 (2005).

¹³⁵ *Id.*

¹³⁶ *Id.*

¹³⁷ *Id.* at 1654.

¹³⁸ *Id.*

¹³⁹ *See id.* at 1653.

¹⁴⁰ *See id.*

these organisms are released, the organism can likely never be brought back under control.

II. REGULATION OF GM INSECTS

The current regulatory framework for GM products is a convoluted, largely unorganized patchwork of administrative regulations and statutes. This section will analyze the current regulatory framework and how it might apply to GM insects. It will begin with an introduction to the Coordinated Framework. Next, it will discuss the statutes and administrative agencies likely involved in regulating GM insects. A final section will briefly cover an international regulatory scheme.

A. *Coordinated Framework*

In the ten years after Cohen and Boyer's report, GM techniques rapidly advanced and were transitioning from the lab bench to the real life applications. These developments, in addition to the confusion associated with the regulation of biotechnology, prompted the Reagan administration to assemble an interagency working group under the White House Council on Natural Resources and the Environment in the Office of Science and Technology Policy (hereinafter "OSTP").¹⁴¹ This group, the Working Group on Biotechnology, initially offered a notice seeking public comment in the Federal Register on the following: (1) U.S. laws related to biotechnology; (2) policies of major regulatory agencies; and (3) how federal agencies should coordinate regulation.¹⁴² After a comment period, the OSTP announced its official policy in the Coordinated Framework in June 1986.¹⁴³

The policy announced in the Coordinated Framework was based on three conclusions. The Working Group was operating under a goal of trying to protect human health and the environment while maintaining

¹⁴¹ Proposal for a Coordinated Framework of Regulation for Biotechnology, 49 Fed. Reg. 50,856, 50,856-57 (Dec. 31, 1984).

¹⁴² *Id.* at 50,856.

¹⁴³ Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302, 23,302 (June 26, 1986).

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relative regulatory certainty to provide incentives for growth of the biotechnology industry.¹⁴⁴ This led to the first conclusion that, for the most part, current laws provide an adequate framework from which biotechnology can be regulated.¹⁴⁵ Second, products of the biotechnology process would be regulated, rather than the process itself.¹⁴⁶ The final conclusion was that relative to non-biotechnology goods, biotechnology products pose no unique risks.¹⁴⁷ Based on those conclusions, the Coordinated Framework established a broad regulatory network.

The regulatory network adopted in the Coordinated Framework is a patchwork grouping of federal agencies. The Coordinated Framework includes six federal agencies: FDA, EPA, USDA, NIH, the National Science Foundation (hereinafter “NSF”), and the Occupational Safety and Health Administration (hereinafter “OSHA”).¹⁴⁸ Although the NIH,¹⁴⁹ NSF, and OSHA are vital for biotechnology regulation, the major agencies for implementation of the Coordinated Framework are the FDA, EPA, and USDA.¹⁵⁰ The Coordinated Framework concluded that the major statutes associated with each of these three agencies had the ability to cover biotechnology and any changes necessary could be accomplished through the promulgation of administrative regulations.¹⁵¹

The statutes and regulations associated with each of the agencies and how each can be applied to the regulation of GM insects will be covered in the following sections. It is important to realize that the determination of jurisdiction is largely untested;¹⁵² this paper will report on which agency

¹⁴⁴ *Id.* at 23,302-03.

¹⁴⁵ *Id.* at 23,303.

¹⁴⁶ *Id.* at 23,302-03.

¹⁴⁷ *Id.*

¹⁴⁸ *Id.* at 23,303.

¹⁴⁹ The NIH through its Guidelines for Research Involving Recombinant DNA Molecules places contractually binding regulations on researchers, however, if a researcher is doing work *not* funded by the NIH, they are not bound to these guidelines. 51 Fed. Reg. 16,958, 16,959 (May 7, 1986).

¹⁵⁰ See PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 49.

¹⁵¹ Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. at 23,303-04.

¹⁵² To date only two field trials have been approved – GM pink bollworms in AZ and GM mites in FL. See Trevor Thieme, *Building a Better Pest*, POPULAR SCIENCE, Oct. 2001, at 64, 67.

could regulate a particular GM insect. Also, the type of GM insect and its use will heavily dictate which agencies have primary jurisdiction over its regulatory review. It is possible and likely, however, that more than one agency and one set of regulations will apply to any one GM insect. The fact that an agency has jurisdiction over one facet of GM insects does not mean that it will have the capability to assess all relevant risks. This section will be organized by agency; the order will be the FDA, the EPA, and the USDA. Under each agency, different statutes and regulations will be discussed.

B. Food and Drug Administration

The FDA is a vital federal agency which has the main task of regulating food and drugs in the United States. This agency derives its power from the Federal Food, Drug, and Cosmetic Act (hereinafter "FFDCA").¹⁵³ Although the Coordinated Framework concluded that biotechnology products should be regulated, *and not the process* used to create the products, most agencies differentiate biotech products from non-biotech products based on the process and regulate based on a product's GM status. The FDA, however, is the agency that has stayed closest to the ideal of regulating the product and not the process.¹⁵⁴ FDA's evaluation of all drugs (GM insect or not) is based on whether each is "safe and effective," a determination made after several rounds of testing.¹⁵⁵ Prior to an FDA finding of "safe and effective," several steps must occur. First, the FDA must assert jurisdiction over the product.¹⁵⁶ Then, if jurisdiction is proper, the producer must prove their product is "safe and effective" by going through several regulatory steps.¹⁵⁷

¹⁵³ See 21 U.S.C. §§ 310-399 (2006).

