IGERT- Genetic Engineering and Society: The Case of Transgenic Pests

PI: Fred Gould, North Carolina State University

SUMMARY

This IGERT project will create a transformative graduate education program that broadly trains students in technologies needed for manipulating pest genomes as well as methods needed to assess the environmental and social appropriateness of specific products of these manipulations.

The concept of genetically manipulating a pest species to destroy or render it benign dates back to the 1940's, and there have been several major successes in using this approach. However, restricted tools of classical genetics limited the broader use of Genetic Pest Management. Recent advances in molecular genetics have provided much more precise techniques for manipulating the genomes of pests, and efforts are now underway for development and potential release of transgenic mosquitoes and transgenic agricultural pest species aimed at achieving Genetic Pest Management.

The future of this pest management strategy will depend on further technological advances, public understanding of the novel technologies involved, and the creativity and wisdom of researchers and policy makers. Although esteemed scientific groups including the U.S. National Academy of Sciences have repeatedly emphasized that risk assessment for transgenic organisms should focus on the specific product and not the process, the legacy of genetically-engineered crop commercialization has made the logic behind this idea obscure to most people, including many scientists. For new applications of genetic engineering to be developed and judged appropriately, diverse social and cultural groups will need to more deeply examine the ramifications of each application. Broadly trained PhDs in biological and social sciences will facilitate this examination and help foster more sophisticated interactions among policy makers, academicians, and members of societies where Genetic Pest Management may be applied.

Intellectual Merit of this IGERT derives from the fact that this could become the first graduate program in the world that is specifically training graduate students to understand, build, and assess impacts of transgenic organisms. All students will receive basic training that will include molecular biology, ecology, population genetics, epidemiology, economics, public policy, communication, and ethics. Each student will become an expert in one or two of these specialties. Our program is broad in integrating across diverse disciplines, but maintains the focus of students and faculty by specifically studying a small set of species that are targets for Genetic Pest Management. In each of the first years of the program, we will recruit graduate students in biological and social sciences. Groups of about six students, balanced across disciplines, will work together with faculty to choose a single target species as the focus of their respective dissertations. The focus on single species will challenge both student groups and faculty to work together, develop a common vocabulary, and understand how each others disciplines operate. We are developing a set of core courses in the distinct disciplines, which will provide all students with a basic toolkit for working in the field of Genetic Pest Management. Students specializing in the discipline of a specific course will act as mentors to the other students taking the course.

Broader Impacts of this IGERT fall into the following categories: 1) Improvement in the administration and extent of integrated graduate education at NCSU, 2) Impact on US integrated graduate education by testing a specific model of such integration, 3) Increasing the number of students from underrepresented groups that receive interdisciplinary education, 4) Improvement of methodologies for assessing and introducing new technologies, 5) Ph.D.s in biology and social sciences who have tools needed for future interdisciplinary, global work. 6) Education of local communities. Furthermore, most of the target pest species are of importance in poor countries, and we will use existing and newly developed partnerships to set up internships and dissertation projects in these countries. We have developed collaborative relationships with relevant programs at Historically Black Universities in North Carolina, and will use specific fellowship and internship programs at NCSU to recruit students from under-represented groups.

Key words: Biology, Mathematics, Social Sciences; Environmental Sciences

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*Proposers may select any numbering mechanism for the proposal. The entire proposal however, must be paginated. Complete both columns only if the proposal is numbered consecutively.

