U.S. Department of Agriculture
Office of Inspector General

Controls over Genetically Engineered Animal and Insect Research

Audit Report 50601-16-Te
May 2011

United States Department of Agriculture
Office of Inspector General
Washington, D.C. 20250

DATE: May 31, 2011

AUDIT NUMBER: 50601-16-Te

TO: Dr. Gregory L. Parham
Administrator
Animal and Plant Health Inspection Service
ATTN: Joanne L. Munno

Edward B. Knipling
Administrator
Agricultural Research Service
ATTN: Michelle Garner

Chavonda Jacobs-Young
Acting Director
National Institute of Food and Agriculture
ATTN: Edward Nwaba

FROM: Gil H. Harden /s/ Rod DeSmet (for)
Assistant Inspector General
for Audit

SUBJECT: Controls over Genetically Engineered Animal and Insect Research

The report presents the results of our audit of the controls over genetically engineered animal and insect research. The responses from the Animal and Plant Health Inspection Service, the National Institute of Food and Agriculture, and the Agricultural Research Service are included in their entirety as exhibits in this report.

We accept your management decision for Recommendations 1, 3, 4, and 5 for the subject audit. Please follow your internal agency procedures in forwarding final action correspondence to the Office of the Chief Financial Officer, Director, Planning and Accountability Division.

We are unable to accept management decision for Recommendations 2, 6, 7, and 8. Documentation and actions needed to reach management decision for these recommendations are described in the OIG Position sections of the report.

In accordance with Departmental Regulation 1720-1, please furnish a reply within 60 days describing the corrective actions taken or planned, and timeframes for implementing the recommendations for which management decisions have not been reached. Please note that the

regulation requires management decision to be reached on all recommendations within 6 months from report issuance, and final action to be taken within 1 year of each management decision to prevent being listed in the Department's annual Performance and Accountability Report.

We appreciate the courtesies and cooperation extended to us by members of your staff during our audit fieldwork and subsequent discussions.

Table of Contents

Controls over Genetically Engineered Animal and Insect Research

Executive Summary

In recent years, scientists have begun to genetically modify animals and insects for a wide variety of purposes, including enhancing the productivity of food animals and reducing problems posed by agricultural insect pests. Some of this research is conducted and funded by Department of Agriculture (USDA) agencies, such as the Agricultural Research Service (ARS); the National Institute of Food and Agriculture (NIFA), formerly the Cooperative State Research, Education, and Extension Service (CSREES); and the Animal and Plant Health Inspection Service's (APHIS) Center for Plant Health Science and Technology (CPHST). The Office of Inspector General (OIG) initiated this audit to determine if current laws and USDA regulations provide sufficient authority to control genetically engineered[1] (GE) animal and insect research, and to determine if USDA agencies involved in this research have sufficient controls in place to ensure that GE animals and insects would not be inadvertently released, which could cause harm to commerce, the environment, and public health.

GE animals and insects are understood to be encompassed—along with non-GE animals and insects—within broader regulations regarding animal disease and plant pests.[2] To date, no new laws have been codified to specifically address the regulation of GE animals, and authority relevant to the oversight of GE animals and insects is shared between USDA and the Food and Drug Administration (FDA). USDA has authority over GE animals and insects that are animal pests under the Animal Health Protection Act, and GE insects that are plant pests under the Plant Protection Act. FDA has responsibility over GE animal approvals of new animal drugs that could enter the food supply. Within USDA, regulatory authority over GE animal and insect research is triggered when GE animals, animal pests, and plant pests are imported, moved interstate, exported, or field-tested.

We found that APHIS has not issued regulations that pertain specifically to the introduction (import, interstate movement, or field release) of GE animals or insects. The APHIS program units focusing on biotechnology and animal health, respectively, had not coordinated with one another to prioritize the development of a regulatory framework for GE animals and insects. As a result, the requirements that apply to these organisms were not clear to researchers and the public (see Finding 1).

To secure genetic engineering research inside USDA laboratories, USDA agencies are responsible for implementing and managing security and biosafety programs to prevent adverse impacts on the health and safety of USDA employees or the public, and on the environment. USDA agencies that conduct research on GE animals or insects are responsible for overseeing their research and

[1] Genetically engineered products (i.e., animals, plants, and insects) are created by taking the DNA from one organism and inserting it into another. The process passes on certain characteristics to the desired plant, animal, or insect. The resulting organism is called "transgenic." Transgenic organisms are organisms whose DNA includes inserted DNA that originated in a different species. Recombinant DNA (rDNA) is two pieces of DNA from different organisms that have been joined together into a single piece of DNA. In this report, the terms transgenic, rDNA, and GE are used interchangeably.

[2] See Background for a more detailed description of the regulatory authority for GE animals and insects.

ensuring that they follow USDA safety and security policies and the guidelines from the U.S. Department of Health and Human Services' National Institutes of Health (NIH) regarding such research. The NIH guidelines specify physical containment, facility design, and facility access controls for research involving genetic engineering.

Based on our review at the agencies' Headquarters offices and at four research facilities managed or funded by USDA agencies, we found that USDA needs to address specific problems at several laboratories performing research into GE animals and insects.

- NIFA has not implemented a formal process for documenting and monitoring research incidents such as unauthorized releases of GE animals, even though USDA's and NIFA's own research agreements require that researchers report any inadvertent release of GE insects and animals. Agency officials stated that because NIFA is a funding agency and not a regulatory agency, it relies on assurances from universities and reports from other agencies to ensure that researchers are complying with applicable regulatory guidelines. However, this approach has meant that NIFA has often been slow to respond to research incidents, such as when researchers at the University of Illinois allowed 386 pigs—the offspring of GE research animals, and thus potentially transgenic themselves—to enter the food supply (see Finding 2).

- CPHST, the scientific support division of APHIS' Plant Protection and Quarantine program, develops, adapts, and supports technology to detect, identify, and mitigate the impact of invasive organisms. CPHST funds two types of projects, ad hoc and long-term projects. Ad hoc projects are projects that should take 3 months or less to complete and should have immediate agricultural benefit, while long-term projects are projects that take more than 3 months to complete. We found that CPHST lacks a formal process for selecting which projects will receive funding, evaluating the results of the funded project, and summarizing the results of that work. The approval and review process employed by CPHST was undocumented and did not have controls to ensure that all research projects were properly evaluated. CPHST officials stated that because they have had so much success in responding to ad hoc requests they had not developed a formal process for reviewing long-term projects (see Finding 3).

- ARS performs safety, health, and environmental inspections at its laboratories, but it does not adequately track how laboratories respond to recommendations made during these inspections. This occurred because ARS did not have any controls to track recommendations that were open or recommendations that were corrected and closed. ARS officials explained to us that they relied on its inspectors and response letters from its laboratories to ensure that corrective action is taken on recommendations. We noted that this approach to resolving these recommendations has resulted in action not being taken to correct some deficiencies. For example, one laboratory—the Kerrville Research Facility—took more than 36 months to develop a biological safety program, even though inspectors had twice recommended that it do so. This laboratory manipulates human cells that, once modified, could result in a public safety concern if they were inadvertently released (see Finding 4).

- Laboratories operated by CPHST had not developed comprehensive security plans—including incident response plans for events such as break-ins—even though Departmental regulations require them to do so.[3] The CPHST officials who were responsible for laboratory security stated that they were unaware that their laboratories were subject to Departmental regulations requiring a comprehensive security plan, and thus they did not develop this plan (see Finding 5).

Overall, OIG concluded that APHIS needs to develop regulations that clearly define the agency's role in regulating the introduction of GE animals and insects. While the problems noted at laboratories involved in the research of GE animals and insects were relatively minor and did not lead to the inadvertent release of any problematic animals or insects, we concluded that the agencies involved should act proactively to strengthen their controls now so that they can reduce the possibility of future problems.

Recommendations Summary

APHIS should develop a regulatory framework that clearly defines APHIS' scope of coverage and regulatory requirements for the introduction of GE animals and insects, and to develop performance measures and a timetable to ensure that this regulatory framework is developed in a timely manner and meets strategic goals**.**

NIFA should develop and implement a formal process for documenting and monitoring research incidents involving GE animals and insects.

APHIS should direct CPHST to develop management controls for a work plan approval and review process that is transparent and ensures the accountability of funded projects.

ARS should develop and implement a process for tracking the status of inspection recommendations until corrective action has been completed.

APHIS should direct CPHST to create comprehensive security plans for its laboratories.

Agency Response

APHIS, NIFA, and ARS concurred with the recommendations. We have incorporated the agencies' responses in the Findings and Recommendations section of the report, along with the OIG Position. Each agency's response is included in its entirety at the end of this report.

OIG Position

We accepted management decision for Recommendation 1, 3, 4, and 5. The actions needed to reach management decision on Recommendations 2, 6, 7, and 8 are provided in the OIG Position section for each recommendation.