¹⁵⁴ See CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: REGULATION OF GENETICALLY ENGINEERED ANIMALS CONTAINING HERITABLE RECOMBINANT DNA CONSTRUCTS 4 (2009), available at <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM113903.pdf> (stating that the FDA's policy is to regulate the article produced (quoting 21 U.S.C. § 321(g)(1))).

¹⁵⁵ 21 U.S.C. § 321(v)(1)-(2).

¹⁵⁶ See *id.* subsec. (g)(1).

¹⁵⁷ See 21 C.F.R. §§ 312.20, 312.22 (2009).

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1. Regulatory Jurisdiction

Although the FDA has yet to assert jurisdiction over a GM insect release, the FDA has the potential to assert jurisdiction under the *two-pronged* definition of a “drug.”¹⁵⁸ This conclusion comes from a broad reading of the definition of regulated articles.¹⁵⁹ In 21 U.S.C. § 321 (g)(1), Congress defined the *first prong* of the FDA’s regulatory jurisdiction over a “drug” as a product “intended to affect the structure or any function of the body of man or other animals”¹⁶⁰ Genetic modifications could be seen as affecting “the structure or any function” of the transgenic insect because the alterations could affect the insidious function of disease transmission. Also, production of a new protein would alter the structure of the native species in that a new structure would be present. Thus, broadly interpreted, any genetic modification would fall under the FDA’s purview if the intent is to alter the structure or any function of the insect. In fact, in a non-binding guidance statement provided by the FDA’s Center for Veterinary Medicine (hereinafter “CVM”), the CVM claimed jurisdiction over GM insects based solely on the “structure or any function” provision.¹⁶¹

Additionally, techniques using paratransgenesis would also likely fall under this “structure or any function” definition of a drug. The genetic modification of insect symbionts which would prevent the transmission of diseases would, in a very broad sense, alter the function of the disease vector. Thus, the FDA would also likely have regulatory authority over insects altered via paratransgenesis.

The FDA must also satisfy the second part of the “drug” definition to be able to assert jurisdiction. The *second prong* of the definition of “drug” reads “articles intended for use in the diagnosis, cure, mitigation,

¹⁵⁸ See 21 U.S.C. § 321(g)(1).

¹⁵⁹ These broad readings are necessary because the FFDCA was originally drafted in 1906 at a time when none of these biotechnology innovations were remotely contemplated.

¹⁶⁰ 21 U.S.C. § 321(g)(1)(C).

¹⁶¹ CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 5.

treatment, or prevention of disease in man or other animals.”¹⁶² GM insects that have been designed to either eliminate disease vectors, through the SIT, or replace populations of competent vectors with those that are refractory to carrying diseases may fall under this category. Insect symbionts altered through paratransgenesis would likely be seen as preventing disease; this would be another avenue for the FDA to assert regulatory jurisdiction over those organisms. Also, GM insects, designed for the above purposes are created to “prevent disease in man.” Additionally, if an insect was genetically modified to deliver a compound to a human upon feeding (perhaps a vaccine), the GM insect could be viewed as a drug delivery system. Thus, the FDA will likely be able to satisfy both prongs of the jurisdictional requirements, giving it the ability to regulate GM insects.

After a likely finding that GM insects are animal drugs, the FDA must make further findings before regulatory action can be taken. The CVM of the FDA has taken the position that GM animals (insects are animals) are to be regulated like “new animal drugs.”¹⁶³ Under the FFDCa, “new animal drugs” are to be “deemed unsafe” unless: (1) there is an approved new animal drug application (hereinafter “NADA”); or (2) the drug is for investigational uses and it conforms to the requirements of an Investigational New Animal Drug (hereinafter “INAD”); or (3) the drug is in compliance with other exceptions set forth in 21 U.S.C. § 360b(a)(4) or (5).¹⁶⁴ In effect, for a field trial of GM insects, if the FDA asserts jurisdiction, a researcher would have to go through the regulatory phase described below.

When applying for FDA approval, it is important that developers of GM insects have refined their chosen lineage of insect. When directly modifying an insect’s genome via transposon or virus, these genetic constructs can insert almost anywhere in the insect’s DNA, meaning that one hatching of insect offspring can have many different insertions. The FDA has stated that each insertion requires its own approval.¹⁶⁵ Thus, a

¹⁶² 21 U.S.C. § 321(g)(1)(B).

¹⁶³ CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 5.

¹⁶⁴ *Id.* GM insects do not qualify for (3) as mandated by statute. 21 U.S.C. § 360ccc(a)(3)(A).

¹⁶⁵ CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 5.

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manufacturer of GM insects has great incentive to select one lineage of modified insects and seek approval for those after refinement.