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C1. PARTICIPANTS

Table 1. Participating NCSU faculty

NAME/HOME DEPT.	CONTRIBUTION TO IGERT PROJECT
Gould, Fred, Entomology*	**PI**, Population genetics and ecology research, science policy; Teach IGERT courses #1, #2
Haddad, Nick, Biology*	**Co-PI**, Species removal impacts on communities, endangered spp.; Teach IGERT course #2
Haenn, Nora, Anthropology CRDM *	**Co-PI**, Anthropology in Mexico, Culture and perception of GPM; coordinate IGERT course #1
Lloyd, Alun, Biomathematics*	**Co-PI**, Epidemiology of insect vectored diseases, gene drive; Teach IGERT course #5
Thurman, Wally, Economics*	**Co-PI**, Agricultural economics, economics of pest management; Teach IGERT course #5
Apperson, Charles, Entomology	Ecology/genetics of mosquitoes and ticks, public education; Lecturer IGERT course #2
Auerbach, David, Philosophy	Bioethics; Teach IGERT course #3; assistance with IGERT course #1
Berube, David, Communications CRDM *	Public perception and attitudes; Assist with student surveys and focus group analysis
Birkland, Thomas, Public Administration*	Risk assessment and public policy research; Teach IGERT course #4
Bloem, Stephanie, Entomology adjunct*	Course on regulatory aspects of pest management and lecturer in IGERT course #2
Brown, Dennis, Biochemistry*	Molecular biology of flavivirus; assist student work on virus adaptation to GPM mosquitoes
Burrack, Hannah, Entomology*	Farmer education programs, medfly research, Lecturer in IGERT course #2;
Cardoza, Yasmin, Entomology*	Chemical ecology, medfly research; International collaboration liaison; teach IGERT course 1
Dunn, Rob, Biology	Biodiversity, community ecology, natural history, public outreach. Lecturer in Course #2 & #3
Estes, Patricia, Genetics	Developmental genetics, engineering of transgenic strains; lecturer in IGERT course #2
Gross, Kevin, Biology	Population and community ecology, biostatistics, avian malaria; lecturer in IGERT course #5
Jacka, Jerry, Anthropology CRDM	Environmental Anthropology related to agricultural development: lecturer IGERT course #4
Kennedy, George, Entomology*	Research/policy for Transgenic crops, farmer education; lecturer in IGERT course #2
Kinsella, William, Communications CRDM	Rhetoric of science and technology (academic background in Physics); Lecture in Course #4
Mackay, Trudy, Genetics*	Quantitative genetics, adaptation of pest populations to GPM; teach genetics of evolution
Mahaffey, James, Genetics*	Developmental Genetics, engineering of transgenic strains; lecturer course #2
McMillan, Owen, Genetics*	Evolution of *Tribolium Medea*: gene-drive lecturer IGERT course #2
Miller, William, Biochemistry	Mammalian reproductive biology, Development of gene drive in rodents; Lecturer course #2
Minsky, Lauren, History	History of sterile mosquito use in India; interaction of culture & innovation lecture in Course 2
Roe, Michael, Entomology*	Insect molecular biology; mosquito and tick genomics & physiology; transgene development
Rufty, Thomas, Crop Science	Transgenic crops; experience in teaching bioethics; lecture in IGERT course #3
Schal, Coby, Entomology*	Urban pest ecology and genetics; public education, Chemical ecology for GPM, Ethics
Steelman, Toddi, Forestry*	Natural resource policy response to multiple stakeholders: Lecturer in IGERT course #2 & #4
Suiter, Karl, Entomology adjunct	Invasive pest risk assessment, Pest survey in developing countries; Lecturer in course #2
Thompson, William, Plant Biology*	Plant molecular biology research, development of transgenic plants;
Threadgill, David, Genetics*	Molecular biology and transgenesis in mice; Lecturer in IGERT course #2
Vandenbergh, John, Biology	Behavior, physiology, and ecology of rodents; bioethics, federal regulation of transgenics

**** indicates that CV of participant is provided***

IGERT COURSES:

#1 Pest Issues in Developing Nations: Science, Culture, & Infrastructure
#2 Principles of Genetic Pest Management
#3 Ethics in Genetic Pest Management Research
#4 New Technology Emergence & Adoption: Social and Cultural Issues
#5 Systems Thinking and Modeling

C2. VISION, GOALS, AND THEMATIC BACKGROUND

Vision: *"I've been in higher education long enough to know that vision without focus is an illusion," Dr. Charlie Nelms –Chancellor of NC Central Univ.—February 22, 2008.*

Genetic engineering of organisms has attracted a great deal of public attention, both in prosperous and poor countries. Insulin for diabetics, produced by genetically engineered microbes, has been universally embraced. Other products of genetic engineering, such as transgenic crops, have been controversial and tend to dominate public discussion. New applications of genetic engineering are on the horizon, and could benefit society if used appropriately, but their use could be hampered if the technologies are shunned by society, or developed without due regard for risks. One novel application of genetic engineering is the development and release into the environment of transgenic pests to provide Genetic Pest Management **(GPM)**. The pest species that may be managed through such genetic engineering range from insects to

rodents, and from pests of large-scale agriculture to invasive pests of endangered ecosystems. It is too early to predict how widespread the use of this approach will be in the future, but because prototypes of some transgenic pests have been developed and a field test was already conducted, we feel that it is now time to undertake a careful evaluation of this approach. We envision our students helping to lead and shape the development of this technology and its evaluation. Focus on this specific application of genetic engineering offers students/mentors a system where careful, intensive integration of biological and social sciences is needed for appropriate assessment, public education, and product development.

Background: Insect- and tick-vectored diseases such as malaria, dengue fever, and Lyme disease cause human suffering and current approaches for prevention are not adequate. Invasive plants and animals such as Scotch broom, zebra mussels, and gypsy moths continue to cause environmental damage and economic losses. Rodents transmit diseases and cause major pre- and post-harvest losses, especially in less affluent countries (e.g. rats eat enough rice to feed 180 million people/year—Stenseth et al. 2003). Each of these problems might benefit from the developing field of GPM (Gould 2008).

Since the 1940's, researchers have been experimenting with approaches for directly manipulating the genetic systems of pests in order to control their populations, or for replacing pathogen-vectoring pest strains with genotypes incapable of pathogen transmission. These efforts have saved billions of dollars in plant and animal agriculture and decreased pesticide use (for example, screwworms have been eradicated from the US, Mexico, and Central America). However, the number of successes has been limited by the lack of sophisticated genetic tools and inadequate social integration research and practice (Gould and Schliekelman 2004, Dyck et al. 2005). Furthermore, no successful programs have been conducted with taxa other than insects.