[3] Departmental Manual 9610-2, "USDA Security Policies and Procedures for Laboratories and Technical Facilities," page 7, dated April 30, 2003.

Background & Objectives

Background

As biotechnology continues to develop, scientists are genetically engineering new varieties of animals and insects for a wide range of purposes. Scientists are now capable of specifically tailoring animals to grow more quickly, to have healthier meat and flesh, and to resist diseases. Genetically engineered (GE) animals are also created to help medical researchers find cures for diseases.

Scientists are also modifying insects for a number of purposes. One area of research involves using GE insects to help solve agricultural pest problems. Scientists are attempting to modify crop-destroying insect pests in ways that weaken their ability to reproduce or that make them less harmful.

Some concerns exist regarding research into GE animals and insects. In 2002, the National Research Council formed a committee whose task was to define science-based concerns associated with products of animal biotechnology.[4] The committee issued a report detailing the risks and concerns associated with GE animals and insects. The committee stated that it considered environmental issues to be "the greatest science-based concerns associated with animal biotechnology … in large part due to the uncertainty inherent in identifying environmental problems early on and the difficulty of remediation once a problem has been identified …. The release or escape of GE animals could result in a [genetically modified animal] spreading through reproduction with wild type individuals of the same species …. The GE organism eventually might replace its relative or become established in that community if it is more fit than its wild relative in that environment."

Regulations Regarding Development of GE Animals

The responsibility for regulatory oversight of biotechnology products is shared by three Federal agencies: the Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS), the U.S. Environmental Protection Agency (EPA), and the U.S. Department of Health and Human Service's Food and Drug Administration (FDA).

[4] The National Research Council is part of a private nonprofit institution that provides science, technology, and health policy advice under a Congressional charter.

The following table shows the areas of responsibilities for each agency:

Agency	Regulated Biotechnology Products
APHIS	Plant pests, plants, animals, animal pests, veterinary biologics[5]
EPA	Microbial/plant pesticides, new uses of existing pesticides
FDA	Food, feed, food additives, veterinary drugs, human drugs, and medical devices

In 1986, the Office of Science and Technology Policy—part of the Executive Office of the President—published the Coordinated Framework for the Regulation of Biotechnology. This policy document describes the system for coordinating the activities of Federal agencies responsible for regulating all GE organisms (see exhibit A). The Coordinated Framework for the Regulation of Biotechnology was founded on the principle that existing health and safety laws administered by Federal agencies provide a sound network of agency authorities for the regulation of GE organisms.

Under the Coordinated Framework for the Regulation of Biotechnology, agencies that are responsible for regulatory oversight of certain product categories or for certain product uses are also responsible for evaluating the same kind of products developed using genetic engineering (see exhibit B). Therefore, APHIS is responsible for the regulation of GE plant pests, plants, animals, animal pests, and veterinary biologics, just as it is responsible for the regulation of conventional plant pests, plants, animals, animal pests, and veterinary biologics. The laws currently used to regulate the products of GE animals and insects are the Animal Health Protection Act, Plant Protection Act, and the Federal Food, Drug, and Cosmetic Act (which is enforced by FDA).

The Plant Protection Act and the Animal Health Protection Act give APHIS regulatory authority relating to plant health and animal health, respectively.[6] Although FDA's purview includes GE animals and insects in general,[7] APHIS—because of its authority relating to animal pests and animal diseases—has authority over the importation, interstate movement, and field release of GE animals and insects.

[5] Veterinary biologics are veterinary products of biological origin, such as vaccines, antiserums, and diagnostic kits.

[6] Specifically, the Plant Protection Act (Title 7, United States Code (U.S.C.), section 7701 et seq., dated June 20, 2000) authorizes APHIS to regulate any plant, plant product, biological control organism, noxious weed, article, or other means of conveyance of plant pest that could injure, damage, or cause disease in any plant or plant product. The Animal Health Protection Act (7 U.S.C. 8301 et seq., dated May 13, 2002) gives APHIS authority to regulate the importation and interstate movement of livestock animals, insects, and any means of conveyance that may be diseased with, exposed to, or carrying a livestock disease. The Animal Health Protection Act defines "livestock" as any farm-raised animal, and "animal" as any member of the animal kingdom (except humans).

[7] Under the Federal Food, Drug, and Cosmetic Act and FDA's Center for Veterinary Medicine guidance document, "Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," issued in draft form on September 19, 2008, and in final form on January 15, 2009.

Under the authority of the Plant Protection Act, APHIS regulations provide procedures for obtaining a permit or for providing notification, prior to introducing GE organisms that are plant pests. APHIS regulations define the "introduction" of such articles[8] into the United States as including any movement into or through the country, or any release into the environment outside an area of physical confinement. The regulations also describe how the agency may be petitioned to determine that an article should no longer be regulated.

If a person wishes to move any GE organism that is a potential plant pest into the United States or between States, he or she must apply for a permit and provide APHIS with details about the nature of the organism, its origin, and intended use. For the years 2005 to 2009, APHIS issued 58 permits involving GE plant pests. These included 24 interstate movement permits, 25 import permits, and 9 environmental release permits. The nine environmental release permits were for GE pink bollworms—plant pests that feed on the seeds of cotton bolls. Researchers have been interested in modifying pink bollworms to reduce costs and improve the efficiency for the pink bollworm eradication program. APHIS also oversees field testing (environmental release) of GE insects that are considered to be plant pests, or that include gene splices from organisms that are considered to be plant pests. A company, academic research institution, or public-sector scientist wishing to move or field-test a GE insect must obtain the necessary permits before proceeding. An applicant must provide complete information about the insect, including new genes, its origin, the purpose of the test, and the experimental design and precautions to prevent the escape of insects from a field site.

Since FDA and APHIS potentially share regulatory authority over GE animals and insects, the two agencies have been discussing their respective roles. On September 19, 2008, FDA published the draft guidance document "Regulation of Genetically Engineered Animals Containing Heritable rDNA[9] Constructs" in the Federal Register and solicited public comment. On January 15, 2009, FDA published the final version of the guidance document. This guidance explains that, where an rDNA construct in a GE animal is intended to affect the structure or function of the body of the GE animal, that construct is a new animal drug, regardless of the intended use of products that may be produced by the GE animal. The document was intended to clarify FDA's oversight of GE animals under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act. In general, the regulations specify labeling and recordkeeping requirements, shipping requirements, the final disposition of the animals and insects, and conditions under which food from animals used for clinical investigations can be introduced into the food supply. The Federal Food, Drug, and Cosmetic Act requires that each new animal drug application be approved based on a demonstration that it is safe and effective for its intended use. In its guidance document, FDA stated that it intends to exercise enforcement discretion with regard to requirements for certain GE animals. According to its guidance, FDA does not intend to take enforcement action for "GE animals of non-food species that are regulated by other government agencies or entities, such as GE insects being developed for plant pest control or animal health protection, and that are under APHIS oversight …."

[8] The term "articles" means any material or tangible object that could harbor plant pests or noxious weeds.
[9] rDNA, or recombinant DNA, is two pieces of DNA from different organisms that have been joined together into a single piece of DNA.

In the same issue of the Federal Register, APHIS solicited public comment on any potential effects of animals with GE traits on U.S. livestock health. Specifically, APHIS sought input regarding GE animal research currently being conducted or planned for the future, the implications of the importation or interstate movement of GE animals for U.S. livestock health, and activities that APHIS should consider with respect to U.S. livestock under the Animal Health Protection Act that would complement FDA's draft guidance.

Security at USDA Laboratories

To secure GE research inside USDA laboratories, USDA agencies are responsible for implementing and managing security and biosafety programs to prevent adverse impacts on the health and safety of USDA employees, the public, or the environment. USDA uses a risk management approach to establish the Department's policy for safety and security of critical assets (e.g., equipment, facilities, functions, personnel, and research or regulatory material and projects) at USDA facilities that conduct research using rDNA technology.[10] Agencies are required to complete a risk assessment of their research facilities and to develop security policies based on the assessment to reduce and mitigate the risk of potential threats. Agencies are also required to develop a safety program that addresses issues such as personal safety and health, containment, and education.

When constructing and handling rDNA molecules, or organisms or viruses containing rDNA molecules, institutions that receive funding from NIFA are required to follow guidelines from the U.S. Department of Health and Human Service's NIH. These guidelines specify physical containment, facility design, and facility access controls for research involving rDNA technology.

USDA agencies that conduct GE animal or insect research are responsible for oversight of their research and ensuring that their agency is following USDA safety and security policies. Three agencies within USDA conduct or fund research into GE animals and insects:

- APHIS' Center for Plant Health Science and Technology (CPHST)—part of APHIS' Plant Protection and Quarantine program—supports USDA's regulatory decision making and operational process through development work, scientific investigation, analysis, and technology.

- The Agricultural Research Service (ARS) conducts research aimed at developing solutions to agricultural problems affecting Americans' everyday lives.

