6. Risk Assessment Methodologies for Biotechnology Impact Assessment

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No clear basis presently exists for assessing the potential impacts of the application of biotechnology products in the environment. However, there are several possible approaches, employing presently available technology and technology which might reasonably be developed. This chapter therefore focuses on methods of risk assessment and those portions of current methodologies that might be applicable to biotechnology.

Registration of pest-controlling organisms under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides some general features and data requirements equivalent to the comprehensive assessment usually afforded a new chemical pesticide and pertinent to biotechnology products (EPA 1984). About a dozen such “pesticides” have been registered on an ad hoc basis, under rules relieving the registrant of responsibility for massive data development (see chapter 3). In spite of parallels to issues raised elsewhere in this report, such procedures for pesticide registration have not been particularly instructive. Although the release of pest-controlling organisms is deliberate and intended to affect populations in natural ecosystems, the registered organisms used to date already exist in nature. Monsanto Chemical Company recently announced (press conference, 10 December 1984) plans for submission of extensive data in support of a petition to EPA for an insecticidal soil organism generated by genetic engineering of *Bacillus thuringensis × Pseudomonas fluorescens*, constituting the initial experience in this area (Sun 1985).

Current toxic substance regulation also provides little insight—though considerable concern—about the potential for predicting adverse impacts if the Toxic Substances Control Act (TSCA) were to be used as the major regulatory mechanism for controlling deliberate releases of biotechnology products. The vast majority of premanufacturing notifications (PMNs) on new chemical substances, submitted under section 5 of TSCA, lack any substantive data about either chemistry (providing details for exposure assessment) or toxicity (for effects assessment) (Auer 1983). However, as described in chapter 3, it is possible to acquire the requisite data by taking a section 5(e) action. No genetically engineered organisms are presently considered as “existing chemicals in commerce” (TSCA section 4), so there is no particular data base against which data on novel organisms might be compared, further underscoring the difficulty of the problem being addressed. What data might EPA’s Office of Toxic Substances (OTS) need in order to assess a new genetically engineered product and prevent untoward exposure and adverse effects? A wide range of data suggested as pertinent has been reviewed by expert panels and is currently awaiting public comment (OSTP 1984). On the basis of material presented in chapters 4 and 5 of this issue, it is clear that new methods and improved basic knowledge in several fields will be required to provide answers to these questions.

There is an apparent dilemma regarding the development of quantitative risk assessments in the absence of adequate technology to conduct them. Risk assessments, even for conventional chemicals, do not lead to conclusions that are necessarily absolute or ultimate truths. They are conducted within the confines of what is technically possible at the time. Risk assessment methodologies are dynamic processes which must change in accordance with advances in the state of the art in associated technologies. Therefore, it is not inconsistent to expect regulatory agencies to evaluate the potential risks posed by products of genetic engineering while the tools to do so are still under development or improvement. This means that initial assessments which may be accompanied by fairly large areas of uncertainty should be performed on a case-by-case basis. As technologies are developed which improve the quality of risk assessments, these zones of uncertainty should narrow accordingly, as has been demonstrated historically for radiation, pesticides, and so forth, and assessments may eventually take on a more generic character.

The process of developing an effective and efficient assessment methodology involves more than prescribing tests and data-reporting requirements. The assessment paradigm to be used, the tests to meet information needs of such a paradigm, the criteria that might be applied to the results of such tests, and the specific manner in which risk management may interact with testing and risk assessment all are important and are therefore considered here.

The Risk Assessment Paradigm

Risk assessment of environmental impacts of new chemicals regulated under TSCA has been divided into two major components: (a) hazard assessment, in which the potential adverse impacts of the substance...
product on organisms and processes are first identified, then quantified in relation to experimental exposure; and (b) exposure assessment, in which the distribution of the substance/product is described in relation to the activities of the affected species. For a new product lacking data, hazard assessment often involves comparison of known activities of related or similar structures to those of the candidate. Exposure assessment emphasizes the fate of the chemical in the environment and the cumulative amounts which might reach people or other organisms.

These assessments must then be combined with other information to characterize the risk (NAS 1983) on at least a judgmental basis. When data on sources, rates, and so on, are adequate, a more quantitative analysis may be performed through a series of realistic scenarios anticipating situations in the environment. Risk assessments are therefore likely to differ so sufficiently from each other that they must be evaluated on a case-by-case basis.

Risk management seeks to reduce the risk to “reasonable” levels through controls on manufacture, use, and disposal, and through mitigation, monitoring, and other activities. This risk assessment process can be taken a step further, to compare risks and costs to benefits and other values to determine if the risk is or is not “unreasonable.” All of these aspects of risk assessment and risk management, as illustrated for a genetically engineered organism in Figure 1, are interactive and adaptive, evolving with technical experience and shifts in societal values. Whatever paradigm might be applied to biotechnology products deliberately released to the environment, it likely will contain most of these elements. However, the interaction of responsibilities of several federal agencies operating under different legislative mandates and executive orders may require additional considerations.

An alternative model of regulation and assessment might include some absolute notion of safety, such as the Delaney Clause of the Federal Food, Drug, and Cosmetic Act (FFDCA), which prohibits the addition of any carcinogen to feed or food. Quarantines and outright prohibitions are commonly used regulatory tools for exogenous and exotic species, whether pathogenic or not. Essentially, such models ignore any benefits and permit only “zero risk” to be the “reasonable” level of risk. Testing is relatively simple and may be limited to only the single prohibited property of the organism/agent.

FIFRA requires consideration of the “unreasonableness” of risk, and establishes “safety” by defining recommended use patterns, application rates, and methods of use of the agent based on hazard and exposure assessments. To accomplish these and develop risk management, the EPA under FIFRA and its amendments asks for very detailed data to assist in making such judgments, periodically reviews the registration, and collects monitoring data over time to determine the effectiveness of risk management with respect to both the assessment system and the candidate pesticide. Risk is rarely held to zero levels, but many candidates may be rejected because the net outcome (benefits minus risks) is negative.

Other assessment procedures consider either exposure or hazard (but usually not both), which results in establishment of standards for either specific responses to an agent or levels of that agent in specific environments. The Clean Water Act and the Clean Air Act thus largely concentrate on control technologies and waste treatment methods (retrospective and ameliorative approaches) for particular materials with demonstrated hazard. Little predictive testing is employed for exposure or hazard assessments per se, once criteria are developed for the qualifying control technologies. Concern then focuses on whether a given technology is “feasible,” “practicable,” or the “best available” to meet the criteria within economic limits.

By contrast, regulations formulated on a prospective basis—for example, developed under TSCA, FIFRA, FFDCA, RCRA (Resource Conservation and Recovery Act), and the Ocean Dumping Act—combine experience and test data to ascertain risk before a

![Figure 1. Risk assessment and risk management of genetically engineered organisms. In this model of assessment, patterned after that for toxic substances, hazard assessment is combined with exposure assessment in realistic scenarios to yield a risk assessment, which is employed in risk management. These latter activities feed back to alter methods and criteria for decisions as experience is gained in the overall assessment process.](image-url)