CEQ and OSTP Assessment: Case Studies of Environmental Regulations for Biotechnology

I. Introduction

On May 3, 2000, President Clinton directed the Council on Environmental Quality (CEQ) and the Office of Science and Technology Policy (OSTP) to "conduct a six month interagency assessment of Federal environmental regulations pertaining to agricultural biotechnology and, if appropriate, make recommendations to improve them." The assessment was undertaken as part of a larger set of policy measures intended to build consumer confidence and ensure that U.S. regulations keep pace with the latest scientific and product developments.

The President directed this assessment to further long-standing goals of public access to information and maintenance of strong, science-based regulation. The assessment was intended to focus on environmental regulations through the use of a set of case studies to describe in detail how specific products are being regulated or how they may potentially be regulated. The focus on environmental regulations was based on the premise that this aspect of biotechnology regulation is not well understood by the public and is the subject of considerable interest. The analysis was not intended to be comprehensive in scope, but rather to be based on a set of case studies that could illuminate current agency practices, identify strengths and potential areas for improvement.

In the intervening months, the assessment produced a set of working documents that provide rich detail and information on specific case studies for the public and for policymakers. However, due to time limitations, the interagency working group that was assembled to conduct the assessment was not able to conduct the analysis necessary to develop conclusions or recommendations. The selection of these particular case studies in no way indicates specific concern with previous regulatory findings. In fact, no significant negative environmental impacts have been associated with the use of any previously approved biotechnology product.

This introduction to these case studies provides additional background on the assessment, agricultural biotechnology, U.S. regulation of environmental aspects of biotechnology, and a request for public comment. As part of the generation of these case studies, agencies have been reviewing their own procedures and policies, and intend to continue to do so. Should an agency determine that major changes in policy or procedures are warranted, it would only do so through a notice and comment procedure to ensure full public participation.

II. Scope and Organization of the Assessment

For the purposes of this assessment, agricultural biotechnology is defined as the use in the environment of any organism that has been genetically modified using

recombinant DNA (rDNA) techniques. Environmental regulations include those that involve certain aspects of confinement as well as introduction into the environment under conditions with no or minimal physical confinement (e.g., field plantings, net pen aquaculture, and release of biological control agents).

CEQ and OSTP established an Interagency Working Group (IWG) to conduct the assessment. The IWG was composed of individuals from: the U.S. Department of Agriculture (USDA), including representatives from the Animal and Plant Health Inspection Service (APHIS), the Forest Service (FS), and the Food Safety Inspection Service (FSIS); the Environmental Protection Agency (EPA); the Department of Health and Human Services' Food and Drug Administration (FDA); the Department of the Interior (DOI); the Department of Commerce National Oceanic and Atmospheric Administration (NOAA), National Marine Fisheries Service (NMFS); the Office of Management and Budget (OMB); the Department of Justice (DOJ); and the Department of State (DOS). Reviews of the scientific information in the case studies were conducted by the Department of Health and Human Service National Institutes of Health (NIH), National Science Foundation (NSF), USDA Agricultural Research Service (ARS) and Cooperative State Research, Education and Extension Service (CSREES), and the DOI U.S. Geological Survey (USGS). Due to the inherent complexity associated with the regulation of such a diverse array of organisms and uses, the IWG selected a broad, but representative set of case studies for the assessment.

III. Background on Agricultural Biotechnology

Products developed using biotechnology hold enormous promise for increasing agricultural production efficiencies and product quality as well as for improving environmental conditions and human well-being. For example, new crop varieties have been developed that are able to reduce, in many cases, chemical insecticide applications and allow for the utilization of more environmentally benign herbicides. Other applications of biotechnology control diseases that were otherwise impossible to control using more traditional means (e.g., control of some plant viruses). Future applications may boost the use of biofuels and produce inexpensive sources of vaccines and other pharmaceuticals. "Golden Rice" has been developed using biotechnology techniques to produce elevated levels of beta-carotene, the precursor to vitamin A. The production of beta-carotene enriched foods could have a major impact on reducing health problems associated with vitamin A deficiency (e.g., blindness and death) in the world's 800 million malnourished people. These are just a few examples of the potential of biotechnology products. However, the realization of all of these advances is dependent on a comprehensive and scientifically rigorous regulatory system that relies on risk assessment and not only ensures environmental and human health issues are adequately addressed, but are also done so in a way that is credible to the public.

