Rachel Carson and the Adaptation of Biotechnology to Crop Protection

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Biotechnology is the latest breakthrough in the history of agriculture. Like the pesticides that preceded them, transgenic crops such as corn and soybeans were readily adopted at first, then they encountered opposition starting in Europe. Proposals for applications of transgenic insects, however, met with opposition from the beginning. In this article, I give a historical background to the impetus for developing transgenic insects in crop protection from the perspective of a little-known quote from Rachel Carson. I also detail the regulatory experience and public reaction to transgenic pink bollworms and paratransgenic leafhoppers.

Rachel Carson on Pesticide Use

In the preface to their book on insecticide bioassay, Robertson and Preisler (1992) reprinted a quote from Rachel Carson, author of *Silent Spring*: [**AuQ 1**]

> I do favor insect control in appropriate situations, that I do not advocate the complete abandonment of chemical control, ...I criticize modern chemical control not because it controls harmful insects, but because it controls them badly and inefficiently, and because it creates many dangerous side effects in doing so. I criticize the present methods because they are based on a rather low level of scientific thinking. We really are capable of much greater sophistication in our solutions of this problem.

This quote was cited from page 7 of the book *Silent Spring Revisited*, edited by Marco, Hollingworth, and Durham (1987), [**AuQ 2**] in which Shirley Briggs described the public reaction to the first printed versions of the content of *Silent Spring*. The reaction to *Silent Spring* grew in content and volume while I was in graduate school. Pesticide and antipesticide factions were equally vocal. Carson became the target of aggressive criticism, yet many of her critics' charges were indefensible. The use of pesticides had become an integral part of pest control, with excessive practices all too common. By then, insect and weed resistance to pesticides had become a widespread problem. Secondary pest outbreaks that could be attributed to pesticide use were well documented. A new philosophy of pesticide use called integrated pest management (IPM) was designed in response to criticisms of pesticide use, and IPM is now part of the lexicon of agriculture.

Biotechnology Applications

The second part of the quote, which calls for greater sophistication in controlling pests, raised the bar in discovering a new way to deal with pests in agriculture. Advances in biotechnology are offering greater sophistication and alternatives to traditional pesticide use. The most obvious uses of biotechnology in crop protection have included advances such as ice-minus bacteria to protect against frost damage (Fishbein 1985; Lindemann and Suslow 1987; Walbot and Yelton, undated) and transgenic crops with inherent herbicide and insect resistance. The former lead to more efficient herbicide use to reduce weed growth, and the latter resulted in less insecticide use against certain key pests (Ferber 1999, Byrne et al. 2004). According to some sources (PANNA 2004), pesticide use actually increased in response to transgenic crops.

Bacteria and plants were the first objects of gene splicing. Animals came later, except for the early work with P-elements, which were [**Au: ok?**] restricted for technical reasons to *Drosophila melanogaster* [**AuQ 8**] (Rubin and Spradling 1982). The first breakthrough in transgenic insect technology came in 1995 (Loukeris et al. 1995). Since then, several species of insects of different orders have been transformed, one of the most recent being the screwworm fly (Allen et al. 2004).

The possible application of this new technology has been described by several authors (Fryxell and Miller 1995, Thomas et al. 2000, Handler 2002, Robinson et al. 2003, [**AuQ 3**] Wimmer 2003), and the applications will ultimately be put through the regulatory process (Hoy 2000, Miller and Staten 2001). The Pew Foundation (2004) recently reported a study of regulatory needs for newer transgenic insect technologies and held a workshop 20–21 September 2004 at Georgetown University, Washington, D.C., to address social and ethical issues in use of transgenic insects.

Although biotechnology applied to insects is relatively new, some aspects of the new strategies have been dealt with by the regulatory process. Robert Staten (Senior Scientist, USDA–APHIS, Phoenix, AZ) applied for a permit to move the transgenic

Table 1. Movement of transgenic pink bollworm between states.

