# ASSESSING THE RISKS ASSOCIATED WITH BIOTECHNOLOGY: THE REGULATORY PROBLEM

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ABSTRACT

In examining the regulatory problem posed by biotechnology, three areas must be considered: 1) the potential benefits to mankind, 2) the generation of profits to industry, and 3) the mitigation of risk presented to human health and the environment. Environmental risk assessments involving exposure and effects assessments must consider the potential for establishment in the environment, the potential for altering ecosystem processes and the potential for unexpected events as they relate to biotechnology applications. Predictive and analytical tools must be developed and used by regulators to ensure that the rewards of genetic engineering to both mankind and industry are realized with minimal consequence.

KEY WORDS: Biotechnology, Regulation, Genetic Engineering, Risk, Risk Assessment, Environmental Release, Microcosm, Differential Light Scattering.

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Biotechnology presents us with the possibility for solutions to many of mankind's problems and presents industry with unique opportunities for new markets, yet is perceived to present novel risks also - defining a regulatory problem. My objective is to further explore this problem, examining the sources of risk and the techniques that can help to predict and mitigate it.

The genetic engineering of microorganisms involves the introduction of new genetic sequences into existing microorganisms to enhance their capabilities to perform a function. One method of engineering is DNA recombination. Figure 1 presents a simplistic representation of DNA recombination. A selected characteristic present in the donor DNA molecule is removed using restriction enzymes and inserted or recombined into plasmid DNA. The recombinant DNA is then cloned into a bacterial host where the desired function can be expressed. The application of genetic engineering technology by recombinant DNA and other methods has come to be known as biotechnology (OTA, 1981).

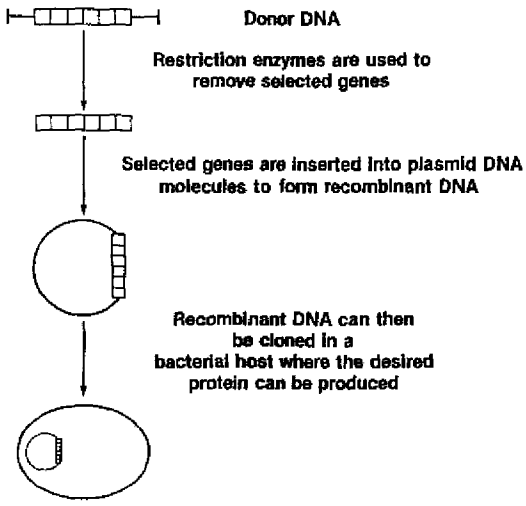


Figure 1

Recombinant DNA

The technique of recombining genes from one species with genes from another

Biotechnology's potential impact for the benefit of mankind is enormous. The treatment of human, animal, and plant diseases may be revolutionized. Commercial applications will enhance the chemical, energy, mining, electronic, textile, and waste treatment industries. Business and market analysts predict that biotechnology may benefit 70% of current US industries, due to the wide variety of potential applications.

Although tremendous potential exists, profits have not been realized to any significant degree, nor have products been marketed to benefit consumers. Notable exceptions are interferon, insulin, and human growth hormone, which are produced by genetically engineered organisms in fermentation cultures. These products have been approved for use by the Food and Drug Administration (FDA). Reasons for the delay in bringing other genetically engineered products to the market are related to the risks posed by the products of biotechnology.

These three possibilities 1) the benefits to mankind, 2) the profitability to industry and 3) the risk posed, combine to describe a regulatory problem. How can we guarantee that the inherent benefits and profitability will be captured while avoiding the potential risks to health and the biosphere?

This is not a new problem, but is one that has been faced by the chemical industry and the nuclear energy industry. A tool that was developed to assist in defining the unknown risks posed by these technologies is risk assessment. Biotechnology has an advantage in that this tool has already been developed; however, it must be modified to allow application to new types of risk.

Risk assessment methods can assist the regulatory community in solving this problem. Regulation should be designed to mitigate risk, and is often based on risk management endpoints. But before risk can be mitigated or endpoints can be determined, the risk must be defined.

Risk questions can be divided into three areas:

1) Potential for establishment in the environment. Engineered organisms may have the ability to find a suitable niche once they are released, and may reproduce, disperse, and evolve in new environments. They may also interact with native species creating new community structures and predator-prey relationships.