Genomic tools of the 21st century are beginning to offer new approaches for manipulating target pest species with much more precision. A major effort sponsored by the Gates Foundation (Gates 2008), and including NCSU researchers, is using the ever-increasing array of molecular genetic methods to manipulate mosquitoes that vector human diseases. A few smaller programs are currently aimed at insects of agricultural importance (Gong 2005, Schetelig 2009) and involve USDA-APHIS scientists at NCSU.

In the next 10-20 years it is likely that the genetic methods being pioneered today will become more routine, and will be broadly applied to diverse taxa of pests that cause damage to the environment, health, and agriculture (Gould 2008). While transgenic crop technology has been led by industry, it is likely that, due to its economic properties, GPM will mostly be developed by academic and government institutions. This contrast may alter social/technical challenges faced in GPM research and application.

Specific Goal: ***The goal of our IGERT project will be to train students in the technologies needed for manipulation of pest genomes and the methods needed to assess the products of these technologies.***

While the molecular technology behind GPM is clearly moving ahead, less effort has been focused on the economic, ecological, social, and ethical issues that must be considered if we are to use this technology wisely. The Gates Foundation, The Pew Initiative in Food Safety, and the USDA have each conducted limited research and/or held symposia on ecological, economic, and social issues (Pew 2004, Gates 2009), and a number of important, high profile articles on these topics have been published (e.g. Scott et al. 2002, Knols et al 2007, Fischetti 2008). However, our web searches and networking indicate that no relevant academic or government program has been developed for long-term study or student training in these areas. The training provided by our IGERT program will focus on GPM, but students will also obtain an education that will prepare them for work in other fields that require interaction among multiple disciplines that each operate with sophisticated methodologies that tend to exclude all but specialists.

Response to Previous Reviewers: We submitted a pre-proposal in April 2008 that ranked in the top 15% of the pre-proposals from that year. The review panel was very positive about our proposed program but asked that we bolster our description of the involvement of ecologists in the assessment of effects of GPM on non-target species, and that we clarify the role of social science researchers and international collaborators in the program. We feel that we addressed these concerns in the full IGERT proposal that we submitted in October 2008, but the NSF staff has indicated that reviews of the 2008 proposals would not be available until after the deadline for this new round of pre-proposals.

Thematic Basis & Unifying Aspects: We envision our program involving the intersection of the biological specialties of Population Genetics, Ecology, and Molecular Biology. The development of a biologically successful transgenic pest method or product will depend on collaboration among researchers in these areas. To be relevant, education and research in these biological sciences will be paralleled by innovative, cross-disciplinary research and education in Economics, Policy, and Social Issues **(EPSI).** Our program will focus on a small set of target pest species that raise challenges in each of these biological and social science disciplines. ***No single student will be trained to be an expert in all of these areas.*** Instead, groups of students will conduct research on single target pest species, with individual students specializing in one or two aspects of the research, but interacting with others in the group to develop a more relevant analysis for that species.

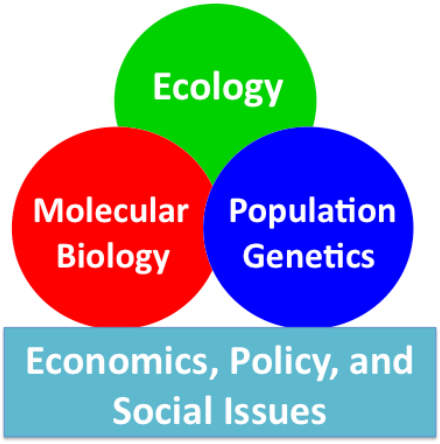

Figure 1.

As a concrete example, Lyme disease has been a major problem in the US, especially in Northeastern states where both the disease-vectoring tick species and a major secondary host, the white-footed mouse, are prevalent. There is no vaccine for this spirochete pathogen, and misdiagnoses can lead to lifelong physical impairment. Research has shown that decreasing either the mouse or tick populations should lower human infection rates. The most straightforward GPM approach to this problem would be to use a gene drive mechanism (see Sinkins and Gould 2006) to force recessive lethal genes into mouse and/or tick populations with the goal of population reduction or eradication. Such an action might be appealing to citizens in the affected area, but these species have roles in biological communities that must be considered (Scheufele et al. 2007). Furthermore, some gene-drive mechanisms could spread recessive lethal genes so effectively that they would cause eradication of these species (and potentially other species). Ecological, economic, and ethical questions are raised by such interventions.

Another approach to controlling this disease would be to drive anti-spirochete genes into the mouse populations so that they would no longer serve as a host for the pathogen. This might be technically more difficult, but its feasibility could be determined by students specializing in molecular biology. Population genetics students could at the same time examine the potential for developing gene drive systems with self-limiting properties that would affect a local area for a limited period of time, so methods could be tested without permanently changing a population. In concert with the biological work, students in EPSI, could conduct analyses in the target location and beyond, to determine the social acceptability of a number of technical solutions to the problem, including the genetic approaches. This short description only touches the surface of issues that students and their mentors would need to address.