Movement Permits under 7 CFR Part 340
All applications received within last 180 days
Sorted in reverse order by BP number.
Biotechnology Regulatory Services
USDA, APHIS, BRS

6. 03-335-01m APHIS

Reg article:	Pink bollworm	
Destination:	AZ	
Interstate		
Receive:	12/01/03	
St atus:	Issued	2/04/04

Copied directly from the online postings of APHIS: http://www.aphis.usda.gov/cgi-bin/parse-brs-states.pl [**AuQ 10**]
The original movement permit request is at: http://www.aphis.usda.gov/brs/arthropod/permits/9824402m/9824402m.html [**AuQ 10**]

pink bollworm strain from the University of California, Riverside, to USDA quarantine facilities in Phoenix. Even though this was a new application, the Biotechnology Permits branch of USDA–APHIS worked through the permit process, first with Orrey Young (OY in Table 1) [**AuQ 4**]and later with Robert Rose (RR in Table 2). Because these requests were for movement from one quarantine facility to another (indicated by the letter "m" on the permit code number), they did not evoke much in the way of public comment.

Table2. Permit Releases for pink bollworm posted by USDA-APHIS.

Release Permits under 7 CFR Part 340
All applications Sorted in reverse order by BP number. Biotechnology Regulatory Services
USDA, APHIS, BRS

20. 04-005-01r APHIS		
Reg article:	Pink bollworm / OO /	
Release State:	NM	
Reviewer:	RR	
Receive:	1/05/04	
Status:	Pending	
36. 03-104-01r APHIS		
Reg article:	Pink bollworm / OO /	
Release	State:	AZ
Reviewer:	RR	
Receive:	4/14/03	
Status:	Issued	7/14/03
37. 03-104-02r APHIS		
Reg article:	Pink bollworm / OO /	
Release State:	AZ	
Reviewer:	RR	
Receive:	4/14/03	
Status:	Void	
107. 01-029-01r APHIS		
Reg article:	Pink bollworm / OO / Visual marker	
Release State:	AZ	
Reviewer:	RR	
Receive:	1/29/01	
Status:	Issued	10/01/01
http://www.aphis.usda.gov/brs/arthropod/permits/0102901r/0102901r.html		
140. 00-158-01r APHIS		
Reg article:	Pink bollworm / OO /	
Release	State:	AZ
Reviewer:	OY	
Receive:	6/06/00	
Status:	Withdrawn	1/31/01
362. 96-159-01r U of California		
Reg article:	Pink bollworm / OO / Cold intolerant	
Release State:	AZ	CA
Reviewer:	OY	
Receive:	6/07/96	
Status:	Withdrawn	6/11/96

Copied directly from the online postings of APHIS: http://www.aphis.usda.gov/brs/status/relday.html [**AuQ 11**]

The Regulatory Process

When Staten applied for a permit to conduct field trials to compare the reproductive behavior of transgenic pink bollworm with the nontransgenic counterpart (Fig. 1), a great deal of public scrutiny was drawn to the application. Rose used a notice of intent in the Federal Register to usher in a period of public response, and he separately called for comments from parties he knew to be interested.

This was followed by a permit to release transgenic pink bollworm into confined field cages for tests of competition between transgenic and nontransgenic moths (BP No. 01-029-01r, issued 1 October 2001 ; and, No. 03-104-01r, issued 14 July 2003).

During the summer of 2001, a notice was posted in the Federal Register by the USDA–APHIS administrator, Craig A. Reed, [Federal Register (21 June 2001) 66 (120): 33226; Docket No. 01-024-01] about proposed field cage studies of transgenic pink bollworm and nontransgenic counterparts in Arizona. Public reaction was received by the regulatory agency, USDA–APHIS Biotechnology Permits branch and was dealt with by the regulatory personnel. A permit was issued that fall.

An Environmental Assessment, written by Robert I. Rose (2001), was issued for this confined field cage study, 1 October 2001. The assessment document contained Finding of No Significant Impact (FONSI), Response to Comments and an Environmental Assessment; it was signed by Michael Firko, Assistant Director, Permits and Risk Assessment, USDA–APHIS.

