*Regulatory Risk Assessment: A View from the Potomac**

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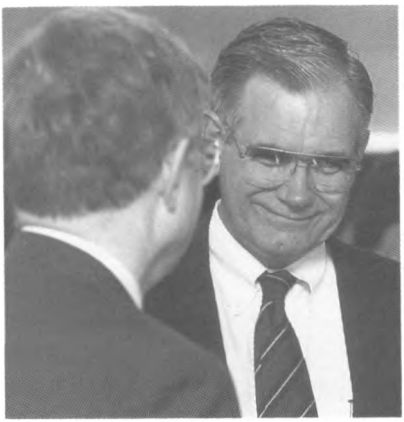

One needs to understand the history of U.S. biotechnology regulations in order to comprehend the present regulatory structure. It all began with the recombinant DNA research in the early 1970s. At that time the hazards of the research were not known and the scientific community formulated its own program for biosafety oversight, managed through the National Institutes of Health (NIH), coordinated through the Recombinant DNA Advisory Committee (RAC), and operated through a distributed network of Institutional Biosafety Committees. The NIH-RAC evolved a series of guidelines for recombinant DNA research that has become the standard for contained laboratory experimentation.

After a decade of successfully using guidelines and institutional oversight, the technology followed its normal sequence of activities leading to small-scale testing to be conducted outside of laboratory containment. Quite independently, but coincidentally, the National Research Council (NRC) published the "Redbook" (NAS, 1983) which set out a new paradigm for risk

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analysis. It is important to understand the dimensions of the NRC risk paradigm because it directly influenced subsequent policy decisions regarding the regulation of biotechnology.

PRINCIPLES OF RISK ANALYSIS

The risk paradigm provided in the "Redbook" described the process of risk analysis as being made up of:

Risk Assessment
Risk Management
Risk Communication

The sequential steps in risk assessment are: the identification of a hazard, followed by an assessment of exposure, and then risk characterization. Exposure is made up of fate and effects, when the focus of the assessment is on the environmental release of an organism. Conceptually taken together the identification of a hazard *times* the exposure is the characterization of a risk, or:

Risk Characterization = Hazard x Exposure,
when
Exposure = Fate x Effects

Risk assessment should be conducted with a sound scientific basis and use inferences as appropriate.

Risk management is the process of determining what to do about a characterized risk. This includes risk prevention, as well as the identification, selection and use of mitigating measures to reduce risk. Environmental risk management considerations often include social, economic and political judgements. The process of risk management should be institutionally separated from risk assessment.

Risk communication is an interactive process that promotes the exchange of information and opinions about risk among individuals, groups and institutions. This process should include providing access for stakeholders, or participation by and appreciation of public perceptions of risks.

THE FEDERAL COORDINATED FRAMEWORK

As the process of biotechnology research approached small-scale testing outside of contained laboratories, the Executive Branch of the Federal government began extensive discussions on how to coordinate regulatory activities to assure adequate protection of public health and the environment *vis-a-vis* biotechnology (ca. 1984). One of the foundations of the Federal Coordinated Framework for Regulation of Biotechnology (OSTP, 1986) is that the regulatory decision should be risk-based, and thus was set in motion the process of applying the "Redbook's" principles for risk analysis.

The first step in risk analysis is the identification of a hazard. It was clearly evident to the Federal Coordinated Framework policymakers that not all biotechnology represented a hazard. For instance, the application of somaclonal variation to crop improvement was definitely biotechnology, but it did not represent an unusual hazard. Additionally, some activities in recombinant DNA biotechnology were accepted as no, low or reasonable risk, and therefore these were not prime candidates for regulation.

What was identified was the fact that some *products* of biotechnology may represent an unusual hazard. Thus, these products should be the subject of risk assessment and regulation. It was therefore asserted that the products of biotechnology, not the process, should be the focus of Federal biotechnology regulation.

Risk assessment should be conducted with a sound scientific basis and use inferences as appropriate.

This distinction eventually became misconstrued by a few zealots of the Federal Coordinated Framework for Regulation of Biotechnology. They took the principle one step further, in an inept attempt to obliterate the distinction between conventional methods and the new biotechnologies. A terminology mind-game reminiscent of the popular book *1984* (Orwell, 1949), dominated Federal regulatory terminology during the Bush Administration. The use of common scientific terms like "genetically modified organisms," "transgenic" and "genetically engineered," was forbidden in regulatory language. As policy was derived from the Federal Coordinated Framework, some creative terminology had to be invented by technical editors (e.g.,"deliberately modified hereditary traits") to comply with these policies.

Another primary principle of the Federal Coordinated Framework was that there would be no new laws. This principle was derived from the assumption that existing statutory authorities were sufficient for Federal regulatory agencies to regulate the products of biotechnology. In the beginning this made a lot of sense. The first applications of biotechnology were emerging as pharmaceuticals and drugs, and this industry had long been regulated. Thus, there was considerable resistance on the part of the drug industry to biotechnology regulation *per se,* inasmuch as the existing regulatory structure seemed clearly sufficient.