Synergy Among Strong Programs: NCSU has been recognized for providing international leadership in the ecologically-based field of Integrated Pest Management (IPM) since the 1960's (Rabb and Guthrie 1970), and in the 1970's NCSU faculty were very active in the debate about ecological and ethical issues associated with early efforts at eradicating pest species. More recently, NCSU's Crop Science, Entomology and Agricultural Economics programs have had major roles assessment of transgenic crops. NCSU has had a distinguished program in Population and Quantitative Genetics for over 40 years, and newer programs in basic and applied aspects of molecular genetics at NCSU have been very successful. Research and extension scientists from the above groups at NCSU began development of a GPM project in 2006 with leadership of an executive committee composed of prominent NCSU faculty (Gould, Haddad, Kennedy, Lloyd, Mackay, Schal, Thompson-see attached CVs)

At about that same time, NCSU's College of Humanities and Social Sciences (CHASS) began a directed effort at hiring senior faculty who could provide expertise in assessment of perception and impacts of new technologies (e.g. Burube, Birkland –see attached CVs). Until recently, this group of faculty had focused its efforts on nanotechnology and natural hazard risk analysis and communication, with major funding from NSF. Discussions between the CHASS group and faculty members in biology and economics led to the realization that there was a natural fit among them in addressing questions about

GPM. Ongoing discussions resulted in recruitment of other faculty to our program from anthropology, history, and natural resource management. This proposal is an outcome of work by this group and support from NCSU administration.

C3. MAJOR RESEARCH EFFORTS

Our research efforts will focus on a small number of potential pest species targets for GPM. Early in their program at NCSU, each successive cohort-team of five to six students will pick one pest system as a focus for study. Each specific project will be organized using the general template in Figure 1, with each disciplinary area covered by students and faculty mentors specializing in that area. Given space limitations, we provide only brief and provisional project sketches of some potential target systems.

***Tribolium* Beetles** are a major cause of post-harvest losses, especially in poor countries. Typically, one to a few *Tribolium* beetles invade locally stored grain, and the population then increases almost exponentially. Any intervention that lowers the reproductive potential of the beetles would be useful. From a molecular biology perspective, the *Tribolium* genus is a useful early target for GPM because its genome was recently sequenced, and some populations naturally harbor a selfish genetic element called *Medea,* which could efficiently drive a recessive lethal gene into a local population (Chen et al. 2007, Lorenzen et al. 2008). Furthermore, they are easy to engineer, and a *PiggyBac* transposon inserted well within 1cM of the *Medea* element has been confirmed as lethal in homozygous form (Marce Lorenzen unpubl. data; Dr. Lorenzen will join our faculty in July 2009).

Research at the population genetics and ecological levels will start with computer simulations and laboratory experiments to determine the rate at which the selfish *Medea* element and the linked recessive lethal allele spread into populations, and how much they decrease reproductive potential. Molecular work in collaboration with Bruce Hay (Cal Tech) will aim at producing strains with synthetic *Medea* elements. Because genetically engineered strains with marker genes are currently available, students in Public Administration will collaborate with biology students and USDA-APHIS personnel on campus to develop federal applications for regulatory approval of transgenic marker strains to be used in population ecology studies. This effort will include academic study of the regulatory approval process. Further work on the system will depend on results of economic analyses and development of synthetic *Medea* elements.

Mosquito Vectors of Human Diseases. We will concentrate on the dengue-vectoring mosquito, *Aedes aegypti*, because Lloyd and Gould have an ongoing NIH grant ($1,300,000) to work with this system, and they are also members of a project funded by the Gates Foundation ($19,000,000) that includes molecular biologists, ecologists, social scientists, and our group (mathematical epidemiology and population genetics). Our membership in Gates project has enabled us to hold workshops at NCSU because our modeling expertise is valuable to all members of the team. Future workshops will be valuable to students in our proposed IGERT project. The molecular and population genetic components of this project are well underway. Transgenic lines with anti-dengue constructs and gene drive are expected to be available for release in 5 years. A novel Killer-Rescue gene drive mechanism conceptualized and analyzed at NCSU is now in development. The IGERT component of this project will center on ecology, evolution, and EPSI issues. Brown (biochemistry) and Katia Koelle (Duke-Biology) are working on molecular and population genetic aspects of dengue virus evolution, respectively. This will be critical because a major concern is virus adaptation to anti-pathogen genes. Mackay (Genetics) will help students work on genetic variation in mosquito RNAi pathways that could lead to breakdown in efficacy. Field studies for the Gates project are focused in Chiapas, Mexico. One specific IGERT project that would involve students in biology and EPSI is assessing the potential for developing cottage industries in Chiapas towns for rearing engineered mosquitoes instead of the typical approach of large-scale factory production. Haenn (Anthropology) has experience in Chiapas and will help with this effort.