Some of our experience with regulatory activity in the pink bollworm project was described by Miller and Staten (2001). Some publicity appeared in an article on the front page of the *Wall Street Journal*, 26 January 2001. The Pew Initiative on Food and Biotechnology report was mentioned in *Business Week* (3 May 2004, p. 75) and on All Things Considered (National Public Radio, 28 June 2004). A number of newspaper articles around the country printed an Associated Press story about the transgenic pink bollworm. Some articles included my picture, a picture of the pink bollworm, or both.

The regulatory agency and I received several e-mails and letters in response to this publicity. I have included a few samples here. [**AuQ 5**]

4 May 2004
I saw a report that you were involved in a proposal to release a batch of moths that carry a fluorescent marker gene inserted by scientists into the wild. The wisdom in doing this release is not sound, and the potential benefits to mankind are miniscule when you compare the potential harm that could result if man continues to attempt to manipulate creation.

10 February 2001
Dr. Miller, I am an older woman, typical of many over 50, and just recently read a brief article about your testing an altered moth in Arizona. This strikes fear in many of us who have lived long enough to see that nature will turn on those who abuse her. I fear that science is abusing nature by acting on the thought that men can do better. Not true without a price to be paid by all of us. I have no doubt that you are an honorable man, but we must stop destruction as a result of scientific curiosity. Science that causes injury or harm to living things is nothing more than abuse of the natural creation. Please reconsider this tinkering before it is too late. Super moths? And what next!!! God help us! And, save us from this science!!!! Thank you for your time.

11 February 2001
Hi, Mr. Miller, I have just been reading about the moths that have been engineered with Jellyfish genes. My question isn't really about these particular creatures, but geneitic modification in general.

Fig. 1. Ernie Miller, USDA-APHIS entomologist checking pink bollworm mating stations in a field cage in Phoenix, AZ, fall 2002 under the auspices of a biotechnology permit.

To be honest it scares the hell out of me that some humans are taking on the role of GOD. No one knows exactly what will happen with these moths, what if one does escape and cause havoc with our ecosystem? Who will accept the blame? Shouldn't we just accept the way nature is and let it be?

12 February 2001
Hi Thomas Miller, I have recently learned that you are currently genetically modifying insects. I am curious what the purpose of changing their DNA code is; and in addition, how hard have you thought about the possible reaction to such changes? Do you really think that [using] insects to fight insects is right? What about a more natural way to do this sort of thing? I am very concerned with what sort of massive problems this may cause. I already do not agree with genetically altering anything. Nature will take care of everything in my mind. I think that proper education would be better spent money, than quick fix-alls. Well, you have a lovely day, and I hope to hear from you soon. Life is lived as many times as you can remember it.

12 February 2001
Dr. Miller, I just ran across a news release about pink bollworm eradication experiments using artificially introduced Trojan genes. Bravo! I'm especially happy to see this work being done by my alma mater. I have been sending e-mails around about this technique off and on for months, including a posting on IPM Net News. Reading an abstract of (Australian researchers) Scott and Heinrich's article, [**AuQ 6**] "A repressible female-specific lethal genetic system for making transgenic insect strains suitable for a sterile-release program", triggered my thinking along these lines. In their ingenious system, a line of insects was developed wherein fertile males produced sterile daughters and fertile sons—who were, in turn, carriers of the sterility trait. Thus, theoretically at least, total extinction of genetically-interacting populations is possible. I presume you are looking at a similar approach? Certainly, a lot of folks would be eager to try such a system on agricultural or forest pests or disease vectors in their [the pest's] native areas (e.g., cotton bollworms, spruce budworms, or tsetse flies), but consideration of the ecological role of such organisms is a prerequisite to such an undertaking. This is less problematic where the pest is clearly an invader and therefore not integral (in fact may be considered, presumptively, to be a disruption) to the local ecosystem. Critical to acceptance of this approach—even for exotic pests—is the evaluation of rate of gene flow back to the location of origin. If there is any appreciable amount of flow (back to India, in the case of the bollworm), then this genetic solution might conceivably lead to complete extinction of the species (which is of debatable desirability). I presume one aspect of your work is evaluating the probability of "escape" of sterility/lethality genes from the continent.(?) Again, congratulations; I think that this line of work has tremendous potential—I have always been a bit uncomfortable with introducing yet more exotics to try to control the ravages of previous, accidental exotic introductions.