In conclusion, it is likely that a broad reading of the FFDCA could be construed to confer the FDA with regulatory authority over GM insects. The next step in the process would be the actual regulatory steps imposed by the FDA on GM insect producers.

2. FDA's Regulatory Process

If the FDA asserts jurisdiction over GM insects (which it likely will), producers will face regulatory steps, which must be completed if they wish to have their insects no longer “deemed unsafe.” The FDA has stated that there are certain circumstances where it will not assert jurisdiction, however, the agency does reserve the right to do so if it sees fit. The two circumstances where the FDA will not require an INAD and NADA approval are: (1) GM insects not intended for food uses that other agencies (such as USDA) will regulate; and (2) GM insects not intended for food uses in a controlled environment, such as an approved laboratory.¹⁶⁶ In light of the recent push toward collaborative science, however, shipping of GM insects for experiments at different facilities may be necessary. This development will likely trigger the requirement for an INAD.

INAD regulations cover testing of GM animals and clinical investigations associated with those animals.¹⁶⁷ INAD regulations generally require diligent record keeping, labeling of any shipping containers, records regarding animal disposition, and whether or not the animals or animal-derived products will enter the food supply.¹⁶⁸ In the case of GM insects under experimental investigation, it is likely that the only requirements associated with an INAD would be for labeling of shipments and record-keeping, as the GM insects are not likely to enter the food supply at this early stage. Thus, prior to any interstate shipping of GM insects, investigators will have to file an application with the FDA for an INAD and meet the labeling and record-keeping requirements of 21

¹⁶⁶ *Id.* at 6.

¹⁶⁷ *See id.* at 8.

¹⁶⁸ *See* 21 C.F.R. § 511.1 (2009).

C.F.R. § 511.1(b). The FDA has urged the biotechnology industry to file INAD notices as early as possible in the development process; however, it is not required to do so until GM insects enter interstate shipping routes.¹⁶⁹

A GM insect producer's INAD application will be reviewed for compliance with FDA regulations, and because the approval of an INAD is a "federal action," the procedural requirements of the National Environmental Policy Act (hereinafter "NEPA") must be met as well.¹⁷⁰ The NEPA requirements are intended to address any potential environmental considerations associated with a "federal action," such as regulatory approval.¹⁷¹ GM insect producers will have to file an environmental assessment of their products¹⁷² or claim a categorical exemption¹⁷³ if they can prove that extraordinary circumstances will not exist, although NEPA considerations must still be noted in every "federal action," regardless of the finding.¹⁷⁴ Producers of GM insects, in their INAD applications, will have to explain any significant potential adverse impacts on the environment and describe containment methods designed to prevent those impacts.¹⁷⁵ Although environmental considerations are highly relevant and important, NEPA considerations are only procedural; the FDA is under no obligation to use those assessments in its decision.¹⁷⁶

INAD applications will be important for GM insect developers in the early stages; however, the actual NADA is the crucial hurdle to mass release of GM insects. Approval of a new animal drug is based on whether the drug's producer demonstrates the drug's safety and efficacy.¹⁷⁷ A NADA is a long and complex document with requirements defined in 21 C.F.R. § 514.1; the technicalities of which are too detailed for this paper. The most important inclusions in the NADA are: (1) how the GM insect was created (including its full genotypic characterization);

¹⁶⁹ CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 8.

¹⁷⁰ *Id.* at 11.

¹⁷¹ *Id.*

¹⁷² 21 C.F.R. §§ 25.15, 511.1(b)(10).

¹⁷³ *Id.* § 25.33(e).

¹⁷⁴ *Id.* § 25.21.

¹⁷⁵ *See* CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 11.

¹⁷⁶ *See id.*

¹⁷⁷ 21 U.S.C. § 360b(a)(1) (2006).

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(2) providing samples of the GM insect; (3) evidence establishing safety and efficacy; and (4) meeting NEPA requirements by filing either an environmental assessment or claiming one of the categorical exemptions.¹⁷⁸

One of the most powerful criticisms of the FDA asserting jurisdiction for the regulation of GM insects stems from the complex nature of the NADA application process. The FDA lacks the expertise to regulate the environmental risks which will likely be a major issue for the release of the GM insects. The FDA is geared toward the regulation of foods and traditional “drugs,” and, therefore, is not prepared to understand the intricacies associated with the release of a GM insect and how it *could* lead to severe environmental impacts. The “safe and effective” standard will have little use when it comes to assessing impacts on ecosystems.

Another complaint regarding the FDA’s regulatory process is its lack of transparency.¹⁷⁹ The NADA process is confidential and the FDA is not allowed to notify the public of a pending application.¹⁸⁰ After approval of an NADA, the FDA would release a summary of the data it used for making its decision.¹⁸¹ In its recent guidance statement, the CVM of the FDA stated that it wished to increase transparency in this process.¹⁸² To accomplish this goal, the CVM stated that it would “hold public advisory committee meetings prior to approving any [GM] animal.”¹⁸³ Although this process has not been applied yet, this may assuage some of the concerns associated with FDA approval of GM insects.

In conclusion, the FDA likely has the regulatory authority over *any* GM insect set to be released. Producers of GM insects will probably have to comply with the INAD application process during the developmental phase and the NADA process prior to mass-release.