For at least 10,000 years, humans have been selecting and cross-breeding plants, animals, and microorganisms to develop organisms with modified traits, such as disease resistance, herbicide tolerance, enhanced production of certain chemicals, and alterations

in growth and development. The concept of genetically modifying organisms is not new and oversight systems have been developed to identify and reduce any environmental risks that might be associated with their use, for example, in plant breeding. However, the recent application of rDNA technology, which vastly expands the potential to introduce new genetic material, required scientists, regulators, and the public to rethink the adequacy of these existing oversight mechanisms.

The National Academy of Sciences (NAS) found in 1987 and again in 2000 that:

- there is no evidence that unique hazards exist either in the use of rDNA techniques or in the movement of genes between unrelated organisms;

- the risks associated with the introduction of rDNA-engineered organisms are the same in kind as those associated with the introduction of unmodified organisms and organisms modified by other methods; and,

- assessment of the risks of introducing rDNA-engineered organisms into the environment should be based on the nature of the organisms and the environment into which it is introduced, not on the method by which it was produced.

These findings do not imply that products of biotechnology should not be evaluated for any potential hazards. For instance, the 2000 NAS report, Genetically Modified Pest-Protected Plants, states that toxicity, allergenicity, effects of gene flow, development of resistant pests and effects on non-target species are concerns for both conventional and transgenic pest-protected plants. Because both conventional (e.g., breeding) and rDNA methods have the potential to produce organisms of high or low risk, the NAS panel agreed that the *properties* of a genetically modified organism should be the focus of risk assessments, not the *process* by which it was produced. For example, genes that confer resistance to biotic (e.g., pests and diseases) and abiotic (e.g., metal toxicity and drought) stressors are utilized in both classical breeding and biotechnological approaches to crop improvement. The risks and benefits associated with these genes, regardless of the method of genetic modification, depends on the combination of the organism, the function of the new gene, and the environment into which the organism will be introduced. These organisms and products should be compared to their conventional counterparts. While there are no apparent unique environmental hazards associated with rDNA technology, the fact that a greater variety of genetic constructs now can be incorporated more quickly into organisms with different genetic backgrounds required regulatory agencies to develop specific regulations and guidance documents to provide appropriate risk-based oversight.

IV. The Coordinated Framework for U.S. Regulation of Biotechnology

In response to concerns about how to best provide federal oversight for products of biotechnology, the Coordinated Framework for Regulation of Biotechnology Products

(Coordinated Framework) was adopted by federal agencies in 1986 (see 51 Fed. Reg. 23302 (June 26, 1986)). The Coordinated Framework is consistent with the judgment of the National Academy of Sciences that the potential risks associated with these organisms fall into the same general categories as those created by traditionally bred organisms. The Coordinated Framework provides a coordinated regulatory approach that is intended to ensure the safety of biotechnology research and products, using existing statutory authority and building upon agency experience with agricultural, pharmaceutical, and other products developed through traditional genetic modification techniques. The development of the Coordinated Framework anticipated that agencies might need to develop specific regulations or guidelines under existing statutory authority. The Framework also anticipated institutional evolution in accord with experience, including modifications made through administrative or legislative actions. Finally, the Coordinated Framework determined that interagency coordination mechanisms were necessary to ensure that policy and scientific questions would be addressed across agencies.

The regulatory approach articulated by the Coordinated Framework invokes many statutes and their implementing regulations and guidelines that potentially apply to products of biotechnology introduced into the environment. Some of these statutes apply only to specific types of products or activities and are administered by only one agency, while others apply across-the-board and thus pertain to all or virtually all agencies. With respect to the former, the principal agencies and statutes that regulate specific organisms are as follows:

- Animal and Plant Health Inspection Service (APHIS), in the U.S. Department of Agriculture:
  - **Animal Quarantine Laws (AQL)**, 21 U.S.C. 101-135.
  - **Plant Protection Act (PPA)**, 7 U.S.C. 7701-7772, which consolidated several previous statutes that APHIS used to regulate genetically engineered organisms, including the **Federal Plant Pest Act (FPPA),** 7 U.S.C. 150aa-150jj, the **Plant Quarantine Act (PQA)**, 7 U.S.C. 151-164a, 166-167, and others. Because no regulations have yet been issued pursuant to the PPA, APHIS continues to regulate biotechnology products according to the regulations issued regarding the FPPA, PQA, etc.
  - **Virus, Serum, Toxin Act (VSTA)**, 21 U.S.C. 151-159.