Science versus Nature is a very volatile subject. [**Au: ok?**] Stem cell research was an issue in the recent presidential race; certainly, the two main candidates held opposing views. The debate between creation and evolution as taught in public schools continues, with the same kind of black-and-white opinions expressed and the negative side coming from a religious basis. [**AuQ 7**] I have been faced with the prospect of explaining what I am doing in entomology before, but mostly to funding agencies, where the opinions have been as contrary as the ones quoted here.

Symbiotic Control

One of our other major research projects has evoked a surprising reaction from an unexpected source. We have been using the paratransgenic solution to Chagas disease that was invented by Frank Richards (Beard et al 1998) as a model to try to find a solution to the Pierce's disease problem in California.

The approach is fairly elegant.

- Find a symbiotic microbe that occupies the same space as the pathogen causing the disease.
- Genetically alter the microbe to produce a product that neutralizes the pathogen.
- Insert the GM symbiont into the disease cycle.

By finding the symbiont already present, the existing biology determines the solution. In fact, only a symbiont that is coevolving with the host and pathogen will work. If you pick any other organism, you are merely making a nonselective microbial pesticide.

Symbiotic Control of Pierce's Disease

My collaborator Carol Lauzon found a symbiont living in the vector insect, the glassy-winged sharpshooter, *Homalodisca coagulata*, [**AuQ 8**] and occupying the xylem of host plants in exactly the same place as the pathogen, *Xylella fastidiosa*.[**AuQ 8**] When Blake Bextine and I first approached the U.S. Environmental Protection Agency (EPA) for permission to field test Carol's symbiont, which had been genetically altered by our collaborator Dave Lampe (Bextine et al. 2004), it took the agency a while to figure out which law applied. Then we were warned that the *Alcaligenes* we were using was suspected as being a nosocomial organism found in secondary infections in lungs of cystic fibrosis patients.

William Schneider of the EPA referred to a report on *Burkholderia cepacia*, [**AuQ 8**] which had been proposed as a microbial nematocide. This microbial pesticide was eventually withdrawn from the registration process amidst protests from the Cystic Fibrosis Foundation and the review committee about the human pathogenic properties of *B. cepacia*. The agency did not have sufficient assurance that side effects would not occur. They chose caution over another pest control product.

The Pierce's disease case is similar, but with some important distinctions. The proposed microbial pesticide (which is the legal term used by EPA for this symbiotic control organism) to combat Pierce's disease is not another pesticide nor a biological control agent. It is the only one. The only other method of protecting vineyards from the glassy-winged sharpshooter (GWSS) is to spray with conventional insecticides. This method is used in southern California in the threatened areas at great expense, but it is the only way to reduce the threat.

Imidacloprid is applied in drip irrigation to citrus in the winter months to decrease the population of GWSS. Citrus seems to attract over-wintering adults and acts as a source for spring movements to neighboring vineyards. This is true in Temecula and Bakersfield, which are both within the GWSS-infested area.