C. Environmental Protection Agency

¹⁷⁸ See 21 C.F.R. § 511.1.

¹⁷⁹ See PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 69.

¹⁸⁰ *Id.*

¹⁸¹ *Id.*

¹⁸² CTR. FOR VETERINARY MED., FOOD & DRUG ADMIN., *supra* note 154, at 12.

¹⁸³ *Id.*

The EPA is the second of the three agencies to have regulatory power of biotechnology products, per the Coordinated Framework. Charged with regulating products, the EPA ensures that each product is safe for the environment and for human use.¹⁸⁴

Similar to the FDA, the EPA has yet to assert regulatory authority over GM insects. The following sections will investigate how EPA *could* assert regulatory jurisdiction over GM insects and the process that would follow.

1. Regulatory Jurisdiction

The EPA has two statutory avenues for the regulation of GM insects: (1) the Federal Insecticide, Fungicide, and Rodenticide Act¹⁸⁵ (hereinafter “FIFRA”); and (2) the Toxic Substances Control Act¹⁸⁶ (hereinafter “TSCA”). If the FDA exerts its authority under the FFDCA, effectively deciding that GM insects are either human or animal drugs; the EPA cannot apply either FIFRA or TSCA.¹⁸⁷

a. FIFRA

FIFRA gives the EPA broad regulatory discretion over “pesticides.” Congress has defined “pesticide” as “any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest.”¹⁸⁸ GM insects designed to eliminate or mitigate the impact of agricultural pests, such as the GM screwworm and GM Mediterranean fruit fly,¹⁸⁹ would fit this definition of a pesticide because of its impacts on those pests. Thus, although once again broadly construed to confer regulatory authority, the EPA could assert regulatory jurisdiction over GM insects based on FIFRA.

¹⁸⁴ See U.S. EPA, About EPA, <http://www.epa.gov/epahome/aboutepa.htm> (last visited Jan. 9, 2010).

¹⁸⁵ 7 U.S.C. §§ 136-136y (2006).

¹⁸⁶ 15 U.S.C. §§ 2601-2695d (2006).

¹⁸⁷ 7 U.S.C. § 136(u); 15 U.S.C. § 2606.

¹⁸⁸ 7 U.S.C. § 136(u).

¹⁸⁹ See *supra* Part I.A.2.

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b. TSCA

TSCA is a broad statute, under which the EPA controls non-drug or non-pesticide compounds.¹⁹⁰ Thus, if the FDA under FFDCA regulated GM insects as a “drug” or if the EPA regulated GM insects as a “pesticide,” this statute would not apply.¹⁹¹ In light of these other two more specific avenues for regulation, it is unlikely that the EPA would assert jurisdiction under TSCA, however, it is still possible. The EPA could use TSCA to gain regulatory authority over GM insects by defining GM insects as a “chemical substance.” Congress has defined a “chemical substance” as “any organic or inorganic substance of a particular molecular identity”¹⁹² This is a *very* broad-sweeping definition and could include any substance as long as it has a “particular molecular identity,” which GM insects would possess because of their extensive genotypic characterization. Thus, GM insects would probably fall under this definition.

Additionally, EPA has used TSCA to promulgate regulations governing GM microorganisms. The EPA has regulations which govern “intergenic microorganisms.”¹⁹³ The agency defines these as including “a microorganism which contains a mobile genetic element which was first identified in a microorganism in a genus different from the recipient microorganism.”¹⁹⁴ Any insects altered through paratransgenesis would be covered by this definition because of the alterations to bacterial flora in their gut, but only if the gene has been transferred from one genus of bacteria to another. Thus, any directly genome modified or paratransgenic insect could be covered by TSCA.

One potential issue with TSCA jurisdiction related to paratransgenic insects is that its review is limited to those GM

¹⁹⁰ See Toxic Substances Control Act, 15 U.S.C. §§ 2601-2695d.

¹⁹¹ See *id.* § 2602(2)(B)(ii), (vi).

¹⁹² *Id.* subsec. (2)(A).

¹⁹³ 40 C.F.R. § 725.3 (2009).

¹⁹⁴ *Id.*

microorganisms “with a commercial purpose.”¹⁹⁵ Many of the current efforts are funded through the NIH, the Gates Foundation, or other entities in a non-commercial setting. In those cases, TSCA could not be used to confer regulatory jurisdiction on the EPA.

Overall, the EPA, through a broad reading of either FIFRA or TSCA could assert regulatory jurisdiction over GM insects.

2. EPA's Regulatory Process

The manner in which the EPA would regulate GM insects would vary depending on which statute the agency decided to utilize to obtain jurisdiction. This section will analyze the regulatory steps for each statute.

a. FIFRA

Prior to the commercial release of any pesticide, it must be registered with the EPA.¹⁹⁶ This would impose upon producers of GM insects the requirement to gain registration status with the EPA prior to introduction of GM insects into the environment.¹⁹⁷ Registration entails a balancing of the risks and benefits associated with any use of the pesticide.¹⁹⁸ To obtain approval, the pesticide must “function without unreasonable adverse effects on the environment”¹⁹⁹ Congress had defined “unreasonable adverse effects on the environment” as: “(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food”²⁰⁰ These standards would have to be met with experimental data provided by producers of GM insects to prove that the potential risks described in earlier sections of this essay do not outweigh the potential benefits.