- Environmental Protection Agency (EPA):
  - **Federal Food, Drug, and Cosmetic Act (FFDCA)**, 21 U.S.C. 321, 346a *et seq*., as amended by the **Food Quality Protection Act (FQPA)**, Pub. Law 104-170 (1996).
  - **Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)**, 7 U.S.C. 136-136y, as amended by FQPA, *supra*,.
  - **Toxic Substances Control Act (TSCA)**, 15 U.S.C. 2601-2692.

- Food and Drug Administration (FDA), of the Department of Health and Human Services:
  - **FFDCA**, 21 U.S.C. 321-397
  - **Public Health Service Act (PHSA)**, 42 U.S.C. 262, 264.

- Food Safety Inspection Service (FSIS), of the U.S. Department of Agriculture:
  - **Federal Meat Inspection Act (FMIA),** 21 U.S.C. 601-691.
  - **Poultry Products Inspection Act (PPIA),** 21 U.S.C. 451-471.
  - **Egg Products Inspection Act (EPIA),** 21 U.S.C. 1031-1056.

The statutes listed below are not currently used but might be potentially applicable to specific transgenic organisms:

- Department of the Interior:
  - **Lacey Act**, 16 U.S.C 3371 *et seq*. and 18 U.S.C. 42; and
  - **Non-Indigenous Aquatic Nuisance Prevention and Control Act**, 16 U.S.C. 4701 *et seq.*

- National Oceanic and Atmospheric Administration/National Marine Fisheries Service, the Department of Commerce
  - **Magnuson-Stevens Fishery Conservation and Management Act**, 16 U.S.C. 1801 *et seq*.
  - **Marine Mammal Protection Act**, 16 U.S.C. 1362 *et seq*.
  - **Coastal Zone Management Act**, 18 U.S.C. 1451 *et seq*.

As mentioned above, several statutes and guidelines exist that apply across-the-board to all agencies involved in regulating environmental uses of biotechnology products. For purposes of this report, the most significant of these are:

- **National Environmental Policy Act (NEPA),** 42 U.S.C 4321-4375, overseen by the Council on Environmental Quality (CEQ), though EPA's regulatory activities are not subject to NEPA because they are considered to be the functional equivalent of NEPA;
- **Endangered Species Act (ESA)**, 16 U.S.C. 1531-1544, jointly administered by the Fish and Wildlife Service (FWS) in the Department of Interior and the National Marine Fisheries Service (NMFS) in the Department of Commerce;
- **Migratory Bird Treaty Act (MBTA),** 16 U.S.C. 703-712;
- **Trade Secrets Act,** 18 U.S.C. 1905 (except when certain information is not statutorily exempt).
- The Occupational Safety and Health Administration laws apply to worker safety.
- National Institutes of Health's **Recombinant DNA Advisory Committee Guidelines** are used by federal agencies and others receiving federal funding to ensure the safety of laboratory research.

Most of the statutes and guidelines referred to above pertain to particular policy interests, and the applicability of each is determined by the presence of specific conditions. In some instances, interagency agreements or understandings also clarify regulatory roles and responsibilities. The actual regulatory coverage of a particular organism depends on a variety of factors, the most significant of which are:

- the stage of development (e.g., is it still in a contained laboratory setting or is it being field tested, or is it ready for commercial use in the United States);
- the uses (e.g., is it intended for bioremediation of pollution or for biocontrol of another organism, is it intended to be a human drug or an animal biologic, or might it eventually be used as food even though that is not its primary use);
- the type of possible hazards (e.g., does it have the potential to harm plants or contain new genetic material that might cause a plant to become a noxious weed, or does it have the potential to release pollutants into the atmosphere or bodies of water); and
- the type of organism (e.g., is it an animal, plant, or microorganism).

