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USDA REGULATIONS FOR TRANSGENIC ORGANISMS

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ABSTRACT

The USDA regulation of organisms and products developed through biotechnology is, in general, related to the Department's mandate from the U.S. Congress to protect the nation's plant and animal health. Under the authority granted by the Federal Plant Pest Act and the Plant Quarantine Act, the USDA regulates the movement into and through the United States of plants, plant products, plant pests and any product or article which may contain a plant pest at the time of movement. Under this broad authority, the USDA regulates a number of potential food products of biotechnology and products used in food animals, including: 1) transgenic plants and microorganisms; 2) veterinary biological products developed through biotechnology. 3) animals used in biotechnology research. The Federal policy statement on biotechnology regulation that was published in final form in June 1986 contains several main elements: 1) the products of recombinant DNA technology will not differ fundamentally from unmodified organisms or from conventional products; 2) the existing laws are adequate for regulating organisms and products developed by the new processes; 3) the product and the risk should be regulated, not the process and 4) regulation should be based on the end use of the product and conducted on a case-by-case baseis. The USDA policy has been consistent with the overall Federal policy and National Academy of Sciences recommendations. The USDA Agency directly concerned is the Animal and Plant Health Inspection Service (APHIS) which has combined a number of existing staffs to create the Biotechnology, Biologics, and Environmental Protection Division.

INTRODUCTION

The National Academy of Sciences (NAS), a nongovernmental advisor to the Federal Government on science issues since 1863, has produced several studies on biotechnology. A 1987 NAS publication entitled "Introduction of Recombinant DNA-Engineered Organisms into the Environment: Key Issues" listed two key findings:

1. There is no evidence that unique hazards exist either in the use of rDNA techniques or in the transfer of genes between unrelated organisms.

2. The risks associated with the introduction of rDNA-engineered organisms are the same in kind as those associated with the introduction into the environment of unmodified organisms and organisms modified by other genetic techniques.

The most recent NAS publication, entitled, "Field Testing Genetically Modified Organisms--Framework for Decisions", was released September 20, 1989. This report discusses scientific issues underlying decisions on the planned environmental introduction of genetically modified organisms and plants under field-test conditions. The report has considered such issues as a comparison of classical and modern biotechnological techniques, the potential for weediness of modified plants, and competitiveness of modified organisms.

In preparing their publication, the NAS steering committee adopted several fundamental principles annunciated in their 1987 report. One such principle was that safety assessment of a rDNA-modified organism "should be based on the nature of the organism and the environment into which it will be introduced not on the method by which it was modified."

Some other major scientific conclusions from the report are:

Plants

1. As the molecular methods become more specific, users of these methods will be more certain about the traits they introduce into plants. Traits that are unfamiliar in a specific plant will require careful evaluation in small-scale field tests where plants exhibiting undesirable phenotypes can be destroyed.

2. At this time, the potential for enhanced weediness is the major environmental risk perceived for introductions of genetically modified plants. The likelihood of enhanced weediness is low for genetically modified plants, domesticated crop plants, on the basis of our knowledge of their morphology, reproductive systems, growth requirements, and unsuitability for self-perpetuation without human assistance.

3. Confinement is the primary condition for ensuring safety of field introductions of classically modified plants.

4. Depending on the crop species, proven confinement options include biological, chemical, physical, spatial, environmental, and temporal isolation, as well as the size of the experiment.

5. Plants grown within field confinement for experimental purposes rarely escape to cause problems in the natural ecosystem.

6. Established confinement options are as applicable to field introductions of plants modified by rDNA as to introductions of plants modified by classical plant breeding methods.

Lastly, the NAS committee developed a "familiarity" framework for the evaluation of risk. Three essential questions were presented:

1. Are we familiar with the properties of the organism and the environment into which it may be introduced?

2. Can we confine or control the organism effectively?

3. What are the probable effects on the environment should the introduced organism or a genetic trait persist longer than intended or spread to nontarget environments?

The report makes it very clear that familiar does not mean safe. "Rather, to be familiar with the elements of an introduction means to have enough information to be able to judge the introduction's safety or risk".

USDA POLICY, ORGANIZATION, AND AUTHORITY FOR REGULATING BIOTECHNOLOGY

USDA policy on the regulation of biotechnology has been consistent with the overall Federal policy and the findings of the NAS. In policy documents published in December 1984, and June 1986, and in practice:

1. USDA has not viewed genetically engineered organisms and products as fundamentally different from those produced by conventional methods.