¹⁹⁵ *Id.* § 725.8(a)

¹⁹⁶ 7 U.S.C. § 136a (2006).

¹⁹⁷ *See id.*

¹⁹⁸ *See id.* § 136a(c)(5).

¹⁹⁹ *Id.* subsec. (c)(5)(C).

²⁰⁰ *Id.* § 136(bb).

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Additionally, to gather any data required to apply for a pesticide permit, GM insect producers would likely need an “experimental use permit.”²⁰¹ This permit would allow for the controlled use of GM insects in confined quarters to gather data for the review process.²⁰²

Overall, under FIFRA, the EPA would have to balance the risks to the environment and to human health with the great potential benefits associated with GM insects before the agency would grant approval.

b. TSCA

TSCA-based regulation requires that a party manufacturing a “chemical substance” must submit a pre-manufacture notification to the EPA at least ninety days prior to beginning manufacture.²⁰³ This submission is not required if the “chemical substance” is on the EPA’s TSCA Chemical Substances Inventory,²⁰⁴ a listing of approximately 83,000²⁰⁵ chemical substances. During this ninety day period, the EPA will review all materials submitted with the pre-manufacture notice including environmental and health effects, intended use, and intended commercial distribution, among others.²⁰⁶ Similar to regulation under FIFRA, if not enough information is known, a balancing of risks against benefits will ensue.²⁰⁷

TSCA regulation can be tricky for GM insects. Depending on the protein expressed, TSCA regulation may or may not be complicated. If the genetic modification results in expression of a protein that is already present on the EPA’s Toxic Substances list, the regulatory steps may be simple because the pre-manufacture notification steps will not be necessary. If the protein is not on the EPA’s list, however, the steps

²⁰¹ See *id.* § 136c.

²⁰² See *id.* subsec. (a).

²⁰³ 15 U.S.C. § 2604(a) (2006).

²⁰⁴ Neil A. Belson, *US Regulation of Agricultural Biotechnology: An Overview*, 3 J. AGROBIOTECHNOLOGY MGMT. & ECON. 268, 273 (2000).

²⁰⁵ U.S. EPA, *What is the TSCA Chemical Substance Inventory?*,

<http://www.epa.gov/oppt/newchems/pubs/inventory.htm> (last visited Nov. 13, 2009).

²⁰⁶ 15 U.S.C. § 2604(a).

²⁰⁷ See *id.* § 2605.

associated with the “pre-manufacture notice” may be more onerous.

The EPA has given some indication that regardless of whether the FDA determines that a GM insect is a “drug,” the EPA believes it can still regulate under TSCA. The EPA believes that the “drug” component of the GM insect is the genetic modification; however, the entire GM insect (including all components – natural or GM) is a “chemical substance” under TSCA.²⁰⁸ This adds to the confusion associated with the regulation of GM insects.

One important positive that would come from EPA regulation is the transparency associated with regulation either under FIFRA or TSCA. Applications to the EPA, under either of these statutes, require a public notice period with a mandatory publication in the Federal Register.²⁰⁹ One exception is confidential business information. Per TSCA, a manufacturer can designate disclosure to the EPA under TSCA as “confidential,” which restricts its release in the Federal Register.²¹⁰ Potentially, a GM insect producer could attempt to deem their product “confidential” and try to restrict its publication in the Federal Register. However, some public comment and discourse on these topics is possible. This may help the public perception of the regulation of GM insects.

In conclusion, the EPA likely has two different routes to regulate GM insects, FIFRA and TSCA. Regulation under these statutes is largely a matter of balancing the risks against the benefits associated with GM insects. Once again, it is entirely possible for the EPA in conjunction with other agencies to assert control, making the regulatory process difficult to apply.

D. U.S. Department of Agriculture

The USDA has broad statutory authority to regulate and promote U.S. agriculture and to protect it from potential threats such as animal illnesses and plant pests. In terms of biotechnology and protecting U.S. agriculture from pests, the USDA largely functions through the Animal and Plant

²⁰⁸ See COUNCIL ON ENVTL. QUALITY, OFFICE OF SCI. & TECH. POLICY, CASE STUDIES OF ENVIRONMENTAL REGULATION FOR BIOTECHNOLOGY (2001).

²⁰⁹ 7 U.S.C. § 136a-1(d) (2006); 15 U.S.C § 2604(d).

²¹⁰ 15 U.S.C. § 2613(a).