- The National Institute of Food and Agriculture (NIFA)—formerly the Cooperative State Research, Education, and Extension Service (CSREES)—seeks to advance knowledge for agriculture, the environment, and human health and well-being by supporting research, education, and extension programs. To accomplish this goal, NIFA funds research grants for universities and other partner organizations.

[10] Departmental Manual 9610-1 for Biosafety Level 3 facilities and Departmental Manual 9610-2 for Biosafety Level 1 and Biosafety Level 2 facilities.

Objectives

The objectives of this audit were to determine (1) which USDA agencies have oversight responsibilities for regulating GE animal and insect research, (2) whether current law and USDA regulations provide adequate authority to control GE animal and insect research, (3) the extent of research activities in the Department and which agencies are involved, and (4) if agencies established sufficient controls to ensure that GE animals and insects are not inadvertently released into the environment.

Section 1: APHIS Regulations Regarding GE Animals and Insects Need to be Strengthened

Finding 1: APHIS Needs to Revise How its Regulations Pertain to GE Animals and Insects

While the Secretary of Agriculture has emphasized the promise that biotechnology offers and the need for market acceptance of GE products, APHIS has been slow in developing regulations regarding GE animals and insects[11] that are comparable to the regulations APHIS already has in place for GE plants and plant pests. APHIS considers regulations for animals and insects a lower priority because there was more genetic experimentation being performed on plants and because the public was making relatively few inquiries regarding GE animals and insects. Recently, however, researchers and the public have expressed concerns about the adequacy of regulations regarding GE animals and insects. Specifically, they are concerned that GE animals and insects are being imported into the United States, but are not being reviewed by the correct regulatory agency or are even identified as GE. Moreover, developing clear regulations concerning biotechnology is critical to building market acceptance and encouraging GE research.

Under the Coordinated Framework for the Regulation of Biotechnology, APHIS is responsible for regulating GE plant pests, plants, animals, animal pests, and veterinary biologics.[12] Additionally, the Plant Protection Act and the Animal Health Protection Act give APHIS regulatory authority relating to plant health and animal health, respectively.[13] The overall jurisdiction over GE animals and insects belongs to FDA,[14] but APHIS—because of its authority relating to animal pests and animal diseases—has authority over the importation, interstate movement, and field release of GE animals and insects. Since the Coordinated Framework for the Regulation of Biotechnology anticipated that future scientific developments will lead to further regulatory refinements, APHIS is responsible for periodically reevaluating its regulatory position in light of scientific developments, determining whether additional regulatory measures are necessary, and, when necessary, amending or adding regulations.

We found, however, that while APHIS has used this authority to promulgate regulations for GE plants and plant pests, it has lagged in developed regulations for GE animals and animal pests. For plants, APHIS published its regulations pertaining to GE plants and invertebrate plant pests in 1987—Title 7, Code of Federal Regulations, section 340, "Introduction of organisms and products altered or produced through genetic engineering which are plant pests or which there is

[11] Specifically, animals and insects that are not plant pests.

[12] Veterinary biologics are veterinary products of biological origin, such as vaccines, antiserums, and diagnostic kits.

[13] Specifically, the Plant Protection Act (7 U.S.C. 7701 et seq., dated June 20, 2000) authorizes APHIS to regulate any plant, plant product, biological control organism, noxious weed, article, or other means of conveyance that could injure, damage, or cause disease in any plant or plant product. The Animal Health Protection Act (7 U.S.C. 8301 et seq., dated May 13, 2002) gives APHIS authority to regulate the importation and interstate movement of livestock animals, insects, and any means of conveyance that may be diseased with, exposed to, or carrying a livestock disease. The Animal Health Protection Act defines "livestock" as any farm-raised animal, and "animal" as any member of the animal kingdom (except humans).

[14] Under the Federal Food, Drug, and Cosmetic Act and the FDA guidance document "Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," issued in draft form on September 19, 2008, and in final form on January 15, 2009.

reason to believe are plant pests." Given advances in biotechnology and the need to respond to changes in the Plant Protection Act, APHIS proposed a revision of these regulations on October 9, 2008.[15]

In contrast, for GE animals and animal pests, APHIS has not issued regulations pertaining specifically to the introduction (import, interstate movement, or field release) of GE animals or animal pests, and instead regards GE animals and animal pests as regulated by regulations promulgated in 1963.[16] These regulations have not been updated to reflect the Animal Health Protection Act, do not clearly define APHIS' scope of coverage for regulating movements and field releases of GE animals and animal pests, and do not describe requirements for developing a GE animal or animal pest for the market. Essentially, these regulations cover GE animals and animal pests by inference only.

While APHIS officials in Veterinary Services[17] and Biotechnology Regulatory Services[18] stated that they are aware of the need to develop a clear and transparent regulatory framework regarding GE animals and animal pests, they stated that they have emphasized GE plants and plant pests because there are few inquiries regarding GE animals and insects—APHIS has not approved any GE animals for field release, and there have been few requests to import GE animals into the United States. Instead, APHIS reacts on a case-by-case basis when researchers request information about regulatory requirements for the movement or field release of GE animals or animal pests.

OIG acknowledges that APHIS' approach has been reasonable for regulating the few instances of experimentation relating to GE animals and insects that have taken place to date. However, APHIS needs to establish its regulations before such experimentation becomes more common. In December 2008, the Advisory Committee on Biotechnology and 21st Century Agriculture, an entity which provides advice to the Secretary of Agriculture on issues related to agricultural biotechnology, expressed concerns that GE animals were being imported from Asian countries without being identified as GE, and that there were no controls for such imports. Additionally, clear regulations for GE research on animals and animal pests are a critical component to building market acceptance of biotechnology. A well-designed regulatory structure should provide a clear pathway to the market for safe and useful products. Without such a framework, consumer confidence decreases, even as the risk increases that GE products might be inadvertently released.

APHIS-Biotechnology Regulatory Services has taken steps to study, plan, and solicit comments regarding the regulation of GE animals and insects, but the pace of progress has been slow. In 2007, Biotechnology Regulatory Services established an Animal Policy Branch to work on animal policy decisions. The branch chief told us that, in coordination with FDA, APHIS-Veterinary Services, and the EPA, the Branch had been working on determining APHIS' role in

[15] Federal Register, "Importation, Interstate Movement, and Release into the Environment of Certain Genetically Engineered Organisms," volume 73, pages 60008-60048, dated October 9, 2008.
[16] Title 9, Code of Federal Regulations, section 122, "Organisms and Vectors."
[17] APHIS' Veterinary Services unit regulates the import and export of GE animals, animal products, and veterinary biologics.
[18] APHIS' Biotechnology Regulatory Services unit regulates the introduction (importation, interstate movement, and release into the environment) of GE organisms that may pose a risk to plant health.

regulating GE animals. The Animal Policy Branch concluded that it needs to propose new regulations and began work on a draft of an advanced notice of proposed regulation that was geared to addressing the risk of transgenic animals and the health of animal herds. However, this document has not yet been finalized.

On July 28, 2008, APHIS-Biotechnology Regulatory Services issued its strategic plan for fiscal years 2009 to 2014 in which it stated that it was "involved in the development of a framework for regulating GE animals including GE insect pests that may pose a risk to animal and plant health." However, the plan does not include any performance measures to assess the agency's progress or hold Biotechnology Regulatory Services accountable for achieving these goals.

On September 19, 2008—in conjunction with FDA's issuance of its draft guidance document[19] on regulating GE animals—APHIS-Biotechnology Regulatory Services published in the Federal Register a request for information[20] seeking public comment and scientific and technical empirical data and information concerning ongoing and future research on GE animals. APHIS explained that its interest was to ensure that GE animals imported into the United States or moved interstate do not present risks to U.S. livestock health. APHIS also sought comment on what types of actions and approaches it should consider in addressing any such risks that would complement FDA's oversight.

APHIS-Biotechnology Regulatory Services officials told us that their review of the comments received in response to the September 2008 request for information indicated that the public had two major concerns. First, scientists felt that there was a need for APHIS and FDA to collaborate to ensure the adequacy of regulations and safeguards regarding GE animals and insects. Second, the public expressed concerns that, because of the overlap in APHIS' and FDA's purview with regard to GE animals, animals that FDA does not review may not be referred to APHIS (for example, in an import situation). Biotechnology Regulatory Services officials stated that they had discussed these issues with FDA and APHIS-Veterinary Services. At the conclusion of these meetings, Biotechnology Regulatory Services stated that it would draft a Decision Memorandum to the Secretary of Agriculture providing information on the issues, and seeking guidance regarding how the agency should respond. Biotechnology Regulatory Services did not, however, set a deadline for completing the memorandum.

In November 2009, Biotechnology Regulatory Services officials told us that they were working on drafting the Decision Memorandum to the Secretary setting forth three possible options for clarifying the regulations that apply to GE animals and insects: (1) arguing that these regulations in their current form give APHIS sufficient authority to regulate GE animals and insects, (2)modifying these regulations to make it clearer how they relate to GE animals and insects, or (3) formulating completely new regulations.