2. USDA has used existing laws to regulate the products of biotechnology.

3. USDA has attempted to focus attention on the product and the risk, rather than on the process used in production.

In keeping with this policy, USDA, like other Federal agencies, has developed an administrative structure under its existing authorities to deal with all aspects of biotechnology research and regulation. Within U.S. agencies, the research and regulatory activities are generally administratively separated.

The USDA Agency directly concerned with regulating genetically engineered plants and microorganisms is APHIS. The USDA agencies engaged in biotechnology research include the Agricultural Research Service (ARS) and the Cooperative State Research Service.

Jurisdiction for biotechnology product regulation of plants is shared by USDA and EPA in some instances (51 FR 23318; 23329; 23358-59). APHIS and EPA coordinate reviews of proposed field releases when jurisdiction is shared. For example, APHIS sends copies of permit applications to EPA for transgenic plants that EPA considers to have pesticidal properties, such as those containing a Bacillus thuringiensis endotoxin gene. USDA and EPA also share jurisdiction over certain microorganisms that are intended for nonagricultural uses, but are also plant pests. Such products are regulated jointly by USDA under the FPPA and PQA and by EPA under the Toxic Substances Control Act (TSCA), 5 U.S.C. § 2601-2929. Other rDNA organisms which are plant pests and are used as microbial pesticides are regulated by USDA under the FPPA and PQA and by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. § 136-136y. Representatives from USDA and EPA meet regularly to discuss specific cases arising under their authorities. USDA and EPA perform simulataneous, coordinated, but independent reviews to ensure that data requests from the applicant are not duplicated.

APHIS also works closely with FDA in regulatory efforts involving the food products of biotechnology. This coordination will enable Federal agencies to anticipate any potential safety concerns with the range of rDNA products used as food, currently under development. As a result of this coordinated approach, USDA, EPA, and FDA jointly sponsored a conference in 1988 on the scientific issues involved in the development of transgenic plants. The proceedings of this conference are available from the agencies.

USDA COORDINATION OF BIOTECHNOLOGY REGULATION

Within BBEP, APHIS has combined a number of existing staffs to create the USDA's lead division for biotechnology regulation. Two BBEP staffs are:

a) The Biotechnology Coordination & Technical Assistance (BCTA) staff coordinates biotechnology regulatory activities within USDA. BCTA takes the lead in liaison between APHIS and other Federal agencies on biotechnology regulatory matters.

b) The Biotechnology Permits staff is responsible for issuing permits for the field testing of certain genetically engineered plants and microorganisms, maintaining liaison with State departments of agriculture, the academic community and scientific societies, and providing technical information for environmental analyses used to issue permits allowing field tests of regulated articles.

The process and requirements for obtaining a permit for release into the environment of a rDNA derived organism are contained in the Federal Register document entitled "Plant Pests; Introduction of Genetically Engineered Organisms or

Products; Final Rule" 52 FR 22892, 1987. These regulations provide that an organism or product altered or produced through genetic engineering would be a "regulated article" if the donor organism, recipient organism, or vector or vector agent used to produce this organism belongs to a group designated in the list in 340.2, and meets the APHIS definition of a "plant pest" 7 U.S.C. 150aa(c), or is an unclassified organism and is being imported, moved interstate, or released into the environment. The organism being considered for release will be regulated if it is a plant pest or if it contains nucleic acid sequences derived from a plant pest and these sequences have been introduced into the "regulated article" via rDNA. Thus, even if the gene donor and recipient are not plant pests, if the vector used to transfer that gene contains sequences from a plant pest, the organism is regulated. In essence, in issuing a permit for release APHIS certifies that there is no plant pest risk even though the organism released into the environment may contain genetic material from a plant pest.

USDA AUTHORITY

USDA has broad regulatory authority to protect the adulteration of food products made from livestock and poultry, to protect U.S. agriculture against threats to animal health, and to prevent the introduction and dissemination of plant pests. This authority is applicable to genetically engineered animals, plants, and microorganisms.