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Health Inspection Service (hereinafter “APHIS”).²¹¹ APHIS regulates all items that could be introduced which could potentially harm U.S. agriculture.²¹² The USDA, functioning through APHIS, could assert jurisdiction over GM insects using two broad statutes, the Plant Protection Act²¹³ and the Animal Health Protection,²¹⁴ and one narrow statute, the Honeybee Act.²¹⁵

1. USDA’s Jurisdiction

a. Plant Protection Act

The Plant Protection Act (hereinafter “PPA”), enacted in 2000 (replacing the Federal Plant Pest Act), was originally intended to prevent the introduction and movement of traditional “plant pests,” but has been broadly interpreted to include products of biotechnology.²¹⁶ The PPA gives APHIS regulatory control over any articles that could be considered “plant pests.”²¹⁷ Congress has defined “plant pests” as “any living stage of any of the following that can directly or indirectly injure, cause damage to, or cause disease in any plant or plant product . . . [including a] nonhuman animal.”²¹⁸ GM insects that are created to limit agricultural pests that have the potential to destroy crops, such as a GM Mediterranean fruit fly, could fit under this definition of a “plant pest” because GM fruit flies are “plant pests” with a genetic modification. Even though the GM fruit fly will mate and produce non-viable offspring, the release of the GM fruit fly would effectively be the release of an organism that could damage hundreds of types of plants. Thus, any GM insect created to alleviate the effects of a “plant pest” would likely fall under this definition.

²¹¹ United States Regulatory Unified Biotechnology Website, Roles of U.S. Agencies, <http://usbiotechreg.nbio.gov/roles.asp> (last visited Dec. 19, 2009).

²¹² See U.S. Department of Agriculture, Animal and Plant Health Inspection Service, <http://www.aphis.usda.gov/> (last visited Jan. 9, 2010).

²¹³ 7 U.S.C. §§ 7701-7786.

²¹⁴ *Id.* §§ 8301-8322.

²¹⁵ *Id.* §§ 281-286.

²¹⁶ See *id.* § 7701; 7 C.F.R. § 340.0 (2009).

²¹⁷ 7 U.S.C. § 7711.

²¹⁸ *Id.* § 7702(14)(B).

The PPA also gives APHIS regulatory authority over “biological control organisms.”²¹⁹ APHIS may regulate use of “biological control organisms,” much like it may regulate “plant pests.” Congress has defined “biological control organisms” as “any enemy, antagonist, or competitor used to control a plant pest”²²⁰ This definition is a more accurate description because all GM insects designed to eliminate or mitigate a “plant pest” are an enemy of that “plant pest.” A GM insect would be created to control a plant pest, like the Mediterranean fruit fly, and thus USDA through APHIS would have regulatory jurisdiction over GM insects under either the “plant pest” or “biological control organism” provisions of the PPA. Additionally, paratransgenic insects may also fit under the definition of a “biological control organism.” The microorganisms, genetically engineered to function as a disease control agent, would be designed to work as an “enemy” or “antagonist” of pests; thus these microorganisms would also likely be covered. Also, to date, APHIS, under the PPA, is the only regulatory body to assert and regulate a field trial of a GM insect, the GM pink bollworm.²²¹

One final note is that the state of regulations under the PPA may be in flux. On October 9, 2008, APHIS published changes to its regulatory scheme in the Federal Register.²²² PPA requested comments and later had to extend the comment period.²²³ Public meetings to discuss regulatory changes were scheduled for April 2009, although no further actions have been taken.²²⁴

²¹⁹ See *id.* § 7712.

²²⁰ *Id.* § 7702(2).

²²¹ PEW INITIATIVE ON FOOD & BIOTECHNOLOGY, *supra* note 26, at 56-57.

²²² Importation, Interstate Movement, and Release into the Environment of Certain Genetically Engineered Organisms, 73 Fed. Reg. 60,008 (proposed Oct. 9, 2008) (to be codified at 7 C.F.R. pt. 340).

²²³ Introduction of Organisms and Products Altered or Produced Through Genetic Engineering, 74 Fed. Reg. 10,517 (proposed Mar. 11, 2009) (to be codified at 7 C.F.R. pt. 340).

²²⁴ *Id.*; see ANIMAL & PLANT HEALTH INSPECTION SERV., U.S. DEP'T OF AGRIC., ISSUE PAPER 2: INCORPORATION OF THE PLANT PROTECTION ACT NOXIOUS WEED PROVISIONS (2009), available at http://www.aphis.usda.gov/biotechnology/340/340_downloads/apr09pubmtg_issuepaper_noxweed.pdf.

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b. Animal Health Protection Act

The Animal Health Protection Act (hereinafter “AHPA”)²²⁵ was enacted in 2002 to aid in preventing, controlling, detecting, and eradicating animal diseases and pests.²²⁶ Under AHPA, APHIS has the broad authority to protect against animal diseases and pests, including disease vectors, such as insects.²²⁷ Congress has defined “pests” as “any of the following that can directly or indirectly injure, cause damage to, or cause disease in livestock . . . [including a]n arthropod.”²²⁸ Similar to the argument for plant pests, GM insects, created to limit diseases vectored by insects, could still cause injury to animals; GM insects may still need to feed on animals to survive. Now, it is possible that only male insects would be released. Generally the male insect does not blood feed and thus does not spread disease, meaning that if only males are released the GM insects would be unable to injure livestock, either directly or indirectly. This would be a consideration for designers of GM insects. Thus, depending on the potential of the GM insect to injure animals, no matter how beneficial it may be in wiping out disease vectors, it may be regulated under AHPA.

c. Honeybee Act

The Honeybee Act was originally enacted to give APHIS the authority to regulate importation of honeybees to limit the impact of “Africanized” bees.²²⁹ Under this act, APHIS has the authority “to prohibit or restrict the importation or entry of honeybees . . . into or through the United States”²³⁰ Although limited to only one type of GM insect, this Act could nonetheless apply. As described above, genetic modification of honeybees is being considered, and under a broad reading of this statute, GM honeybees would be covered. After all, GM honeybees are still

²²⁵ 7 U.S.C. §§ 8301-8322 (2006).