[19] Federal Register, "Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," volume 73, pages 54407-54408. FDA issued the final version of this guidance document on January 15, 2009.
[20] Federal Register, "Genetically Engineered Animals," volume 73, page 54360, dated September 19, 2008.

On May 20, 2010, a Biotechnology Regulatory Services official provided us with a copy of the draft decision memorandum. However, this decision memorandum remains an internal document, no decision has been made, and there is no timeframe for providing it to the Secretary.

The draft memorandum clearly shows that APHIS has not yet made a firm decision about how it should proceed with regulating GE animals and insects. We believe that APHIS should revise its regulations governing the introduction of GE animals and animal pests by adding provisions in the same areas that it has proposed to revise in its regulations on GE plants and GE plant pests—namely, to (1) revise the scope of the regulations so that researchers can clearly determine if a GE organism is subject to APHIS regulations; (2) reorganize the agency's permit application and evaluation procedures to make them more transparent and clearly reflect the procedural steps in the application, evaluation, and issuance of a permit; and (3) provide greater detail about the application requirements for permits for importation, movement, and environmental release. APHIS also should establish timeframes and performance measurements that hold Veterinary Services accountable for developing a regulatory framework that is transparent, clear, and allows for public participation.

Recommendation 1

APHIS should develop an action plan, including timetables and performance measures, which ensures that APHIS' regulatory framework for GE animals and insects is developed in a timely manner and meets the agency's strategic goals.

Agency Response

In its response, dated May 2, 2011, APHIS stated that it would develop an action plan by December 31, 2011, that includes timetables and performance measures which ensure that APHIS' regulatory framework for GE animals and insects is developed in a timely manner and meets the agency's strategic goals.

OIG Position

We accept management decision for Recommendation 1.

Recommendation 2

APHIS should develop a regulatory framework that clearly defines APHIS' scope of coverage and regulatory requirements for GE animals and insects, and parallels the proposed revised regulations for GE plants.

Agency Response

In its response, dated May 2, 2011, APHIS stated that it would develop a regulatory framework that clearly defines its scope of coverage and regulatory requirements for GE animals and insects. APHIS does not agree that the framework should necessarily parallel the proposed revised regulation for GE plants. According to APHIS, the GE plant regulations were proposed

but have not been finalized and much work remains to be done. Nevertheless, APHIS does acknowledge the need to clarify for the public the APHIS regulatory framework for GE animals and insects. APHIS stated that it will develop the framework in accordance with the action plan developed in response to Recommendation 1.

OIG Position

We agree with the planned corrective action. However, APHIS must ensure that in its development of the regulatory framework, the controls and oversight to regulate the importation, interstate movement, field release, and the deregulation of regulated GE animals or insects are clearly defined to the public and researchers. In order to reach a management decision, APHIS needs to provide information indicating the timeframes in which the regulatory framework will be completed and issued.

Section 2: USDA Agencies Need to Strengthen Their Controls over Research

Finding 2: NIFA Needs to Develop a Formal Process for Reporting and Monitoring Research Incidents Involving rDNA

NIFA has not implemented a formal process for documenting and monitoring research incidents, such as unauthorized releases of transgenic[21] animals produced by manipulating rDNA. Agency officials stated that because NIFA is a funding agency and not a regulatory agency, it relies on assurances from universities and reports from other agencies to ensure that researchers are complying with applicable regulatory guidelines. As a result, NIFA has been slow to react to, and sometimes unaware of, incidents such as the entry of potentially transgenic pigs—produced with NIFA grant funds—into the food supply. In order to ensure the public's health and safety, the agency needs to improve how it receives reports of such incidents and how it responds to the incidents.

Institutions receiving NIFA funding for research are responsible for protecting human subjects, treating animals humanely, and monitoring the use of rDNA. They must also report to NIFA any serious illnesses, accidents, releases, or safety problems involving rDNA.

For the years 2002 to 2008, NIFA (then CSREES) funded 51 GE animal and insect research grant projects and 4 workshop conferences totaling over $5.4 million. Included in the 51 research grants were 17 animal and 34 insect research projects. We found, however, that NIFA did not have a formal process for receiving such reports and addressing research incidents involving rDNA. While recipients of research funding are required to report incidents to NIFA, the agency did not have an established point of contact who receives reports of such incidents.

In one serious incident, we found that from September 2000 to August 2004, NIFA (then CSREES) approved grants totaling $300,000 to the University of Illinois to conduct rDNA research on potentially transgenic pigs that were later released into the food supply. The research involved two groups of pigs. One group had been modified using a cattle gene, and another was modified using a human gene. The researchers' goal was to increase the sows' milk production, which the researchers hoped would allow more piglets to survive to adulthood. By decreasing the piglets' mortality rate, the researchers would have achieved a significant economic breakthrough for U.S. agriculture. In late 2002, the researchers notified FDA that they had rendered a transgenic pig from this study. FDA identified this as a violation of its regulations and initiated an investigation in January 2003. This investigation showed that not only had the researchers rendered one pig, but between April 2001 and January 2003, the university had released at least 386 pigs from this study for sale for slaughter as human food.[22] The researchers claimed that these pigs, which were the offspring of transgenic animals, did not inherit the inserted genetic material, but FDA could not confirm this assertion.

[21] Transgenic organisms are organisms whose DNA includes inserted DNA that originated in a different species.
[22] According to Title 21, Code of Federal Regulations, section 511.1(b)(5), dated April 1, 2002, edible products of investigational animals are not to be used for food unless authorization has been granted by FDA or USDA.

The FDA's investigators reported that the researchers did not conduct sufficient evaluations or keep sufficient records to assess whether the offspring inherited the genetic material. Further, an FDA inspector stated that FDA had not approved the test that the researcher used to determine if the transgenic pig's offspring inherited the transgene. The FDA investigator stated that under the terms of the study protocols—agreed to by FDA and the university—animals involved in this particular study were to be destroyed by incineration to prevent their introduction into the human food supply. Accordingly, FDA sent a warning letter to the university reminding it that study animals may not be used for food without prior FDA authorization. Although the university failed to comply with the protocols of the study, FDA did not believe that any product derived from these animals would have to be removed from commerce for public health reasons, and USDA concurred with this determination. However, FDA and USDA officials could not provide documentation to OIG supporting their determinations.

During our review, NIFA officials stated that they learned of the incident only after the fact, and could not produce any evidence of the incident having been reported to the agency. Furthermore, although NIFA's assurance statement signed by the university required the researchers to dispose of experimental animals correctly, report any inadvertent releases, and follow NIH guidelines, we found that NIFA had not provided researchers with a contact for reporting incidents. When we discussed with NIFA officials their response to this incident, they stated that they did not have a formal process for receiving reports of research incidents of this sort. NIFA's research integrity officer stated that, although she receives allegations of "misconduct," incidents involving the release of transgenic animals would not necessarily qualify as research misconduct. In this specific incident, NIFA did not determine misconduct on the part of the researchers and, from September 2005 through August 2008, continued funding grants totaling almost $372,000. We concluded that the agency needs a process for handling incidents of this nature, as well as receiving reports of any serious illnesses, accidents, releases, or safety problems involving rDNA.

In response to our review, NIFA revised the agreements it signs with researchers to include a point of contact for reporting and monitoring accidents and releases involving rDNA. In addition, OIG concluded that NIFA can improve its controls by including in its new agreement specific language about requirements for reporting accidents and releases involving rDNA. Once the permanent, revised agreement is in place, NIFA stated that it will provide training to its staff on the protocols for receiving reports of research incidents.

Recommendation 3

NIFA should develop and implement a formal process for documenting and monitoring research incidents involving rDNA.

Agency Response

In its response, dated March 15, 2011, NIFA stated that it would amend its Research Award Terms and Conditions to specifically require all awardees to document and report any incidents involving the release of rDNA to NIFA within 48 hours. The amended Research Award Terms and Conditions will be completed by June 30, 2011.

OIG Position

We accept management decision for Recommendation 3.

Recommendation 4

NIFA should establish a central point of contact for receiving reports of accidents and releases involving rDNA.

Agency Response

In its response, dated March 15, 2011, NIFA agreed to provide a central point of contact for receiving reports of accidents and releases involving rDNA by June 30, 2011.

OIG Position

We accept management decision for Recommendation 4.

Finding 3: APHIS' Center for Plant Health Science Technology (CPHST) Needs a Formal Research Approval and Review Process

From 2007 to 2008, CPHST spent about $550,000 on GE projects intended to improve methods to eradicate plant pests that pose a risk to agriculture and the environment. Projects included plant pests such as the pink bollworm, the Mediterranean fruit fly, and the Mexican fruit fly. We found, however, that the center lacks a formal process for selecting which projects will receive funding, evaluating the results of funded projects, and summarizing the results of that project. The approval and review process employed by CPHST was undocumented and did not have controls to ensure that all projects were properly evaluated. CPHST officials stated that, since they have had so much success in responding to their short-term ad hoc requests, they had not developed a formal process for reviewing longer-term projects. Because of the informal nature of the process for determining which projects would receive funding, CPHST lacks assurance that it is effectively prioritizing projects that will result in positive outcomes for the U.S. Government.