Under the authority granted by the Federal Plant Pest Act (FPPA) May 23, 1957, as amended, and the Plant Quarantine Act (PQA) of August 20, 1912, as amended, USDA regulates the movement into and through the United States of plants, plant products, plant pests, and any product or article which may contain a plant pest at the time of movement. These articles are regulated to prevent the introduction, spread, or establishment of plant pests new to or not widely prevalent in the U.S. The regulations which implement this statutory authority are found in 7 CFR Parts 300 through 399.

Specifically, under regulations codified at 7 CFR 330.200, APHIS administers a program which prohibits the movement of any plant from a foreign country into the U.S. or interstate unless authorized under a permit issued by USDA. APHIS also excercises remedial measures to prevent the spread intrastate of a plant pest which constitutes a threat to agriculture. These requirements are imposed by APHIS in regulating the movement of nongenetically engineered organisms, products, and certain articles which are plant pests or could harbor plant pests.

USDA published a new rule on June 16, 1987, under the authority of the FPPA and PQA, which established a permit requirement for the introduction of genetically engineered organisms which are plant pests as an extension of the existing regulations in 7 CFR 330.200.

This final rule, which became effective on July 16, 1987, provides that an organism or product altered or produced through genetic engineering would be regulated if the donor organism, recipient organism, or vector or vector agent belongs to a group designated in the list in 340.2, and meets the APHIS definition of "plant pest", or is an unclassified organism and is being imported, moved interstate, or released into the environment. These regulations are risk based and process specific.

Since July 1987, APHIS has issued 92 permits for field tests under 7 CFR 340. Several others are pending. Environmental assessments and findings of no significant impact were prepared for each of the permits for field tests, and notice of their availability was published in the Federal Register. These environmental analyses were conducted in accordance with the provisions of the National Environmental Policy Act and Departmental environmental regulations. The number of documented field trials with rDNA organisms approved by regulatory agencies of the U.S. greatly exceeded approvals by any other country. In the area of regulatory field test approval, as with scientific advancement, the U.S. is recognized as the world leader. These significant accomplishments demonstrate the benefits to be derived from consulting the regulatory agencies responsible for protecting agriculture, human health, and the environment before releasing rDNA organisms into the environment.

Among the first generation of field tests about half were for herbicide tolerance in tomato and tobacco. The remaining half were nearly all for insect and phytopathogen resistance, also in tomato and tobacco. This years applications show a much greater range of plants used for experimentation, including maize, rice, potato, and soybeans and a more complex range of characters. Three permits were issued for the field trials of a microorganism engineered to contain a gene which is toxic to the European corn borer. Based on this limited sample, I think we can say that breakthroughs involving major crop plant diseases and quality characteristics from these field tests are under way.

THE PERMITTING PROCESS

I would like to briefly review the procedures we have developed at APHIS to issue permits to field test genetically engineered plants and microorganisms and to assure the safety of such tests to human health and the environment. I will deal only with the permits for release although we also have issued over 500 permits for importation and movement. In general, APHIS regulates an organism if it is included on the list of organisms considered to be plant pests. The organisms will be regulated if the organism itself is a plant pest, or if it contains nucleic acid sequences derived from a plant pest and these sequences have been introduced through the use of rDNA technology. If a vector or vector agent is used and the vector is derived from a

plant pathogen, the resulting modified organism to be field tested is reviewed.

The permit application for release contains 14 points which must be addressed before the application is considered complete. This information includes a detailed description of the organism to be tested, who is responsible for conducting the test, where the organism is to be tested, and descriptions of how the organism will be prevented from dissemination into the environment during transport and during the field test. The review period of 120 days, which is required in regulations, includes these features:

1. Notice of receipt of the application is published in the Federal Register.

2. A copy of the application and the preliminary review are sent to the State in which the test will take place within 30 days after the application is received. The State agencies have 30 days to comment after receiving the application.

3. An environmental assessment (EA) is prepared by the reviewing scientist, and the EA is subject to peer review by the scientific staff.

4. When the EA results in a finding of no significant impact (FONSI), the permit is issued, and notice of the action and the availability of the EA and FONSI is published in the Federal Register.

5. Currently, site inspections are conducted near the time of initiation of the field trial.

6. The permit may contain special conditions which must be met, one of which involves the collection and submission of test data to APHIS. This data will be used to evaluate subsequent field applications of the same or similar organism.

7. In addition to the copy containing confidential business information (CBI), the permit application must contain a copy with any CBI deleted. Confidential business information is protected from disclosure under the Freedom of Information Act (5 U.S.C. 552(B).