The following table lists common uses for which there is a statute that currently is used as the primary means of regulation:

Use	**Statute**	**Agency**
Food & food additives	FFDCA	FDA
Meat, poultry, egg products	FMIA, PPIA, EPIA	FSIS
Pesticide residues	FFDCA	EPA
Production of pharmaceuticals		
Human drugs	FFDCA	FDA
Human biologics	PHS Act, FFDCA	FDA
Animal drugs	FFDCA	FDA
Animal biologics	AQL, VSTA	APHIS
Production of pesticidal substances in plants	FIFRA	EPA
	PPA	APHIS
Production of herbicide tolerance in plants	PPA	APHIS
Herbicide usage on plants	FIFRA	EPA
Microbial pesticides	FIFRA	EPA
Microbial products other than pesticides	TSCA	EPA
Biocontrol of plants	PPA	APHIS
	FIFRA	EPA
Biocontrol of plant pests	PPA	APHIS
	FIFRA	EPA

As is inevitable with an emerging technology, not all aspects of biotechnology regulation were anticipated and addressed when the Coordinated Framework was issued. Therefore, regulatory policy is evolving, including through formal and informal understandings between agencies with respect to how a particular organism or set of

organisms will be regulated. It is likely that more than one statute potentially applies to a particular organism or, in some cases, it may be unclear if any statute applies. In these cases, it may be necessary to consult the agencies to determine an appropriate regulatory oversight strategy.

V. The National Environmental Policy Act

The National Environmental Policy Act (NEPA), 42 U.S.C. 4321 *et seq*., establishes a consistent process by which federal agencies must consider the consequences of their proposed actions on the human environment prior to a decision. NEPA requires federal agencies to prepare a detailed "environmental impact statement" (EIS) for all major Federal actions significantly affecting the quality of the human environment. 42 U.S.C. 4332(2)(C). The Council on Environmental Quality (CEQ), an agency established by Congress in NEPA, has promulgated regulations that are applicable to federal agencies in their compliance with NEPA. See 40 C.F.R. 1500-1508. As well as specifying the process for preparation of an EIS, the CEQ regulations provide that federal agencies may prepare an environmental assessment (EA) to determine whether a proposed action is likely to have a significant impact on the environment, thus triggering the need to prepare an EIS. 40 C.F.R. 1501.3, 1501.4(e); 1508.9; 1508.13. CEQ regulations also provide that certain types of federal activities may be "categorically excluded" from NEPA review if the class of actions have no significant environmental effect, either individually or cumulatively, and there are no extraordinary circumstances in a given situation. 40 C.F.R. 1508.4. Public involvement and the participation of state, tribal and local governments is an important component of the NEPA process. Each federal department and agency is required to publish procedures, in consultation with CEQ, that identify how NEPA will be implemented for its typical actions. 40 C.F.R. 1507.3. EPA's decision making under statutes relevant to this assessment has been deemed to be "functionally equivalent" to the NEPA process.

VI. Case Studies

The cases studies cover a range of biotechnology products, some of which government agencies have already approved for commercial production, others of which are currently under regulatory consideration, and still others which have not been presented for regulatory review. To the extent that the case studies address products that have already been reviewed by the government, the case studies are intended to be descriptive of the process the agency (or agencies) actually followed. Since an agency may have changed its past practices, such case studies should not be regarded as modifying any current policies or procedures. By the same token, to the extent that case studies address hypothetical future reviews, the case studies are intended to describe how current statutory authorities, policies, and procedures may be applied. Such case studies are not meant to articulate new policies or procedures, and therefore, they do not constitute binding rules on any regulated entity.

Based on criteria of representation of types of organisms, range of statutes used, and levels of public interest, the IWG decided to prepare the following six case studies and four shorter sidebars:

1. **Salmon:** The production of genetically engineered salmon in net pen aquaculture was selected as a case study because it is a near-term regulatory issue (a regulatory determination has not yet been made) and, with net pen aquaculture, there is a high probability for escape of fish into open waters. The principal statutes involved in this case study are FFDCA, ESA, and NEPA. The Lacey Act, the Non-Indigenous Aquatic Nuisance Prevention and Control Act, and the Section 10 provisions of the Rivers and Harbors Act are also discussed. The lead drafting agency for the case study was FDA. NMFS and DOI were also on the drafting team. The hypothetical goldfish sidebar is meant to explore the regulation of transgenic ornamental fish, which are not produced in net pens. The principal statutes discussed in this sidebar are the Lacey Act, TSCA, the ESA, and the Non-Indigenous Aquatic Nuisance Prevention and Control Act. DOI was the lead drafting agency.