²²⁶ *Id.* § 8301(1).

²²⁷ See *id.* §§ 8301-8322.

²²⁸ *Id.* § 8302(13)(G).

²²⁹ PEW INITIATIVE FOR FOOD & BIOTECHNOLOGY, *supra* note 26, at 57.

²³⁰ 7 U.S.C. § 281(a).

honeybees with added genes.

In conclusion, the USDA, through APHIS, could easily assert regulatory jurisdiction through a broad reading of the PPA, AHPA, or the Honeybee Act.

2. USDA's Regulatory Process

One of the first steps in APHIS' regulatory process is consideration of the NEPA procedural requirements.²³¹ Similar to what was described in the FDA section, APHIS must consider an environmental assessment to determine if the release under the PPA, AHPA, or the Honeybee Act would cause a major environmental concern.²³² If APHIS determines that the release of a GM insect (only the GM insect applying for a permit) would not pose a significant environmental threat, APHIS will issue a finding of no significant impact.²³³ If APHIS has concerns about the environmental impact, the agency can order an environmental impact statement to be prepared.²³⁴ Interestingly, for the release of the GM bollworm in Arizona, APHIS issued a finding of no significant impact.²³⁵ Although not required, APHIS proceeded to carry out an environmental impact statement, in spite of the finding of no significant impact.²³⁶ The environmental impact statement illustrated there were no expected environmental concerns associated with the field testing of the GM pink bollworms.²³⁷

Currently, APHIS has developed rules that could be, and have been, used for the release of GM insects under the PPA. Prior to the release of a GM organism, APHIS must be notified and may require a permit to be

²³¹ See 7 C.F.R. § 372.1 (2009).

²³² PEW INITIATIVE FOR FOOD & BIOTECHNOLOGY, *supra* note 26, at 60.

²³³ *Id.*

²³⁴ *Id.*

²³⁵ Availability of Environmental Assessment and Finding of No Significant Impact for Confined Field Test of Genetically Engineered Pink Bollworm, 67 Fed. Reg. 1434 (Jan. 11, 2002).

²³⁶ Environmental Impact Statement; Genetically Engineered Pink Bollworm, 67 Fed. Reg. 5086 (Feb. 4, 2002).

²³⁷ *Id.*

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issued.²³⁸ APHIS has the power to place certain articles under an exemption for a permit, requiring only notice, but not a permit.²³⁹ This, however, may change in the proposed revisions to the USDA regulations²⁴⁰ discussed above. There are several requirements that must be met to fit under the exemptions list, one of which is that the article must be a plant,²⁴¹ thus GM insects will not fit under this exemption list.

APHIS' permit process is similar to other agencies' regulatory processes. GM insect producers would be required to provide copious amounts of information so that the agency can perform a risk assessment as to whether the organism can be controlled.²⁴² Similar to the EPA's requirements, APHIS requires information regarding the GM insect's genotype, ecological considerations, biology, mating fitness, a risk assessment, and control mechanisms, among other information that can be used in a risk balancing manner.²⁴³

A permit will not be issued or will be cancelled once issued, if the safeguards associated with containing the "plant pest" are not adequate or if the risks of dissemination outweigh the benefits.²⁴⁴ This point can be important for later commercial development of GM insects. The containment procedures for field testing are understandable; APHIS does not wish to allow GM insects to spread until it knows that the insects will properly function. However, GM insects' entire purpose will be dissemination and population eradication or replacement. If defined as a "plant pest," conflict could arise in allowing full release. To date, no GM insects have been fully released (SIT insects aside), thus, the regulations, and how each will be adapted to that process, have yet to be tested.

APHIS, although likely possessing jurisdiction under AHPA and the Honeybee Act, has not yet promulgated regulations to address how GM

²³⁸ 7 C.F.R. § 340.4 (2009).

²³⁹ *Id.* § 340.3.

²⁴⁰ See Performance Specification and Quality Assurance Requirements for Continuous Parameter Monitoring Systems, 73 Fed. Reg. 59,956 (Oct. 9, 2008).

²⁴¹ 7 C.F.R. § 340.3(b)(1).

²⁴² See *id.* § 340.4; Animal and Plant Health Inspection Service, Transgenic Insect Permit Guidance, <http://www.aphis.usda.gov/biotechnology/arthropods.shtml> (last visited Nov. 13, 2009).

²⁴³ Animal and Plant Health Inspection Service, *supra* note 242.

²⁴⁴ 7 C.F.R. § 330.204.

insects could be regulated under these statutes.