Mosquitoes and Endangered Bird Species. Evidence to date indicates that until the recent arrival of the mosquito, *Culex quinquefasciatus,* in the Hawaiian Islands, the native bird species had not been exposed to bird malaria (*Plasmodium relictum*). The native Hawaiian birds are typically more susceptible to malaria than invasive bird species from continental areas. A number of studies have produced strong evidence associating bird malaria with declining densities or complete absence of specific native bird species from low- and mid-altitude forests where *C. quinquefasciatus* thrives, and future increases in global temperatures may push native birds to even higher altitudes or to extinction

(Benning et al. 2002). The problem associated with bird malaria appears to be spreading to native birds of New Zealand and the Galapagos Islands. Conventional control efforts for *C. quinquefasciatus* have failed. *C. quinquefasciatus* has been transformed in the laboratory. Genome sequencing of *C. quinquefasciatus* is almost complete and will provide additional genetic tools.

A typical public concern with environmental release of transgenic organisms is whether or not there will be side-effects that threaten biodiversity. In this case, the driving force behind the engineering project itself is to preserve biodiversity, offering a useful contrast for the public. One safety issue with this system entails whether transgene-induced resistance to these bird diseases could decrease refractoriness of *C. quinquefasciatus* to human pathogens. Assessing such a risk would be a worthwhile project for a student focusing on molecular and epidemiological issues (Brown and Lloyd will advise). Economic estimates of the dynamic paths of costs and benefits from bird species preservation would also be needed for a balanced analysis (Thurman).

Apperson (Entomology) has had many years of experience working on the ecology and management of *Culex* species. Haddad and Dunn (Biology) have expertise on the population dynamics of endangered species. Dr. Susan Jarvi (University of Hawaii) has been studying the interactions between native Hawaiian birds and malaria for eight years. She attended our March 2009 conference and has agreed to work with IGERT student interns.

Mice and Rats are major post-harvest pests and vector diseases. They are compelling targets for GPM because of their ecology and impacts (Gould 2008). Genomes of both taxa have been sequenced and, especially for mice, advanced tools for transgenesis are available. Miller (Biochemistry) has been working with transgenic mice with altered estrogen cycles based on manipulation of FSHbeta subunit. This work has pre-adapted his lab for his new work on development of transgenic mouse strains with female infertility genes that can be rescued with a second construct. This type of system would be ideal for testing the Killer-Rescue gene drive system developed at NCSU. Threadgill (Genetics) who is an expert in mouse transgenesis would help in developing synthetic *Medea* and meiotic drive systems in rodents.

Because natural segregation distorter alleles and Robertsonian chromosomal translocation are available, and both result in gene-drive, we would be able to conduct population replacement studies with non-transgenic animals in outdoor enclosures. We could also conduct such studies on isolated islands if these experiments could be developed in an ethically appropriate way. Vandenbergh (Biology) developed methods for using island habitats for studying population regulation and behavior of rodents and could work with us on the studies. For *Mus* and *Rattus* species, our goal will be reduction in population growth. If possible, we will also work with the white-footed mouse that serves as a reservoir for Lyme disease in many areas. Recognizing the EPSI issues here, our faculty in Anthropology and Public Administration will lead efforts at risk assessment. Grant Singleton (IRRI, Philippines) attended our March conference and is committed to work with interns to examine ecological feasibility of transgenic rodents in SE Asia.

Fruit Flies in the genera *Rhagoletis, Ceratitis, Bactrocera, and Anastrepha* (not *Drosophila*), are worldwide pests of diverse fruits. The USDA-APHIS personnel at NCSU are collaborating with the Guatemalan government in the field-cage testing of transgenic strains of Medfly *(C. capitata)* that exhibit conditional lethality. Unlike many of the other transgenic pest methods described here, the conditional lethal approach is expected to result in transgenes dying out (Heinrich and **Scott** 2000). These strains are being considered as a replacement for the current use of radiation in the ongoing international sterile release programs. The Guatemalan Medfly facility currently produces over one trillion Medflies per year for international use. Although there are financial, safety, and operational benefits to switching from use of radiation to transgenics, the USDA-APHIS is rightly concerned about EPSI issues and wants to conduct broad assessments of this technology, including public perception and understanding of the technology. The USDA has indicated its interest in interacting with our students in their ecological and EPSI work (see attached letter). Hannah Burrack (Entomology) has worked with *Ceratitis* and *Bactrocera* control programs. We have begun a dialog with USDA-APHIS regarding obtaining permission to rear specific *Anastrepha* and *Bactrocera* species in NC, so that we can investigate other potential molecular manipulations. While not closely related to the true fruit flies, *Drosophila* can serve as a model system for manipulations to be transferred to these economically important fruit flies (Chen et al. 2007). Mahaffey