This was not however the case for much of the rest of the applications of biotechnology, especially in agriculture. Much of the agriculture research enterprise had never been regulated, and existing authorities to deal with clearly identified special threats (such as plant pests; pesticides; toxic substances; animal viruses, serums and toxins; meat and poultry inspections; and food additives) stretched this eclectic collection of authorities over the domain of agricultural biotechnology. This became a challenge that has

pretty much been met successfully. This success was achieved through the promulgation of new regulations under existing legislative authorities, individual efforts and a commendable level of interagency coordination to get the job done.

In spite of the extraordinary efforts to make the Federal Coordinated Framework fit the structure of agricultural biotechnology, some gaps and overlaps still exist. For example, it is still not clear how transgenic fish will be regulated, either in the research stage or as commercial products. U.S. Federal authority for the regulation of aquatic species is yet to be resolved, and as a consequence there is no existing statutory authority for fish and shellfish biotechnology products. Similar situations exist for non-pest insects, amphibians, reptiles, plants that have been transformed with sequences not from plant pests, and non-pest and non-pesticidal microorganisms when the research has no commercial intent (e.g., some types of university research with rhizobium). Moreover, the final promulgation of the Environmental Protection Agency (EPA) authorities under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA) has yet to take place.

If the regulation of biotechnology is to be risk-based, a clear and general agreement on what constitutes a hazard needs to be reached.

Given the above considerations some have called it remarkable that the Federal Coordinated Framework has been so successful for agricultural biotechnology regulation. A lot of the credit for this success goes to a few people in the Federal regulatory agencies that have given extraordinary effort to make it succeed.

THE NEXT GENERATION

As the technology progresses through its normal sequence, many of the products of agricultural biotechnology are ready for larger-scale performance testing, pre-commercial evaluations and eventual commercialization. As a consequence there are considerations that go beyond small-plot testing during these subsequent stages of product development that will place further strain on the processes of the Federal Coordinated Framework. Certainly the experiences and knowledge gained from small-scale testing can be used to better predict performance in larger-scale testing and commercial use, but not everything is directly translatable. The identification of the hazards of large-scale testing, the consideration of exposure, the numerics of large populations, and the probability values for fate will all take on new dimensions in large-scale tests. The question now being asked is: Is the Federal Coordinated Framework for Regulation of Biotechnology fully adequate to address today's and tomorrow's questions regarding the risks of biotechnology?

As the question on the Federal Coordinated Framework's adequacy is asked, is this the time to revisit the fundamental principles upon which it rests?

The regulatory issue of product versus process is not truly a settled issue, at least in the minds of many. The process of biotechnology and the transforming of organisms with foreign DNA represents to many an identified hazard requiring risk analysis. This perspective is no doubt related to the U.S. Food and Drug Administration's (FDA) May 1992 request for more public comment on its policy regarding the labeling of foods derived from new plant varieties. The FDA wants to know:

—Should all foods derived from new plant varieties developed using "genetic engineering" techniques be required to be labeled as such?
—Should labeling the source of introduced DNA be required?
—Under what circumstances is ingredient labeling appropriate?
—How can required labeling for food allergies be accomplished?
—What are the practical difficulties and economic impacts of labeling "genetically engineered" foods?

Clearly the regulatory issue of hazard identification for biotechnology is not resolved. Different perspectives on what constitutes a hazard complicates the development of a consensus. Without completing the first step of risk assessment, the application of scientific objectivity to the rest of the process will not be sufficient for those with opposing views.

WHAT IS NEEDED?

If the regulation of biotechnology is to be risk-based, a clear and general agreement on what constitutes a hazard needs to be reached. This involves reconciliation of the different views of the world where commercial interests advise the use of marketplace determinants; regulators prefer the use of a hierarchial, authoritative decision-making process; scientists assert the need for a rational process; and those concerned for the environment wish to apply a natural standard to the identification of a hazard.

Adding further complication is how different standards of objectivity are judged. Scientific objectivity is based on standardized techniques which permit experimental reproducibility. Social inquiry studies are considered objective if devoid of personal bias. Legal proceedings are considered objective if the participants adhere to the principle of disinterestedness. A lawyer would hardly view a scientist as objective if the scientist has an interest in that brand of science. Conversely, a scientist would accuse the lawyer of being subjective if the judgements were not truly reproducible. Social scientists share similar concerns for jurisprudence and biological science as they do not see them as necessarily free of personal bias. Who then is to provide objective judgements for biotechnology regulation?