Finally, the transparency of APHIS' process is similar to the EPA. APHIS will provide (and has provided in the case of the GM pink bollworms) notice of regulatory actions in the Federal Register, allowing time for public comment and hearings. This will be helpful in assuaging the public's concerns with the regulatory process.

In conclusion, the USDA, through APHIS, has regulatory jurisdiction over GM insects. Its regulatory process has already experienced the granting of a permit for GM pink bollworms for limited, contained release in Arizona. Although APHIS has only experienced minor testing of its process, it appears to have been successful. With the proposed rule changes that were published in the Federal Register last year, this process will likely change, with unknown consequences.

E. *International Regulation*

The final destination of some GM insects developed in the United States will be abroad. As detailed in earlier sections, one of the significant motivations for the design and release of GM insects is to limit the transmission of tropical diseases. These diseases are endemic abroad, thus international regulations will be highly relevant for GM insect producers.

The current state of international regulation is in flux. In 2002, the Food and Agricultural Organization of the United Nations, in conjunction with the International Atomic Energy Association held a meeting in Rome to discuss GM insects, including their regulation.²⁴⁵ One of the conclusions from the conference was that "[c]urrent national regulatory processes, including the availability of suitable risk analysis protocols, may be insufficient to address any eventual release of transgenic arthropods."²⁴⁶ This illustrates how difficult it will be for developers of GM insects to obtain regulatory approval, if even available in target countries.

²⁴⁵ FAO/IAEA AGRICULTURE & BIOTECHNOLOGY LAB., INT'L ATOMIC ENERGY AGENCY, STATUS AND RISK ASSESSMENT OF THE USE OF TRANSGENIC ARTHROPODS IN PLANT PROTECTION 3 (2002), available at http://www-pub.iaea.org/MTCD/publications/PDF/te_1483_web.pdf.

²⁴⁶ *Id.* at 4.

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Another concern is the stability of target countries. It is entirely possible that a regulatory regime, similar to what is available in the United States, will not be present in a target country because of the lack of stability of governments in some of these developing nations. These concerns highlight just some of the problems that producers of GM insects will face when seeking regulatory approval abroad.

In spite of this uncertainty, one regulatory mechanism that will likely apply is the Cartagena Protocol on Biosafety (hereinafter "Protocol"). This Protocol was adopted as a part of the Convention on Biological Diversity to apply to "transboundary movement, transit, handling and use of all living modified organisms that may have adverse effects on the conservation and sustainable use of biological diversity" ²⁴⁷ The Protocol defines "living modified organism" as "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology." ²⁴⁸ Thus, a GM insect would likely fall under the Protocol, especially because of its ability to move not only across ecosystems, but also across transnational boundaries. The Protocol does, however, exempt living modified organisms which can serve as pharmaceuticals. ²⁴⁹ Thus, if a GM insect was created to transmit a vaccine-like dose of an antigen for human use, the Protocol may not apply.

Although GM insects would likely fall under the Protocol, this document serves only as a notification system among countries that are signatories to the Protocol. The Protocol requires that advanced notice be given to the country where the living modified organisms are to be shipped. ²⁵⁰ This notice only applies to organisms that will be released into the environment and includes detailed information about the GM organism. ²⁵¹ Also, to date, the United States is not a signatory to the

²⁴⁷ Cartagena Protocol on Biosafety to the Convention on Biological Diversity art. 4, Jan. 29, 2000, 2226 U.N.T.S. 257, *available at* http://untreaty.un.org/unts/144078_158780/6/5/13663.pdf.

²⁴⁸ *Id.* art. 3(g).

²⁴⁹ *Id.* art. 5.

²⁵⁰ *Id.* art. 8.

²⁵¹ *Id.* art. 7, annex I.

Protocol, and is not subject to its requirements.²⁵² Currently, the Protocol functions only as an advanced warning system for countries into which GM insects would be shipped; there is not a liability or redress system associated with it.

Overall, prior to implementation of a strategy using GM insects, much more work will have to be done to implement a regulatory framework that is capable of dealing with their release. Aside from a purely domestic regulatory framework, which may or may not be present, an international set of regulations would be beneficial to all involved.

CONCLUSION

In conclusion, GM insects will likely be a necessary part of our future. Many needs for GM insects are present. Those needs include mitigating public health disasters associated with tropical disease, assuaging the burdens of crop and livestock pests, and the endless potential that comes with altering insects to produce pharmaceuticals. Although, there are different views on the risks and rewards associated with GM insects, the regulatory process helps to balance the two. The Coordinated Framework has created a system wherein the FDA, the EPA, and the USDA will be (and have been) able to regulate GM insects. There is, however, a lack of adequate clarity on which agency will regulate GM insects and whether the insect's intended use or some other measure will govern which agency regulates which GM insect. Finally, there is a dearth of information regarding international regulation. Producers of GM insects will need to know how their products will be regulated on foreign shores because so many of the motivations for GM insects are abroad. Overall, GM insects will become a necessary part of our future.

²⁵² See Convention on Biological Diversity, List of Parties, <http://www.cbd.int/biosafety/parties/list.shtml> (last visited Jan. 9, 2010) (listing countries with their date of ratification and further listing the United States without a date of ratification).