2. **Bt-Maize:** Bt-maize was selected because it is grown widely in the United States and possible non-target effects of Bt pollen have been the subject of recent public and scientific debate. The food safety issues associated with the Bt Cry9C protein, which is found in StarLink corn, are not treated here, but are being addressed through extensive interagency collaboration and interaction with consumers, scientists, and industry. The principal statutes involved in this case study are FIFRA, FFDCA, FPPA, PQA, and PPA. The Migratory Bird Treaty Act and ESA are also discussed. EPA was the lead drafting agency. APHIS and DOI were also on the drafting team. The virus sidebar is included to describe how microbial pesticides, rather than Bt plant pesticides, are regulated. This sidebar briefly discusses FIFRA, FPPA, PQA, and NEPA. EPA was the lead drafting agency. APHIS and DOI were also on the drafting team.

3. **Herbicide-Tolerant Soybean:** A herbicide-tolerant soybean was selected because this type of genetically modified plant is grown widely in the United States and has the potential to alter significantly how herbicides are used to control agriculturally important weeds. The principal statutes involved in this case study are FPPA, PQA, PPA, FIFRA, FFDCA, FQPA, NEPA, and ESA. APHIS was the lead drafting agency for this case study. EPA and DOI were also on the drafting team. A hypothetical pharmaceutical-producing plant was included as a sidebar to describe the oversight of a plant with a different set of environmental exposure issues under some production conditions. The principal statutes discussed in this sidebar are the Virus-Serum-Toxin Act, Public Health Service Act, FFDCA, PPA, and NEPA. FDA was the lead drafting agency. APHIS was also on the drafting team.

4. **Animals Producing Human Drugs:** This hypothetical example was selected to describe the regulation of animals whose primary function is to produce pharmaceuticals. Depending on the confinement conditions, these animals potentially

present to the regulator a different set of environmental exposure issues. The principal statutes involved in the case study are the Public Health Service Act, FFDCA, and NEPA. FDA was the lead drafting agency. APHIS and FSIS were also on the drafting team. The animal biologics sidebar is included to describe how animal biologics, rather than human or animal drugs or human biologics, would be regulated. The principal statutes discussed in this sidebar include the Virus-Serum-Toxin Act, the Animal Quarantine Laws, TSCA, and the Animal Welfare Act. APHIS was the lead drafting agency. FDA and FSIS were also on the drafting team.

5. **Bioremediation Using Poplar Trees:** This case study, though not commercially developed, was selected to demonstrate the oversight of a perennial plant. Perennial plants present the regulator with a different set of environmental exposure issues compared to those of annuals like corn or soybean. The principal statutes involved in this case study are FPPA, PQA, PPA, and TSCA. FS was the lead drafting agency. APHIS, EPA, and DOI were also on the drafting team.

6. **Bioremediation and Biosensing Using Bacteria:** This case study was selected to describe the regulation of bacteria that are not plant pests or pesticides. The principal statute involved in this case study is TSCA. EPA was the lead drafting agency. DOI and APHIS were members of the drafting team.

VII. Request for Comments

In order to further the assessment process, OSTP and CEQ believe it would be beneficial to have public input on federal regulation of environmental aspects of biotechnology informed by the case studies. Following public comments and other input, OSTP and CEQ will continue the IWG and assessment process, and recommend any appropriate steps to strengthen the science-based regulatory system. Public comments are requested by May 1, 2001.

Based on an initial review of the case studies, CEQ and OSTP request public comment in the following broad areas of overall federal regulation of environmental aspects of biotechnology:

- **Comprehensiveness and rigor of environmental assessment.**
- **Comprehensiveness and strength of statutory authority.**
- **Transparency of the environmental assessment and the decision making process**.
- **Public involvement**.
- **Interagency coordination**.
- **Confidential business information (CBI).**

VIII. Address for Public Comments

Public comments are requested by May 1, 2001 and should be directed to:

Chair
Council on Environmental Quality

Director
Office of Science and Technology Policy

Executive Office of the President
17th and G Streets, NW
Washington, DC 20500
Attention: CEQ/OSTP Biotechnology Assessment