and Estes (Genetics) are currently developing a Killer-Rescue system in *Drosophila* as a "proof of concept" experiment. Max Scott will join our faculty in January 2010 and will work with *Anastrepha*.
Broader Research: Some of the EPSI research projects on specific single species systems are described above, but other EPSI research addresses broader issues that could fit into any of the single species projects. We provided some detailed projects in our full proposal, but here we offer a few sketches to provide a sense of the questions of interest.
1) While the issue of neighboring countries speaks to the bilateral aspects of GPM, students might also explore the multilateral settings and conventions that address GPM as a global phenomenon. The World Trade Organization, working groups within the United Nations, and multilateral frameworks (e.g., NAFTA, and the African Union) have been important to delimiting the preferences of individual countries, and in bolstering the position of transnational corporations and NGOs (non-government organizations. A recent review (Knols et al. 2007) has called for the UN-WHO to establish guidelines and/or regulate GPM; however, the feasibility of such an approach has not been studied in detail.
2) What strategies are used to communicate GPM efforts to local populations, and to what effect? Although communicating GPM efforts may seem straightforward, given the diversity of literacies in any given community, people will likely re-interpret messages surrounding GPM activities. This re-interpretation may be based on the less tangible issues such as tone and past relationships with individual messengers. This re-interpretation may also be based on identity differences involving gender, class, age, and ethnicity.
3) Where do specific agencies, especially various NGOs, stand on GPM and alternatives? Studies could draw on theories of the policy process to identify how coalitions form around GPM issues and why some policy ideas succeed while others fail to gain acceptance.
4) Given the heightened debate surrounding transgenic crops, how do development agencies balance economic and other values-based initiatives when developing technologies for local implementation? To what extent, in which agency contexts, and in what local conditions will values (moral obligation) override economics?

C4. EDUCATION AND TRAINING:
Progress to Date: Faculty discussions started in 2006, and resulted in establishment of an executive committee and a plan of action. A new 1-credit seminar class on GPM was held weekly in Fall 2007. In addition to students/postdocs, at least 8 faculty members from 4 departments attended over 50% of the classes, and 7 sat in on a number of classes. We co-organized a 26-participant, international workshop on gene-drive in December 2007 in coordination with and funding from the NSF-supported National Evolutionary Synthesis Center. A second, new 1-credit seminar focused on the selfish genetic elements underlying gene-drive was taught in Spring 2008 (led by McMillan (Genetics) & Gould). This more specialized seminar had 17 participants, including 5 faculty members from diverse departments. Haddad (Biology), with help from Haenn (Anthropology), Thurman (Economics) and Gould raised over $30,000 from 5 sources and organized an international conference on "Genetic Manipulation of Pest Species: Ecological and Social Issues" which was held at NCSU, March 4-6, 2009. We had over 70 participants with researchers from China, England, Germany, Mali, Mexico, Panama, and the Philippines. Representatives from 6 groups that have been critical of transgenic crops participated (e.g. Union of Concerned Scientists, Physicians for Social Responsibility, Sierra Club). Graduate students/postdocs attended (18), and 3 NCSU graduate students took notes that were used to stimulate discussions on the final day. Two publications are expected; A video of the entire conference will be posted on the web.
Curriculum: ***The curriculum for each student will be tailor-made, but all students will take 5 required courses. Each student will receive a degree in an academic department with a concentration in GPM*** (Lomax letter). In preparation for our 2008 full proposal, we worked out details of practical interfacing of departmental and Program requirements. This is an intensive curriculum and we will adjust it based on yearly program assessments.
Required courses: ---(for guest lecturer names see page 1 of proposal)
#1 Pest Issues in Developing Nations: Science, Culture, and Infrastructure (2 credits). The course will be offered to incoming students in the last week of July and the first two weeks in August before their

first campus classes begin. Three major goals of this course are: 1) team building, 2) introduction of the students to the environments in which many of the products of GPM will be used, and 3) experience with field research in biology and social sciences. This three-week course will be held in Mexico and Central America. Haenn, Cardoza (Entomology), and Gould will co-coordinate the course.

Our first location will be Tapachula, Mexico–an ideal place to start because of our ongoing mosquito research at this location and established relationships with colleagues in the Tapachula area working in public health and agricultural pest management. Although fluency in Spanish will be useful to students in this course, it will not be critical because we have sufficient translation ability. The three major projects in this location are: 1) The Gates Foundation center in Rio Florido where a large $2.5-million enclosure is now being built, and will serve as the focus for experiments with transgenic *Ae. aegypti*, including those involving NCSU faculty. 2) Centro Regional de Investigación en Salud Pública (CRISP) in Tapachula, is one of the partners in the Gates Foundation project and hosted an NCSU graduate student last summer. 3) MoscaMed which rears millions of medflies is located one hour from Tapachula.

The second location will be Guatemala City and El Pino, Guatemala, where there is ongoing research with transgenic medfly. Contrasts between the political systems and pest management policies of Guatemala and Mexico will be highlighted. Our final locations will be Honduras. We will visit The Panamerican School of Agriculture (Zamorano), considered one of the best agricultural universities in Latin America, and the Universidad Nacional Autonoma de Honduras. NCSU has formal collaborations with both universities. NCSU's Cardoza received her BS equivalent at Zamorano. Honduras is the only Central American country (2008) to permit the commercialization of transgenic corn. Before flying back to the U.S., we will meet with Honduran agricultural policy-makers in Tegucigalpa.