8. Changes in the permit application may be submitted as amendments both before and after the permit is granted.

The environmental analysis is a key component in the permit review process. It is the public's assurance that APHIS has thoroughly considered the possible consequences of releasing the regulated article into the human environment. This analysis, documented in an EA, is made available to anyone who requests it, free of charge. The EA contains the following sections:

1. A summary describing the purpose of the EA, Departmental regulations, the conditions under which the permit is issued or denied, precautions against environmental risk, the background biology of the organism tests, and the possible environmental consequences of the field test.

2. A complete description of the environment that will be affected by the field test and the precautions developed for protecting that environment, including field plot design, field inspection and monitoring, test plot security, and disposal plans.

3. The environmental consequences of the test are examined from all possible perspectives. Consideration is given to the biology of the recipient, donor, and vector, and to the potential for biological containment based on knowledge of this biology. Any possibility of risk to native flora and fauna is examined, as is any potential impact on human health.

An instruction manual for completing the permit application is being prepared to educate and assist an applicant in the scientific community. The manual will provide, among other things, an up-to-date list of APHIS' staff who can answer questions about the permit process and a list of questions and answers to assist the applicant in determining whether the organism to be field tested is regulated.

CONCLUSIONS

The following points may be concluded.

1. The public must be assured that environmental releases of rDNA organisms are being reviewed to prevent unknown or unintended effects.

2. Each review must be scientifically based to assure public credibility and the industry's voluntary compliance.

3. Evidence must be made immediately available that such reviews have taken place.

4. Regulations should result in "informed decisions" which have considered and analyzed the various alternatives and are rational and appropriate. Procedures for effective "public" participation are essential.

5. Coordination is necessary among government agencies, and between governments.

As safe products are developed and successfully marketed, public acceptance will grow. Establishing a regulatory scheme which provides for such technology transfer while protecting

against any potential danger is one of the most difficult and challenging aspects of modern government. These are critical times in the development of a new generation of rDNA modified organisms. In our society, public perception can be as influential as scientific fact. Public perception underscores public acceptance and therefore it must be favorably shaped to facilitate the acceptance of products derived from genetic engineering. If the technological advances that are an outgrowth of a tremendous public and private investment by this nation, are to be of the greatest benefit, the efforts to develop the appropriate effective regulatory framework are more than justified and positive public perception is a necessity. We have made much progress, and through cooperation we can assure ourselves of continued progress in this vital area.

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Disclaimer

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REFERENCES

Animal and Plant Health Inspection Service, "Plant Pests; Introduction of Genetically Engineered Organisms or Products; Final Rule," S2FR 22882-22914, June 16, 1987.

McCammon, S.L., Medley, T.L. 1989. Certification for the planned introduction of transgenic plants into the environment. In: Molecular and Cellular Biology of the Potato, Chap. 17. Vayda, M.E. and Park, W. (eds.).

Medley, T.L. 1988. Issues in assessing the environmental impact of veterinary biologics produced through biotechnology. Food Drug Cosmetic Jour. 1988:821-829.

National Academy of Sciences. 1987. Introduction of recombinant DNA-engineered organisms into the environment: Key Issues. National Academy Press, Washington, D.C.

National Academy of Sciences. 1989. Field testing genetically modified organisms: Framework for Decisions. National Academy Press, Washington, D.C.

Office of Science and Technology Policy, "Coordinated Framework for Regulation of Biotechnology; Announcement of Policy and Notice for Public Comment," 51 FR 23302-23350, June 26, 1986.

Organization for Economic Cooperation and Development. 1986. Recombinant DNA safety considerations. OECD, Paris, France.

The Keystone Center. 1989. Biotechnology decisionmaking: Perspectives on the objectives of public participation. Issue Report Series. The Keystone Center, Keystone, Colorado.

The Keystone Center. 1989. Transgenic Plant Conference. The Keystone Center, Keystone, Colorado.

U.S. Federal Government Publications: 7 C.F.R. § 300-399; 7 C.F.R. § 330.200; 7 C.F.R. § 340.2; 5 U.S.C. § 552[b]; 5 U.S.C. § 2601-2929; 7 U.S.C. § 136-136y; 7 U.S.C. § 150aa-150jj; 51 F.R. 23318 (1986); 51 F.R. 23329 (1986); 51 F.R. 23358-59 (1986).