Agency managers are responsible for developing and maintaining effective internal controls. These internal controls are the organization, policies, and procedures used to reasonably ensure that (1) programs achieve their intended results; (2) resources are used consistently with the agency's mission; (3) programs and resources are protected from waste, fraud, and mismanagement; (4) laws and regulations are followed; and (5) reliable and timely information is obtained, maintained, reported, and used for decision-making.[23] For an agency that does scientific work such as CPHST, controls over how funding for projects is distributed are fundamental to the center's proper functioning.

[23] Office of Management and Budget Circular A-123, "Management's Responsibility for Internal Control," dated December 21, 2004.

To determine how research will be funded, the CPHST Director or national science program leader staff solicit scientists to submit work plans based on APHIS' prioritized needs list, which is developed through meetings with APHIS managers and working groups specific to emergency programs. Once the work plans are submitted, they are reviewed by the CPHST Director and national science program leader staff and are approved, disapproved, or modified based on the available budget and the adequacy of the work plans. Approved plans are subject to two levels of review. First, the CPHST Director and national science program leader staff annually review new and existing projects to determine if the proposed work meets the requirements of APHIS' prioritized needs list for CPHST projects. Second, annually scheduled technical meetings conduct reviews of laboratories to make recommendations for the future direction of projects.

We found that CPHST's approval and review process was not transparent. The center lacked documented controls for tracking whether reviews were performed or documenting the results of the reviews. The CPHST Director stated that, with short-term and long-term work plans, the center effectively developed two parallel approval systems. He also stated that it became difficult to distribute resources between these two parallel systems, for which the approval process was not accountable, and that tracking the results of research projects was inefficient.

CPHST has recently recognized its need to improve its process for approving and reviewing the research it funds. In its 2007 to 2012 strategic plan, for instance, the center stated that it needed a transparent review process for funding new research. When we spoke to the CPHST Director about what progress was being made towards this goal, he informed OIG that the center has been overhauling its current system and is in the process of implementing its new system in stages.

In order for CPHST to achieve its objective of implementing a transparent work plan approval and review process, it must develop and implement formal management controls that will help ensure the accountability of funded research projects.

Recommendation 5

APHIS should direct CPHST to develop written management controls for a work plan approval and review process that is transparent and ensures the accountability of funded projects.

Agency Response

In its response, dated May 2, 2011, APHIS stated that CPHST is in the process of implementing a new SharePoint-based project management system called the CPHST Project Information Assistant (CPIA). CPHST will also develop a manual describing the project approval and review process and how to use the new system to manage this process. The CPIA and manual will be fully implemented by September 30, 2011.

OIG Position

We accept management decision for Recommendation 5.

Section 3: USDA Needs to Improve Security at Laboratories Researching GE Animals and Insects

Finding 4: ARS Needs to Develop a Process for Tracking Recommendations from its Safety, Health, and Environmental Evaluation Inspections

ARS performs safety, health, and environmental inspections at its laboratories, but it does not have a process for tracking recommendations from these evaluations and ensuring that laboratories take corrective action to remedy any deficiencies. This occurred because ARS did not have any controls to track recommendations that were open or recommendations that were corrected and closed. ARS officials explained to us that they relied on their inspectors and response letters from their laboratories to ensure that corrective action is taken on recommendations. However, we noted that this approach to resolving these recommendations has resulted in action not being taken to correct some deficiencies. In particular, we found that one laboratory—the Knipling-Bushland U.S. Livestock Insects Research Laboratory located in Kerrville, Texas—did not respond to an inspector's recommendation to develop a biological biosafety program until 3 years after the recommendation was made. This laboratory manipulates human cells that, once transformed, could result in a public safety concern if they were inadvertently released.

ARS requires that qualified and properly equipped personnel perform periodic inspections of all agency laboratories, and that laboratories take appropriate corrective actions in response to those inspections.[24] These inspections are intended to ensure that ARS facilities are in compliance with Federal, State, and local regulations, and that the laboratory is safe for employees and the surrounding community.

For fiscal years 2005 to 2007, ARS conducted five GE animal and insect research projects (four insect projects and one animal project) at its laboratories. Together, these projects totaled over $16 million in funding. As part of the process for ensuring that GE research is conducted safely, we visited the laboratory in Beltsville, Maryland, where the GE animal research project was conducted, and the Knipling-Bushland U.S. Livestock Insects Research Laboratory in Kerrville, Texas, where one of the GE insect research projects was conducted. Although ARS personnel were performing required safety inspections of the agency's laboratories, we found that ARS does not have a process for tracking the results of these inspections and was thus unable to state how many recommendations had been made, how many were still outstanding, or what corrective action had been implemented in response to any given recommendation. Without such a process, ARS could not ensure that laboratories followed through and that they corrected any deficiencies identified by inspectors.

We found that the Knipling-Bushland U.S. Livestock Insects Research Laboratory, where one of the GE insect research projects was being conducted, was slow to correct such deficiencies. ARS inspected this facility in 2005 and 2007 and, on both occasions, the inspector recommended that the laboratory develop a biological biosafety program, since the facility works with a line of

[24] USDA Research, Education, and Economics Manual, "Safety, Health, and Environmental Management Program No. 230.0," section 11, Responsibilities, dated December 5, 2005.

transformed human cells that is tumorigenic (i.e., that produces or tends to produce tumors). However, we found during our fieldwork that the laboratory did not develop a biosafety program. Subsequently, as a result of OIG's finding, laboratory officials reported and provided evidence that a new biological biosafety program was implemented at the laboratory in July 2008, after our fieldwork was concluded. Corrective action was not performed until after our review at the laboratory and 3 years after the initial recommendation was made. We concluded that this was an unacceptably long delay in implementing corrective action necessary to ensure the health and safety of the laboratory employees and the public.

When we spoke to an ARS official about this long delay in implementing corrective action at this facility, he stated that the recommendation just "fell through the cracks." He explained that ARS relies on response letters from laboratories to ensure that adequate corrective action is taken in response to inspections, but in this case, the facility did not provide a response letter. This fact was not noted until OIG reviewed the facility's inspection reports.

We concluded that ARS could improve its oversight of the inspection process by developing a process for tracking the status of recommendations made by its inspectors.

Recommendation 6

ARS should direct the agency's laboratories to develop and implement a process for tracking the status of inspection recommendations until corrective actions have been completed.

Agency Response

In its response, dated April 26, 2011, ARS stated that it has policies and mechanisms for implementing corrective actions identified during health and safety inspections. From ARS' perspective, ARS Manual 230, section 22, specifically addresses health and safety inspections. ARS stated it is in the process of improving ARS Manual 230, section 22. The updates will include: new language and guidance that requires workplace safety and health hazards to be addressed timely; the development and implementation of a hazard abatement plan if a condition or situation cannot be corrected within 30 days; additional USDA authorities who will be added that cover biosafety programs and biohazardous waste decontamination, management, and quality controls at laboratories and technical facilities; and an "accountability statement" that will be placed within the Deputy Area Director for Business Management's performance standards, which will hold the incumbent responsible for tracking and following recommendations to abate any hazard identified during the inspection process.

OIG Position

We concur with the actions being undertaken by ARS. However, to reach a management decision, ARS officials need to provide information indicating the dates that ARS will update and improve ARS Manual 230, section 22, and the Deputy Area Director for Business Management's performance standards to ensure that corrective actions from inspections are timely completed.

Finding 5: APHIS' CPHST Needs to Develop a Comprehensive Security Plan

Although CPHST laboratories dealt with security concerns on an "as-needed" basis, we found that they had not developed a comprehensive security plan including incident response plans. At one facility, for instance, although officials took reasonable steps to improve security after a break-in took place, they did not follow an established plan. This occurred because officials at CPHST responsible for laboratory security were unaware that Departmental regulations requiring a comprehensive security plan applied to their laboratories. As a result, they failed to comply with this requirement. Developing a comprehensive security plan will help these laboratories respond more effectively to future security problems.

Departmental regulations require that each USDA laboratory and technical facility create a plan for security. The plan must include inventory control procedures, physical security systems, cybersecurity systems, personnel suitability reviews, and incident response plans.[25] The plan should be based on a risk assessment, which all USDA labs must complete and review at least once every 5 years.

We found, however, that officials responsible for security at the seven CPHST-operated laboratories were unaware that these Departmental regulations applied to their laboratories. When we visited the Decision Support and Pest Management Systems Laboratory in Phoenix, Arizona, we asked to review the laboratory's security plan. Agency officials stated that they had not developed a comprehensive security plan, as they had not been aware of the requirement. Once they learned of the requirement, however, they agreed that the laboratory was subject to the regulation.