#2 Principles of Genetic Pest Management (4 credits) This course is being developed based on the experience gained from the Fall 2007 course, but it will be more intensive, and will combine lecture, discussion, and activity sections with topics and case studies covering all of the disciplines in figure 1. Faculty from all disciplines will have active involvement with this course. Students specializing in the discipline being covered in a specific section of the course will serve as mentors to other students to ensure comprehension of the information. *Because there is no required course devoted specifically to molecular genetics, the syllabus of this course will be structured to provide students in all disciplines with a working knowledge of molecular tools used in GPM.* This is the first core course a cohort of students takes on campus, and will assist in their selection of target research species and tentative thesis topics.

#3 Ethics in Genetic Pest Management Research (2 credits) will be taught in two parts. The first part will focus on general principles and will be taught by Auerbach (Philosophy) whose teaching time will be supported by the Graduate School (see Lomax letter). The second part of the course will examine ethical issues specifically associated with case studies of past and future GPM research projects. Faculty who have worked with genetically engineered crops will lead discussions based on their experience with ethical issues surrounding that technology. Auerbach will sit in on all discussions to ensure rigor.

#4 New Technology Emergence and Adoption: Social and Cultural Issues (3 credits) will introduce all IGERT and non-IGERT students to key social and cultural issues that influence new technology emergence and adoption. Such issues are crucial to successful technology management and a necessary point of engagement between biological and social science students. Birkland (Public Administration), and Haenn will lead this class which will present real-life cases, ethnographic accounts, and lectures that introduce students to issues and research methods for learning "on the ground" conditions that constrain and enable technologies (Birkland 2005, Haenn 2005). The course will use specific GPM cases and examples, teaching students how to use empirical methods for risk assessment and public policy development and analysis.

#5 Systems Thinking and Modeling (3 credits) is designed to provide all students with a basic understanding of how analytic and numerical models can be used to understand system-wide ramifications of GPM, and will provide specific students with more advanced knowledge. The course will be taught in 3 modules of increasing complexity. Students with no background in modeling will attend the first 2 modules, and students with some background in modeling will take the 2nd & 3rd modules. (Students who already have substantial knowledge of modeling will act as mentors during the course.) This course will explore the use of modeling as a methodology for the integration of biological, social, and economic knowledge/data within a quantitative framework. The limitations of modeling approaches

and the need for careful communication of model results to non-specialists will be highlighted. This course will be taught by Lloyd and Thurman (Economics). Other faculty will give specific lectures.
Other Courses: A large number of relevant specialty courses are available to students, including those taught by the NCSU Biotechnology program. General courses at the NCSU Biomanufacturing Training & Education Center are accessible to students without college biology training. Bloem from USDA-APHIS will add more GPM examples to her course on regulatory issues. We have commitments for short-courses to be taught in summers by faculty collaborators from beyond NCSU (e.g. Bruce Hay, Cal Tech).
Beyond Coursework: Our major mechanism for ensuring interdisciplinary education is the development of student/faculty teams working on specific target pests from diverse perspectives. We will have formal meetings within and among teams on a regular basis. For first year students, we will provide one large office to foster informal discussions. We will host a professional development workshop each year in collaboration with the Keck Graduate Training Program. These workshops will include presentations by each student related to their ongoing research or a proposed project. Roundtable discussions will be held at the end of each workshop. Past workshops of this type have been very helpful in getting all participants to understand each other's research. We will invite internationally recognized leaders in the field of GPM to participate in the workshops.

Each year we will have one program-wide project. For example, EPA Science Advisory Panels (SAPs) which examine proposed rules, allow public comment. Student groups will examine biological and social issues addressed in a proposed EPA ruling that is of relevance to genetic engineering. Students will then attend the SAP in Wash, DC, where representative students will make verbal comments. A second example is that Social Science projects will include focus group work. Students in other disciplines will be invited to observe some of these focus groups and will participate in analysis of the information gathered. In all years, we will continue to build a web site to educate the public about GPM.

At our March 2009 international conference, 5 collaborative arrangements for international internships were solidified. Some of the details are presented in the Research Section.
Student Recruitment: We will identify and recruit a special category of students who have an innate desire to work in an interdisciplinary setting. Our experience is that some of the best undergraduate students have trouble making a decision to go to graduate school because they enjoy multiple disciplines and are reluctant to specialize. We can offer such students a diverse academic experience while moving them into well-focused research projects and training. In Septembers, we will email with colleagues who teach Seniors to locate excellent students who are co-majors in biological and social sciences. We will contact each of these students and will encourage applications and visits by those who are most appropriate. We will also make use of normal NCSU recruiting tools and IGERT websites.
Focus on Underrepresented Groups: Our IGERT group is creating cooperative education projects with historically black universities in North Carolina. Lloyd and Gould have given lectures at NC A&T University in Greensboro, NC, to students in its NSF-sponsored undergraduate Biomathematics Program, and have discussed approaches for cooperative programs with Drs. G. Goins and D. Clemence. Gould has followed up with visits to NC A&T administrators and other students. As indicated by Goins (see attached letter), it would be beneficial for his students to do summer internships at local North Carolina research universities, so that their connection with their summer research lab can be maintained through the year. We are also working to achieve a cooperative agreement with NC Central University. It is our hope that these relationships will lead students from HBUs to pursue graduate degrees in STEM. Dr. Haenn, who was on the faculty of Arizona State University, will lead our efforts to recruit Hispanic students. In addition to more general efforts, Dr. Haenn will use her position as a board member of the Anthropology and Environment section of the American Anthropological Association to advertise the NCSU IGERT while working more intensively with colleagues at Arizona State University and the University of Arizona to recruit Hispanic students. NCSU has a large number of underrepresented groups in its student body, and many of them have done excellent work in our labs, competed successfully in undergraduate research symposia, and gained acceptance to STEM programs at Duke University, Johns Hopkins University, and other prestigious schools. We expect this to continue.