2) Potential for altering ecosystem processes. Releases and establishment of novel organisms could cause changes in decomposition pathways, primary production, oxygen consumption, and/or nitrogen fixation. Climatic and geologic processes could also be affected as pointed out in Eugene Odum's recent letter to Science. Normal, wild type ice-nucleating bacteria cause frost to form on potato crops as the temperature drops. Recently it has been suggested that these normal bacteria decompose contributing their lipoprotein coats to detritus, which is blown about into the atmosphere. Here the coat fragments serve as nuclei for raindrop formation. The use of ice minus strains, strains deficient for the character that causes frost formation, might reduce frost damage to potato crops. However, the establishment of ice minus strains in the environment might ultimately result in the reduction of total rainfall amounts, since nuclei for raindrop formation would not be contributed. The reduction in overall rainfall would be worse for crops than frost damage (Odum, 1985).

3) Potential for unexpected events. Novel genes and genetic changes cannot be specifically controlled or predicted, nor can the stability of genetic changes within an organism be assured. Conjugation and plasmid transfer can take place between organisms that are not generically related. Figure 2 shows some of the pathways of possible genetic exchange that have been demonstrated under laboratory conditions. Exchange is possible between many microorganisms, although spontaneous transfers in nature have not been investigated to any degree. Another point for consideration is that this gene transfer may result in transfer of genetic change from one ecosystem to another, such as from aquatic to terrestrial communities. Instability of genetic change could result in the loss of desired traits, as well as the creation of undesirable traits such as virulence or pathogenicity.

Most researchers are convinced that the chance for untoward events is very small. Surveys of science, environmental, and religious policy leaders demonstrate perceptions that the benefits of biotechnology far outweigh the risks (C & E News, 1985). Most agree that biotechnology risk factors can be classified as low probability/high consequence, and that environmental endpoints must be considered in addition to human health endpoints.

Environmental risk assessment will be more important to the regulation of biotechnology products than they have been with any other technology. These assessments must reflect the complex interaction of wide spectrum of animals, plants, and microorganisms with inanimate processes such as nutrient cycling and material balances.

Environmental risk assessments for deliberately released, genetically engineered products will involve the familiar components of exposure

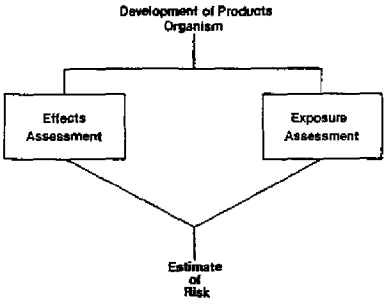


Figure 2

Environmental Risk Assessment

assessment and effects assessment, which will be combined to yield an estimate of risk (See Figure 3). Exposure assessments will rely on models of release, dispersal and persistence to estimate the probability that organisms and ecosystem processes will be exposed. Effects assessment will be used to define the magnitude and likelihood of response of organisms and ecosystem processes produced by the estimated range of exposure.

Two factors compromise our ability to conduct environmental risk assessments for the products of biotechnology: a lack of predictive tools and a lack of appropriate analysis techniques.

With regard to predictive tools; tools must be developed to allow simulation of environmental conditions. Simulated, contained conditions are needed so that we can gather data from which to make predictions.

Microcosms are laboratory systems that allow for this simulation. A variety of designs are possible, ranging from flasks containing soils and microbial communities to larger systems containing vertebrates and higher plants. They have advantages (safety, cost and time effectiveness, and simplification of complex interactions) and disadvantages (may be unrepresentative of natural conditions in surface-to-volume ratio, oversimplification, and elimination of immigration and emigration for population studies). Microcosms seem the obvious tools to utilize, yet development and standardization are needed to make them a viable regulatory tool (Pritchard, 1982).

Appropriate analysis tools are also needed. They must allow for the detection and identification of genetically engineered organisms, and their unique genetic sequences. Biotechnology products must be identifiable by their functional character before they are released into the environment. Detection and quantification will be important after release in microcosms for testing and in the environment for monitoring sites of release.