We also noted that, because officials at CPHST were unaware that they should be following these Departmental regulations, they had not revised their risk assessments in more than 5 years. For example, the Phoenix laboratory had performed a risk assessment, but it was more than 5 years out of date. Updating the laboratory's risk assessment would be helpful for developing a security plan, since it would enable security officials to identify areas of greatest concern. Again, once we brought this issue to the attention of CPHST officials, they agreed that their laboratories were subject to this requirement.

We concluded that, by complying with these Departmental requirements, CPHST could better identify threats, risks, and critical assets; assess its vulnerabilities; and recommend effective security countermeasures.

Recommendation 7

APHIS should direct CPHST to develop and implement comprehensive security plans for its laboratories.

[25] Department Manual 9610-2, "USDA Security Policies and Procedures for Laboratories and Technical Facilities, section 6, Responsibilities, and section 9(f), Physical Security," dated April 30, 2003.

Agency Response

In its response, dated May 2, 2011, APHIS stated that it will develop and implement comprehensive security plans for its laboratories conducting work with GE insects. APHIS will follow the instructions detailed in Departmental Manual 9610-2, "USDA Security Policies and Procedures for Laboratories and Technical Facilities," when developing these security plans. APHIS stated that it will complete the security plans for its laboratories by September 1, 2011.

OIG Position

We agree with the planned corrective action. However, to reach management decision, APHIS needs to develop comprehensive security plans not only for those laboratories conducting work with GE insects, but for all its laboratories that meet the requirements of Departmental Manual 9610-2.

Recommendation 8

APHIS should direct CPHST to review and update its risk assessments, and perform reviews of each laboratory at least once every 5 years.

Agency Response

In its response, dated May 2, 2011, APHIS stated that it will review and update laboratory risk assessments, and perform reviews every 5 years for the laboratories conducting GE insect research. APHIS stated that it will complete the review and update of risk assessments by September 1, 2011.

OIG Position

We agree with the planned corrective action. However, to reach management decision, APHIS needs to review and update its laboratory risk assessments and perform reviews every 5 years, not only for those laboratories conducting work with GE insects, but for all its laboratories that meet the requirements of Departmental Manual 9610-2.

Scope and Methodology

Our audit work focused primarily on identifying USDA controls over research involving GE animals and insects, including safety and security policies used to prevent the release of GE animals and insects into the environment. During the years 2002 to 2009, there were a total of 63 USDA-funded research projects and grants totaling over $22 million involving GE animals and insects.

Based on the laboratories' proximity and our projected travel costs, we judgmentally selected four research facilities conducting such research and reviewed their safety and security policies. We visited laboratories operated by ARS and APHIS' CPHST, as well as one independent laboratory that conducted NIFA-funded research. We evaluated whether current law and USDA regulations provide these agencies with adequate authority to control GE animal and insect research and whether agencies had established sufficient controls to ensure that GE animals and insects are not inadvertently released.

We conducted fieldwork at the Headquarters of USDA agencies and laboratories belonging to ARS and APHIS' CPHST from August 2007 to February 2008. We also conducted fieldwork at a NIFA-funded research laboratory during the same period. We solicited additional documents and conducted followup interviews through May 2010.

To accomplish our audit objectives, we:

- interviewed agency representatives and evaluated agency policies and procedures to determine agency roles and responsibilities related to GE animal and insect research;
- submitted written questionnaires, requested documents, reviewed documentation, and conducted interviews at applicable USDA agencies;
- interviewed FDA, EPA, APHIS, and USDA-Office of the General Counsel officials to determine the responsibilities of FDA, EPA, and APHIS with regard to GE animal and insect research;
- visited ARS and APHIS laboratories and an independent laboratory where a NIFA-funded research project was taking place;
- reviewed USDA laboratory safety and security policies as well as NIH guidelines to develop pro forma questions for review of USDA laboratories that conduct research into GE animals and insects;
- reviewed APHIS' process for issuing permits for GE animal movements and field releases for calendar year 2007 and evaluated APHIS' management controls over these permits;
- reviewed APHIS', ARS', and NIFA's processes for approving and evaluating the results of GE animal and insect research projects; and
- reviewed applicable legislative history, laws, regulations, and agencies' internal reviews, including Federal Managers' Financial Integrity Act reports.

We conducted our audit in accordance with generally accepted Government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions.

Abbreviations

APHIS… ..... Animal and Plant Health Inspection Service

ARS..... Agricultural Research Service

CPHST…… ...Center for Plant Health Science and Technology

CPIA……...CPHST Project Information Assistant

CSREES…..... Cooperative State Research, Education, and Extension Service

EPA ..... Environmental Protection Agency

FDA…..... Food and Drug Administration

FSIS…….....Food Safety and Inspection Service

GE ..... Genetically Engineered

NIFA… ..... National Institute of Food and Agriculture (formerly CSREES)

NIH… ..... National Institutes of Health

NSF……. ..... National Science Foundation

OIG… ..... Office of Inspector General

rDNA..... Recombinant DNA

S&E..... Science and Education Division

U.S.C. ……....United States Code

USDA..... Department of Agriculture

Exhibit A: Coordinated Framework – Approval of Commercial Biotechnology Products

This chart and the narrative description that follows (on the next page) are adapted from the Coordinated Framework for Regulation of Biotechnology, Federal Register, volume 51, page 23302, dated June 26, 1986.

Subject	Responsible Agency/Agencies
Foods/food additives	FDA*, FSIS[1]
Human drugs, human medical devices, and human biologics	FDA
Animal drugs (veterinary drugs)	FDA
Animal biologics (veterinary biologics)	APHIS
Other contained uses	EPA
Plants and animals	APHIS*, FSIS, FDA[2]
Pesticide microorganisms released in the environment	EPA*, APHIS[3]
All other uses (microorganisms):	
Intergeneric combinations	EPA*, APHIS[3]
Intrageneric combination:	
Pathogenic source organism:	
1. Agricultural use	APHIS
2. Nonagricultural use	EPA*[4], APHIS[3]
No pathogenic source organisms	EPA (requires only a report)
Nonengineered pathogens:	
1. Agricultural use	APHIS
2. Nonagricultural use	EPA*[4], APHIS[3]
Nonengineered nonpathogens	EPA (requires only a report)

* Indicates the lead agency.

[1] The Food Safety and Inspection Service (FSIS), under the Under Secretary of Agriculture for Food Safety,[26] is responsible for food use.

[2] FDA is involved when in relation to food use.

[3] APHIS is involved when the microorganism is a plant pest, animal pathogen, or regulated article requiring a permit.

[4] EPA requirements will only apply to environmental release under a "significant new use rule."

[26] At the time the Coordinated Framework for Regulation of Biotechnology was published in 1986, both FSIS and APHIS were under the Assistant Secretary of Agriculture for Marketing and Inspection Services, a position that no longer exists. FSIS is now under the Under Secretary of Agriculture for Food Safety, and APHIS is under the Under Secretary of Agriculture for Marketing and Regulatory Programs.

Narrative description of the preceding chart:

Jurisdiction over the varied biotechnology products is determined by their use, as has been the case for traditional (nonbiotechnology) products.

Food, food additives, human drugs, human biologics, human medical devices, and animal drugs are reviewed or licensed by FDA. Food products prepared from domestic livestock and poultry are under FSIS' jurisdiction.

Veterinary biologics are reviewed by APHIS. APHIS also reviews plants, seeds, plant pests, animal pathogens, and "regulated articles" (i.e., GE organisms containing genetic material from a plant pest). An APHIS permit is required prior to the shipment (movement) or release into the environment of regulated articles, or the shipment of a plant pest or animal pathogen.

"Other contained uses" refers to the closed-system uses of those microorganisms subject to the Toxic Substances Control Act that are intergeneric combinations (microorganisms that contain genetic material from dissimilar source organisms). These are subject to EPA's premanufacture notification requirement.

Microbial pesticides will be reviewed by EPA, with APHIS' involvement in cases where the pesticide is also a plant pest, animal pathogen, or regulated article requiring a permit. (FDA may become involved in implementing pesticide tolerances for foods.)

"Intrageneric combinations" are those microorganisms formed by genetic engineering other than intergeneric combinations. For these, when there is a pathogenic source organism and the organism is used for agricultural purposes, APHIS has jurisdiction. If the microorganism is used for nonagricultural purposes, then EPA has jurisdiction, with involvement from APHIS in cases where the microorganism is also a regulated article requiring a permit. Intrageneric combinations with no pathogenic source organisms are under EPA jurisdiction and require only an informational report.

"Nonengineered pathogens" that are used for an agricultural use will fall under APHIS' jurisdiction. Those that are for a nonagricultural use come under EPA jurisdiction, with APHIS' involvement in cases where the microorganism is also a plant pest or animal pathogen requiring a permit. Nonengineered, nonpathogenic microorganisms are under EPA jurisdiction and require only an informational report.