Beyond our group's specific activities, NCSU has broadly relevant programs including: AGEP, which enables students to transition into graduate education and provides extra mentoring; HBCU

programs with NC A&T and Johnson C. Smith University for retention of undergraduates in STEM disciplines; and NC-MSEN aimed specifically at students in mathematics. NCSU also has a number of REU programs focused on underrepresented groups. In addition to a number of $2-4,000 stipend enhancements available to recruit underserved minorities to NCSU, we have received a $1.5 million grant from NIH for recruitment of underrepresented groups to NCSU health and behavioral sciences programs. A number of our participating faculty are involved with this grant that will provide 2 years of funding for 10 graduate students. STEM students in the IGERT will qualify for this funding.

The NCSU program, "Preparing the Professoriate", has been especially useful to female students interested in academic careers so we will especially urge them to enroll in this program. Entomology has a seminar on "Women in Entomology". We will broaden this to be available to all IGERT students.

Student Placement: The field of GPM is expected to grow over the next 5 years, resulting in demand for our graduates in academic, government, and private settings. ***We expect to be the first graduate program in the world that is training students in the diverse aspects of Genetic Pest Management.*** The cross-disciplinary training of our graduates will also prepare them for positions in other fields that require skills for work and communication between biological and non-biological disciplines.

Monitoring and Measurement: We will take two approaches to assessment by external groups. In years 3 and 5 of our program we will invite research scientists from each of our disciplines to observe our student workshops, interview students and faculty, and prepare assessments. In all years, Dr. Denis Gray, from the Psychology in the Public Interest Program at NCSU will conduct formal assessments.

C5. INSTITUTIONAL COMMITMENT:

NCSU is a Land Grant University that has had a typical departmental structure that does not encourage cross-departmental interactions. As stated in the Lomax letter, NCSU is committed to changing this structure. This is evidenced by a number of cross-disciplinary programs that have recently been developed, and by the clear support for our IGERT proposal. The College of Humanities and Social Sciences has proven their commitment to integrated research through its recent hires of prominent faculty members whose research programs bridge the fields of social, physical, and biological sciences (see Braden letter). The College of Agriculture and Life Sciences has just made job offers (March 2009) to one associate professor (Genetics Dept.), one assistant professor (Entomology Dept.), and one high-level technical staff member to work in the area of transgenic pest research. This is a major commitment of resources during difficult economic times. This commitment will last well beyond the 5-year span of an IGERT grant.

The Provost of NCSU has committed one-month release time for 3 social science faculty members in years 2-5 of the IGERT (total salary and fringe =$194,800 see Lomax letter). The NCSU Kenan Institute of Engineering, Technology and Science will provide $150,000 over the five-year term of the IGERT grant to support workshops, meetings, minority outreach, and faculty release time (see Lommel Letter).

C6. OTHER RESOURCES AND CONNECTIONS:

In addition to our collaboration with USDA-APHIS on Campus, we also have interactions with the NSF-sponsored Center for Integrated Pest Management (IPM) on Campus. The ongoing projects at the center will be valuable to our students in their training to use sophisticated web-based tools for both risk and economic analyses of target pests. The IGERT at the University of Minnesota on "Risk Analysis for Introduced Species and Genotypes" has committed to specific collaborations with our group. Dr. David Andow from UM participated in our March 2009 conference. We will budget funds for students to visit the UM IGERT when they are having internal and external symposia. We will also invite their students to NCSU for symposia and internships.

C7. PREVIOUS EXPERIENCE IN GRADUATE TRAINEESHIP PROJECTS:

A number of our faculty members have participated in NIH training programs, and a Keck Foundation training program that resulted in one of the strongest interdepartmental programs at NCSU (see Lomax letter). We have also participated in recruitment and summer programs for underrepresented groups. NCSU had an IGERT in Genomic Sciences. The long-term impact of this IGERT was the establishment of an inter-college genomics graduate program at NCSU. The funding and accomplishments resulting from this IGERT led to "departmental buy-in" and the hiring of a number of key faculty members who have helped expansion of the graduate program.

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