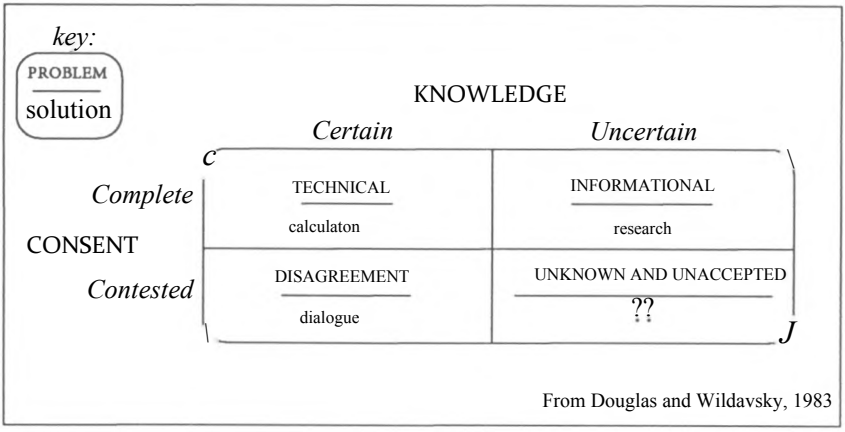
Until we can resolve the issues of what constitutes a biotechnology hazard and who will make the objective judgements, it is not very likely that a consensus will emerge on how to proceed.

CONSENSUS BUILDING

Figure 1, taken from Douglas and Wildavsky (1983) presents the four problems of consensus building in risk analysis. In each of the four cells there is represented a risk problem, and a proposed solution. The dimensions of the block are knowledge and consent. In the upper left cell knowledge is certain and consent is complete. If there is a technical problem, it is merely a matter of making a calculation to derive a solution.

In other circumstances knowledge is uncertain, although consent is complete (upper right cell). In these situations the problem is not enough

FIGURE X



From Douglas and Wildavsky, 1983

information and the indicated solution is to conduct risk assessment research to resolve the problem. This is the approach that the U.S. Department of Agriculture (USDA) has implemented through Section 1668 of the 1990 Farm Bill. The USDA sets aside 1.0 percent of its biotechnology research outlays to conduct risk assessment research to fill knowledge gaps. This year the Department will award competitively $1.7 million for risk assessment research projects to help facilitate science-based, regulatory decision-making.

In those cases where knowledge is certain, but consent is contested, the problem becomes one of disagreement and the solution is dialogue (lower left cell). The role of organizations such as the National Agricultural Biotechnology Council (NABC) is very important in this type of circumstance. Through public dialogue, understanding can be built on existing, certain knowledge and perspectives of divergent views being more clearly understood.

It is the fourth cell (lower right cell) that represents the most difficult situation. In this case knowledge is uncertain *and* consent is contested. Presently, there is not a good solution for this type of situation. Clearly dialogue would be desirable. And more research might help resolve the unknown. But bringing together the information and divergent views for problem resolution represents one of the most tricky responsibilities facing science, government, public and private institutions, and the concerned public.

WHAT IS BEING DONE?

Discussions are now underway as to the adequacy of the Federal Coordinating Framework for Regulation of Biotechnology. As research discoveries progress along the path to commercialization, closing the information gaps, eliminating unnecessary duplication, and deregulating technologies known to be safe seem to be important items for our national agenda. Some of these changes can be seen with the recent implementation of an Animal and Plant Health Inspection Service (APHIS) notification and petition process for plant biotechnology regulation under the Plant Pest Act authority.

Also, the USDA's Marketing and Inspection Service is meeting with the FDA to coordinate new regulations for meat and poultry biotechnology and to close the gap for fish and shellfish. This latter gap may however require new legislation and this would represent a departure from a major principle embedded in the Federal Coordinated Framework. Other existing regulatory gaps may require similar gap-filling legislation.

There is clearly a need for more biosafety information exchange, both nationally and internationally.

There is clearly a need for more biosafety information exchange, both nationally and internationally. The Stockholm Environmental Institute recently established a free advisory service for Third World countries wishing an evaluation of the safety of field tests with genetically modified organisms. U.N. agencies are now looking at their role in information support systems for biotechnology on a global basis. The Organization of Economic Cooperation and Development is continuing to provide international leadership on the principles of biotechnology regulation and safety, and the European Economic Committee is working with the U.S. government to coordinate research and regulatory activities.

A major issue in these efforts is the extent to which the U.S. scientific community can and should become involved in the international exchange of information. If biotechnology is expected to be a major advantage in U.S. competitiveness in global markets, how much information should the U.S. share, given the advantage of a technological lead? Opportunities to collaborate in biotechnology risk assessment, biosafety data exchange, and regulatory

practices seem to be obvious areas for international collaboration for mutual benefit. But to be successful, greater organizational and financial support for such international collaboration is needed.

There is a clear need for national educational programs in biotechnology that would organize factual information to be shared with the interested public, both youth and adult. The USDA's National Biological Impact Assessment Program is sponsoring a pilot project with the University of California,Davis, targeting school-age children with teaching materials on the scientific principles of biotechnology. The Agricultural Research Institute is looking for partners to assist in the development of a biotechnology educational program focused on adults. These are but two examples of what has been started in biotechnology public education.

Finally, there is a need for more national biotechnology dialogue, as there is not so much the absence of factual knowledge, but clearly different views on values, standards and preferences. NABC should continue to play an important role by providing a forum for continued biotechnology dialogue that will hopefully diminish disagreements and build toward a consensus on a national direction for agricultural biotechnology.

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