Exhibit B: Coordinated Framework – Biotechnology Research Jurisdiction

This chart and the narrative description that follows (on the next page) are adapted from Coordinated Framework for Regulation of Biotechnology, Federal Register, volume 51, page 23302, dated June 26, 1986.

Subject	Responsible Agency/Agencies
Contained research, no release into environment	
1. Federally funded	Funding agency[1]
2. Non-Federally funded	NIH or S&E[27] voluntary review
Foods/food additives, human drugs, medical devices, human biologics, animal (veterinary) drugs:	
1. Federally funded	FDA*, NIH Guidelines and review
2. Non-Federally funded	FDA*, NIH voluntary review
Plants, animals, and animal (veterinary) biologics:	
1. Federally funded	Funding agency[1], APHIS[2]
2. Non-Federally funded	APHIS*, S&E voluntary review
Pesticide microorganisms:	
Genetically engineered	
Intergeneric	EPA*, APHIS[2], S&E voluntary review
Pathogenic intergeneric	EPA*, APHIS[2], S&E voluntary review
Intrageneric nonpathogen	EPA*, S&E voluntary review
Nonengineered	
Nonindigenous pathogen	EPA*, APHIS
Indigenous pathogen	EPA*[3], APHIS
Nonindigenous nonpathogen	EPA*
Other uses (microorganisms) released in the environment	
Genetically engineered	
Intergeneric organisms	
1. Federally funded	Funding agency[1], APHIS[2], EPA[4]
2. Commercially funded	EPA, APHIS, S&E voluntary review
Intrageneric organisms	
Pathogenic source organism:	
1. Federally funded	Funding agency[1], APHIS[2], EPA[4]
2. Commercially funded	APHIS[2], EPA (if nonagricultural use)
No pathogenic source organism	EPA (requires only a report)
Nonengineered	EPA (requires only a report)*, APHIS[2]

* Lead Agency. The lead agency designation depends on which research agency is funding the research (e.g., National Institutes of Health (NIH), Science and Education Division (S&E), or the National Science Foundation (NSF)) or which regulatory agency reviews specific-purpose research (e.g., pesticides). The authority refers to approval of the actual execution of experiments and not to their funding.

[1] Review and approval of research products conducted by NIH, S& E, or NSF.

[2] APHIS issues permits for the importation and domestic shipment of certain plants and animals, plant pests, and animal pathogens, and for the shipment or release into the environment of regulated articles.

[3] EPA jurisdiction for research on a plot greater than 10 acres.

[4] EPA reviews Federally funded environmental research only when it is for commercial purposes.

[27] USDA's S&E. At the time the Coordinated Framework for Regulation of Biotechnology was written, USDA had an Assistant Secretary for Science and Education. This Assistant Secretary oversaw the Office of Agriculture Biotechnology.

Narrative description

For contained Federally funded research for biomedical and agricultural purposes, research approval will be granted by the funding agency. The NIH guidelines relate primarily to biomedical experiments and only to those using rDNA techniques. Research on foods/food additives, human drugs, medical devices, and human biologics will continue to rely on the NIH guidelines, with NIH approval required for certain experiments such as human gene therapy, and FDA permission required for clinical trials.

Fashioned after the NIH guidelines, the USDA's S&E guidelines apply to agricultural research on plants, animals, and microorganisms, and provide guidance for laboratory and field testing of organisms derived using rDNA manipulation and other technologies. Adherence to the appropriate set of guidelines is required for institutions receiving financial support from NIH, S&E, or NSF. These guidelines specify what types of review procedures are required for specific categories of experiments. Some experiments require individual approval by the respective agency providing institutional support. For those experiments that require agency approval, advisory committees at NIH, S&E, and NSF, composed primarily of non-Government scientists, may be asked to provide expert review. In addition, research on plants, animals, and animal biologics will come under APHIS' permit requirements if a regulated article, plant pest, or animal pathogen is involved. An APHIS permit is required prior to the shipment (movement) or release of a regulated article, or the importation or shipment of a plant pest or regulated article used in any research experiment.

EPA has authority for all environmental research on microbial pesticides, regardless of whether research is Federally funded. EPA will regulate research under a two-level review system based upon its evaluation of the potential risks posed by various types of microoganisms, with lesser notification required for level I reporting and full review required for level II.

For the "other uses" category, jurisdiction for release may be under S&E, NSF, APHIS, or EPA, depending primarily upon the source of the funding, but also upon the purpose of the research and the characteristics of the GE microorganism. Thus, Federally funded research conducted for an agricultural use will require adherence to S&E guidelines and approval of certain experiments by S&E or NIH, depending on which is the funding agency. EPA will review commercial research. APHIS' jurisdiction applies to issuing permits for regulated articles, plant pests, or animal pathogens. EPA will require an informational report for nonengineered microorganisms released into the environment, with APHIS' involvement for the review of plant pests or animal pathogens.

USDA'S

ANIMAL AND PLANT HEALTH INSPECTION SERVICE,

AGRICULTURAL RESEARCH SERVICE, and

NATIONAL INSTITUTE OF FOOD AND AGRICULTURE

RESPONSE TO AUDIT REPORT

United States Department of Agriculture

Animal and Plant Health Inspection Service

Washington, DC 20250

MEMORANDUM **May 2, 2011**

TO: Gil H. Harden
Assistant Inspector General
for Audit

FROM: Gregory L. Parham /s/
Administrator

SUBJECT: APHIS Response and Request for Management Decisions on OIG Report, "Controls Over Genetically Engineered Animal and Insect Research" (50601-16-TE)

Thank you for the opportunity for the Animal and Plant Health Inspection Service (APHIS) to comment on this report. We have addressed Recommendations specifically addressed to APHIS, with our planned corrective actions and the timeframes for implementation of these actions.

Recommendation 1: APHIS should develop an action plan, including timetables and performance measures, which ensure that APHIS' regulatory framework for GE animals and insects is developed in a timely manner and meets the agency's strategic goals.

APHIS Response: APHIS agrees with this Recommendation. APHIS has a rigorous regulatory system in place to examine and mitigate the risks of GE insects that are plant pests. We agree that further clarification of our regulatory system as it pertains to GE insects as animal pests is an important and timely issue. APHIS will develop an action plan by December 31, 2011 that includes timetables and performance measures which ensure that APHIS' regulatory framework for GE animals and insects is developed in a timely manner and meets the agency's strategic goals. The regulation of GE insects has been raised to the level of the Office of Science and Technology Policy (OSTP), Agricultural Biotechnology Working Group (ABWG). The ABWG has an intergovernmental subgroup that will evaluate the current state of research and development and discuss potential risks and statutory authorities associated with the control of GE insects. APHIS is actively engaged in the interagency discussions lead by OSTP. These discussions will inform the APHIS action plan.

Under the 1986 Federal Coordinated Framework for the Regulation of Biotechnology, APHIS is one of the Federal agencies with regulatory responsibilities over certain products of biotechnology. The Coordinated Framework is a policy statement that describes the comprehensive federal

regulatory policy for ensuring the safety of biotechnology research and products. Further, the 1992 Notice of Federal Policy described a risk-based, scientifically sound approach to the oversight of planned introductions of biotechnology products into the environment, focusing on the characteristics of the product not the process by which the product was created. Therefore, existing statutes are considered adequate to provide safe, risk-based oversight of biotechnology and resulting products and there may not be a need for new regulations for GE insects. We may determine following the ABWG discussions that issuing a guidance document to clarify the regulatory oversight of GE insects is sufficient.

Recommendation 2: APHIS should develop a regulatory framework that clearly defines APHIS' scope of coverage and regulatory requirements for GE animals and insects, and parallels the proposed revised regulations for GE plants.

APHIS Response: APHIS agrees in part with this Recommendation. We agree the Agency should develop a regulatory framework that clearly defines APHIS' scope of coverage and regulatory requirements for GE animals and insects. APHIS will develop the recommended regulatory framework in accordance with the action plan the Agency will prepare in response to Recommendation 1. While we are committing to the development of a regulatory framework, we are not necessarily committing to a change in current regulations. The regulatory framework will identify current regulations and how they address the animal health risks associated with GE animals and GE insects. If we need to clarify our current authority over GE animals and insects, we will determine the most transparent way of accomplishing this goal.

We do not agree that the framework should necessarily parallel the proposed revised regulations for GE plants. The GE plant regulations were proposed but have not yet been finalized and much work remains to be done on that rule.