Symbiotic Organisms Permit

We were given a permit (TERA R-03-01) to do field studies of the marked *Alcaligenes* bacterium, but the permit conditions required the grapevines to be burned and the soil at the root ball sterilized afterwards and the vines had to be covered to prevent insects from gaining access to them during the tests. We chose to do the 2003 season tests in Napa, Temecula, and Bakersfield and on the UCR campus (Figs. 2 and 3). However, before we even arranged the test plots in commercial vineyards, the grape and wine industry signaled a new concern. They are adamantly opposed to any transgenic organism associated with their crops. Indeed, at the end of a Pierce's disease research symposium held 9–11 December 2003 in San Diego, an industry spokesperson said they would not under any circumstances accept a transgenic grapevine as part of the solution. This was met by stunned silence by the researchers because developing a disease-resistant papaya by inserting coat protein genes of the ring spot virus had already saved the papaya industry in Hawaii in an event that is now famous. [**AuQ 9**] And an approach like that might lead to PD-resistant grapevines.

The industry reaction changed the purpose of our field tests. We originally intended to find out if the symbiotic bacterium would establish in the xylem fluid and so be available for attacking the pathogen. Instead, we were faced with the prospect of having our symbiotic control approach rejected if the transgenic symbiont wound up in the berries or stems of the grapevines.

The first year's trials proved negative. Indeed, the marked *Alcaligenes* could not be found in the grapevines three weeks after initial inoculations. We are still doing this work a year later and have just obtained a grant from CSREES to do risk assessment, a new topic in the biotechnology era.

The symbiotic control approach might qualify for what Rachel Carson asked for in the 1960s: a more "sophisticated" method of crop protection that would replace insecticide use. However, we have made the public uneasy about the proposed new solutions. A number of my colleagues have embraced the cautionary approach and are actively lobbying against release of transgenic organisms.

Fig. 3. Funeral pyre of Globe table grapevines that were used in a field test for movement of genetically marked transgenic symbiotic bacteria. Conditions of the permit required that the plants be destroyed as soon as the test was over. The dirt around the root ball had to be sterilized as well. Bakersfield, CA, fall 2003.

Concluding Thoughts

The cost of developing transgenic pink bollworms, *Pectubiogira gossypiella* (Saunders), has been borne by the cotton industry and by federal agencies charged with supporting it. So far, private industry has shown no interest in developing the technology. This means that the application for federal permits has not involved proprietary information, and the review process is relatively transparent to public view. The recent Pew Foundation meeting on transgenic insects helped the whole process along by providing a forum.

Right now, we lack field data on the behavior of transgenic insects. The kind of data needed can only come from genuine field trials; simulations won't provide what is needed. Laboratory experiments are poor substitutes for field data. Our transgenic symbiotic bacteria behave one way in the laboratory and quite differently under field conditions. The sooner the safety requirements are identified and met, the sooner we can move on to assessments that will lead to improvements.

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Fig. 2. Blake Bextine (left) and Carol Lauzon checking on Merlot grapevines before inoculation of genetically marked symbiotic bacteria. Summer 2003 near Napa, CA. Note the white cage material behind the plant that was used to cover the grapevine during the test.

References Cited

Allen, M. L., A. M. Handler, D. R. Berkebile, and S. R. Skoda. 2004. PiggyBac transformation of the New World screwworm, *Cochliomyia hominivorax*, produces multiple distinct mutant strains. Med. Vet. Entomol. 18: 1–9.

Beard, C. G., R. V. Durvasula, and F. F. Richards. 1998. Bacterial symbiosis in arthropods and the control of disease transmission. Emerg. Infect. Dis. 4: 581–591.

Bextine, B., C. Lauzon, S. Potter, D. Lampe, and T. A. Miller. 2004. Delivery of a genetically marked *Alcaligenes* sp. to the glassy-winged sharpshooter for use in a paratransgenic control strategy. Curr. Microbiol. 48: 327–331.

Briggs, S. A. 1987. Rachel Carson: Her vision and her legacy, pp. 3–11. *In* G. J. Marco, R. M. Hollingworth, and W. Durham [Eds.], Silent spring revisited. American Chemical Society, Washington, DC,.

Byrne, P., S. Ward, J. Harrington, and L. Fuller. 2004. Transgenic crops: An introduction and resource guide. http://www.colostate.edu/programs/lifesciences/TransgenicCrops/current.html. Department of Soil and Crop Sciences, Colorado State University, Fort Collins.