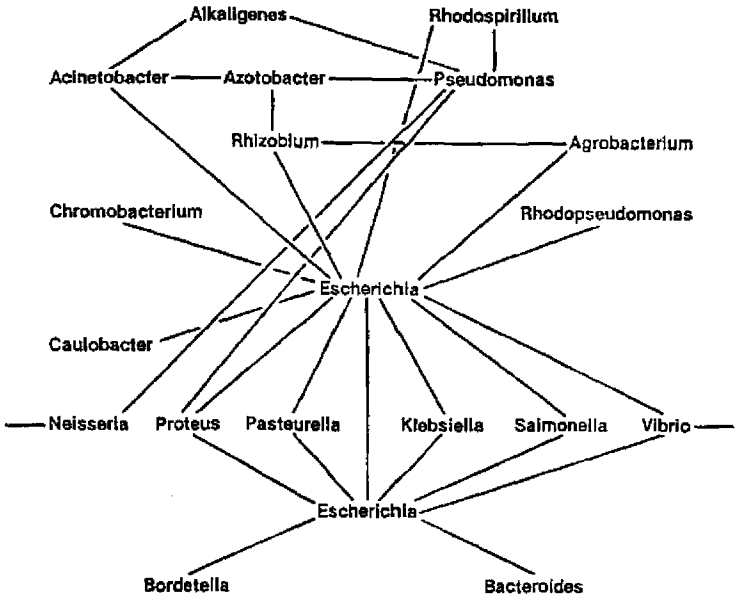


Figure 3

Pathways of possible genetic exchange
(after Reaney et al.; 1982)

Possible methods include the addition or insertion of unique genetic sequences, such as antibiotic resistance markers, as identifiers. However, these sequences may be transferred from species to species with or without the traits being monitored. Spontaneous mutation may also alter both the marker and the useful trait.

Another analysis technique is under investigation. This technique utilizes a battery of 19 recombinant DNA mutants of Bacillus subtilis. The isogenic Bacillus mutants differ only by defects in DNA repair which involve specific recombination, excision or polymerase activity. A laser beam is used to produce unique differential light scattering patterns based on bacterial count, morphology and size, and will monitor changes produced by exposure of the test organisms to various physiological conditions. Distinctive signatures or fingerprints are generated by input of the laser readout data directly into a computer system to produce a visual image. We hypothesize that this system will allow identification of newly introduced novel genetic sequences, thereby allowing us to develop an assay designed to detect and monitor genetically engineered organisms and the products produced by biotechnology (Feikner, 1983).

Further research and development in these areas, and in microbial ecology as a science, will allow us to better predict the ecosystem consequences posed by the release of engineered organisms. This predictive ability will allow the regulatory community to define endpoints

that can be used as indicators of safety for the management of biotechnology products.

A clear framework must be devised to ensure that a balance is achieved between risk and reward or cost and benefit. As biotechnology leaves the developmental stage and moves into the applied, industrial arena, the framework of regulations designed to control medical, agricultural, and industrial products will be applied.

This application must be tempered by risk management decisions that rely on environmentally based assessments. These assessments should examine the potential of genetically engineered organisms to become established in the environment, to alter ecosystem processes, and to cause unexpected events. Both predictive and analytical tools will be needed to ensure that the rewards of genetic engineering to both mankind and industry are achieved with minimal consequence.

REFERENCES


Anon. Biotechnology gets good marks in survey. Chemical and Engineering News (C & E News) 63(34): 16, August 26, 1985.

Falkner, IC. Rapid Detection of Genotoxic Chemicals in the Environment; IN: Proceedings of the ASCE Specialty Conference on Environmental Engineering, p.204, 1983.

Odum, Eugene P. Biotechnology and the biosphere (letter). Science 229:1338, September 27, 1985.

Office of Technology Assessment (OTA). Impact of Applied Genetics: Micro-Organisms, Plants, and Animals, p.5, April, 1981.

Pritchard, P.H. Model Ecosystems; IN: Conway, Richard A (Editor) Environmental Risk Analysis for Chemicals. Van Nostrand Reinhold Co., New York, 1982.

Reanney, DC et al. Genetic interactions among microbial communities; IN: Bull, A.T. and Slater J.H. (Editor), Microbial Interactions and Communities. Academic Press: London, 1982.