We wish to emphasize that the Food and Drug Administration (FDA) now has a rigorous mandatory approval process for GE animals that examines, among other things, the health of the animal. As described in the OIG report, FDA published Guidance to the Industry which described how FDA's New Animal Drug Authority will be used to evaluate the safety of GE animals. At the same time, APHIS solicited public comment in the Federal Register in the form of a Request for Information. APHIS sought information on any potential effects that animals with GE traits may have on U.S. livestock health and on activities APHIS should consider under the Animal Health Protection Act that would complement FDA's Guidance. The majority of comments APHIS received referenced FDA authority over the labeling of edible products of GE animals, or indicated that such products should not be allowed in the food supply. The substantive comments encouraged APHIS to regulate GE insects to meet the needs of rapidly emerging technologies, and stressed the need to collaborate with FDA over the approval of GE livestock.

No information was provided through the public comments which indicated that a GE animal would in itself pose a risk to the health of U.S. livestock by the dissemination of pests and diseases. These results validated previous efforts made by APHIS to determine, through a comprehensive literature search and collaboration with the Agricultural Research Service, any documented risks to livestock health due to biotechnology.

Further, APHIS has effective programs in place to prevent, detect and mitigate the introduction and dissemination of animal diseases. These include regulations that govern the import of animals, animal products and vectors (including insects) that could introduce or disseminate animal diseases. These regulations cover animals, products and vectors regardless of whether or not they are genetically engineered. We acknowledge, nevertheless, the need to clarify for the public the APHIS regulatory framework for GE animals and insects.

As indicated in our response to Recommendation 1, APHIS is an integral part of the ABWG and its interagency subgroup which will evaluate risks associated with GE insects and recommend actions. APHIS believes that working through the ABWG is a fundamental step that must be completed before we complete our regulatory framework. Since APHIS already has a regulatory system in place to examine and mitigate the risks of GE insects as plant pests, APHIS will consider the future direction for the regulation of GE insects as animal pests based on the outcomes of the ABWG discussions.

Recommendation 5: APHIS should direct CPHST to develop written management controls for a work plan approval and review process that is transparent and ensures the accountability of funded projects.

APHIS Response: APHIS agrees that there should be a transparent work plan approval and review process for project management. APHIS' Center for Plant Health Science and Technology (CPHST) is in the process of implementing a new SharePoint-based project management system called the CPHST Project Information Assistant (CPIA) that will be accessible throughout our Plant Protection and Quarantine program area. Project requests will be entered, approved, and tracked through CPIA. Work plans, budgets, and progress reports will also be entered for each project. As part of the implementation plan, CPHST will also develop a manual describing the project approval and review process and how to use CPIA to manage this process. The final testing and initial entry of projects are currently ongoing. CPIA will be fully implemented by CPHST laboratories by September 30, 2011.

Recommendation 7: APHIS should direct CPHST to develop and implement comprehensive security plans for its laboratories.

Recommendation 8: APHIS should direct CPHST to review and update its risk assessments, and perform reviews of each laboratory at least once every 5 years.

APHIS Response: APHIS agrees to develop and implement comprehensive security plans for laboratories conducting work with GE insects. In addition, APHIS will review and update laboratory risk assessments, and perform reviews every 5 years for the laboratories conducting GE insect research. APHIS will follow the instructions detailed in the Departmental Manual 9610-2, "USDA Security Policies and Procedures for Laboratories and Technical Facilities," when developing these security plans. Our proposed completion date is September 1, 2011.

April 26, 2011

SUBJECT: Management's Response to Recommendations in Audit 50601-16-TE Controls over Genetically Engineered Animal and Insect Research

TO: Jon M. Holladay
Acting Chief Financial Officer
Office of the Chief Financial Officer

Gil H. Harden
Assistant Inspector General for Audit
Office of the Inspector General

FROM: Michelle D. Garner /s/
Acting Director, Financial Management Division

The Agricultural Research Service (ARS) appreciates the opportunity to provide comments to the Draft OIG Audit Report 50601-16-TE and would like to provide the following comments, which should be addressed in the final report.

Finding 4: ARS Needs to Develop a Process for Tracking Recommendations from its Safety, Health, and Environmental Evaluation Inspections

Recommendation 6

ARS should direct the Agency's laboratories to develop and implement a process for tracking the status of inspection recommendations until corrective actions have been completed.

Agency Response

ARS has policies and mechanisms for implementing corrective actions identified during health and safety inspections. ARS Manual 230, Section 22, specifically addresses this issue from an Agency perspective. Section 22 states that the inspection and abatement program is implemented at the location level.

The Agency provides checklists and abatement forms for use by the location. *ARS Form 404, Safety, Health, and Environmental Inspection Checklist* serves as a guide and reference tool for conducting inspections. The Form 404 checklist, abatement forms, and inspection procedures can be found at the ARS Facilities Division/Safety Health & Environmental Management Branch home page: http://www.afm.ars.usda.gov/shem/index.htm. There was a lapse at a specific ARS location and we have provided a timeline of events and when the corrective action was implemented at that location (Please see ARS Technical Comments Document). To further emphasize the importance of following up on all internal/external safety inspections, the Agency will be placing an accountability statement within each Deputy Area Director for Business Management's performance standards. This statement will hold the incumbent responsible for tracking and following any management actions or recommendations to abate a hazard that were identified during the inspection process.

- The following sections of Manual 230 are also relevant to inspections and abatement of findings:

  - Section 3 states Research, Education, and Economics policy regarding Safety and Health policy, which is "… to eliminate or minimize losses incurred by the agencies, individual employees, and the general public as a result of actions or incidents involving or producing injury, illness, and property/environmental damage in the workplace…." This is achieved through mechanisms detailed in Section 3, to include developing standard operating procedures that minimize or eliminate potentially hazardous conditions or adverse environmental effects and taking appropriate action to correct deficiencies.

  - The most relevant authorities that are listed in Manual 230 are:
    - 29 CFR, Part 1910, Occupational Safety and Health Standards; and
    - 29 CFR, Part 1960, Basic Program Elements for Federal Employee Occupational Safety and Health Programs.

  - ARS is in the process of updating and improving Manual 230, with an anticipated release date of the new document during the first quarter of the 2011 calendar year. The updates will include the following:

    - New language and guidance will be added to Section 22, **Hazard Abatement Plans:** All identified workplace safety and health hazards will be addressed in a timely manner. If a condition or situation cannot be corrected within 30 days, the work area supervisor and safety representative will develop and implement a Hazard Abatement Plan. The Plan will include the following information:

- an explanation of the circumstances contributing to the delay in abatement,
- a proposed timetable for the abatement,
- a summary of the steps being taken in the interim to mitigate the hazard and protect employees, and
- a requirement that the supervisor be responsible for providing the information contained in the Plan to the employees in the work area by either posting a copy in an accessible location or by providing copies to the employees.

- Authorities will be added, to include the Department of Agriculture (USDA) DR4400.007, Biosafety Program, and USDA DR9630.001, USDA Policies and Procedures on Biohazardous Waste Decontamination, Management, and Quality Controls at Laboratories and Technical Facilities.
- To further emphasize the importance of following up on all internal/ external safety inspections, ARS will be placing an "accountability statement" within each Deputy Area Director for Business Management's performance standards. This statement will hold the incumbent with tracking and following any management actions/recommendations to abate any hazard identified during the inspection process.

Questions regarding this memorandum can be directed to Robert H. Magill, Assistant Director, Financial Management Division on 301-504-1257 or via email at Robert.Magill@ars.usda.gov.

United States Department of Agriculture

Research, Education, and Economics

National Institute of Food and Agriculture

1400 Independence Avenue SW
Washington, DC 20250

March 15, 2011

TO: Gil H. Harden
Assistant Inspector General for Audit

FROM: Roger N. Beachy /S/
Director
National Institute of Food and Agriculture

SUBJECT: Audit Report No. 50601-16-TE - Controls over Genetically Engineered Animal and Insect Research

This is in response to your February 14, 2011, memorandum requesting our written response to the official draft of the subject audit, specifying corrective actions taken or planned on each audit recommendation and proposed completion dates for implementing such actions.

The National Institute of Food and Agriculture (NIFA) agrees with recommendations Nos. 3 and 4 concerning NIFA in the subject report and the Attachment provides our responses to both recommendations. NIFA plans to complete both corrective actions by June 30, 2011. Below is our response to your overall recommendation in the "Executive Summary":

Recommendation:

The NIFA Director should direct laboratories that perform NIFA-funded research to develop and implement a formal process for documenting and monitoring research incidents involving GE animals and insects.

Agency Response: NIFA is in the process of amending its Award Terms and Conditions to formalize the process for documenting and monitoring Incident Reporting. NIFA is also establishing a central point of contact to receive accident or release reports involving genetically engineered animals and insects.

NIFA appreciates the audit work done by the OIG auditors as their efforts have and will contribute to improved monitoring and documenting of research incidents involving NIFA funding.

Questions regarding this memorandum can be directed to Edward Nwaba, Oversight Branch Chief and Interim Agency Audit Liaison Official on (202) 205-5799 or via email at enwaba@nifa.usda.gov.

Attachment

cc: Jon Holladay, OCFO