Ferber, D. 1999. Risks and benefits: GM crops in the cross hairs. Science 286: 1662–1666.

Fishbein, G. W. 1985. Environmental Protection Agency to grant advanced genetic sciences permit on ice-minus experiment soon. Genet. Eng. Lett. 5(19): 1–2.

Fryxell, K. J., and T. A. Miller. 1995. Autocidal biological control: A general strategy for insect control based on genetic transformation with a highly conserved gene. J. Econ. Entomol. 88: 1221–1232.

Handler, A. M. 2002. Prospects for using genetic transformation for improved SIT and new biocontrol methods. Genetics 116: 137–149.

Hoy, M. A. 2000. Deploying transgenic arthropods in pest management programs: Risks an realities pp. 335–367. *In* A. M. Handler and A. A. James [Eds.] Insect transgenesis, methods and applications. CRC Press, Boca Raton, FL.

Lindemann, J., and T. V. Suslow. 1987. Competition between ice nucleation-active wild type and ice nucleation-deficient deletion mutant strains of *Pseudomonas syringae* and *Pseudomonas fluorescens* biovar I and biological control of frost injury on strawberry blossoms. Phytopathology 77: 882–886.

Loukeris, T. G., I. Livadaras, B. Arcà, S. Zabalou, and C. Savakis. 1995. Gene transfer into the medfly, *Ceratitis capitata*, with a *Drosophila hydei* transposable element. Science 270: 2002–2005.

Miller, T. A., and R. T. Staten. 2001. The pink bollworm. Tale of a transgenic tool. Agrichem. Environ. News. 182 (June): 1–5. http://www.tricity.wsu.edu/aenews.

PANNA (Pesticide Action Network North America). 2004. GE crops use more pesticides. http://www.panna.org/resources/panups/panup_20040109.dv.html. San Francisco.

Pew Initiative on Food and Biotechnology. 2004. Bugs in the system? Issues in science and regulation of genetically modified insects. http://pewagbiotech.org/research/bugs/. Washington, DC.

Robertson, J. L., and H. K. Preisler. 1992. Pesticide bioassays with arthropods. CRC Press, Boca Raton, FL.

Robinson, A. S., G. Franz, and P. W. Atkinson. 2004. Insect transgenesis and its potential role in agriculture and human health. Insect Biochem. Molec. Biol. 34: 113–120.

Rose, Robert I. 2001. Confined study of a transgenic pink bollworm, *Pectinophora gossypiella* (Lepidoptera: Gelechiidae). USDA–APHIS, Environmental Assessment. http://www.aphis.usda.gov/brs/arthropod/permits/0102901r/02901rea.pdf

Rubin, G. M., and A. C. Spradling. 1982. Genetic transformation of *Drosophila* with transposable element vectors. Science 218: 348–353.

Thomas, D. D., C. A. Donnelly, R. J. Wood, and L. S. Alphey. 2000. Insect population control using a dominant, repressible, lethal genetic system. Science 287: 2474–2476.

Walbot, V. and M. Yelton. 2002. Introduction to biotechnology. Stanford University class web notes. Biotechnology in microbes, plants, and animals. Three snapshots. http://www.stanford.edu/class/bio4/ClassLinks/october4.htm

Wimmer, E. A. 2003. Applications of insect transgenesis. Nat. Rev. Genet. 4: 225–232.

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Author Queries

1. If possible please find the original source for this quote.
2. Add reference for Marco, Hollingworth, and Durham.
3. 2004 in References Cited. Please check.
4. No receiver is listed in Table 1. Dr. Young is listed in Table 2.
5. I have corrected spelling and punctuation in this section. Without using a lot of [*sic*], it would appear that the mistakes were our mistakes. I think the text itself conveys the writers' intent.
6. Is there any chance of getting a reference for this article?
7. suggest "base" or "bias" instead of "basis".
8. Please give the author name.
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