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Commercial Biotechnology: Technological Risks and Management

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Content

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1. Introduction

For the past two decades, new technologies of genetic engineering, such as "recombinant DNA (r-DNA)" for micro-organisms and "cell fusion" for hybridomas and "monoclonal antibodies" for higher organisms, have been progressed more rapidly than anticipated. The short time lag between basic research and quick commercialization was called a specific attention to industrial policy for developing bio-industry as one of the key high-tech industries as well as to an urgent necessity for some kind of regulation before products are widely distributed in the market. By virtue of its technological nature, biotechnology hold a great potential, not only for contributing to solving many of world major problems such as health, foods and energy, at the same time, it could bring catastrophic bio-hazards to human and natural ecosystem.

The commercial application of biotechnology is to link the new genetic engineering principles or techniques with traditional industrial technologies to meet the social demands for goods or services either in short supply or with no inexpensive substitutes. It, therefore, requires a systematic procedure to join an innovative framework of new scientific practices with a mature system of conventional technologies that provide the basic environment for commercialization as illustrated in Table 1.

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Whatever cautious regulations for the genetic researches might be implemented in research laboratory, there are many other sources of technological hazards involved in the commercialization. From our definition of commercial biotechnology, three categories of risk problems will logically follow:

i) risks from new technology,
ii) risks from traditional technology,
iii) risks from a combination of new and traditional technologies.

Those are, firstly, risks from the newly emerging technology of genetic engineering, secondly risks from conventional technological development such as bio-processing, refine chemical and fermentation processing, and thirdly risks from the combined systems technology of integration and management in new and traditional technologies. The scientific glory of gene-splicing has sometime made scientists forget refining, purifying and recycling processes supported by computer, new materials and other types of high technologies. The last risk issue involves; (1) human factors in the operation and management of complex systems, and (2) institutional factors in regulatory procedures.

In this paper, we examine risk problems associated with commercial applications of biotechnology with the goals of identifying a systematic way of managing hazards of this newly emerging technology. Our objectives are:

(1) to identify the particular risk issues posed by integration of new scientific knowledge and mature traditional technologies,
(2) to examine the past debates over biotechnology risks on the basis of the identified "structural characteridtics" of biotechnology risks at the stages of its commecialization,
(3) to compare commercial biotechnology with "nuclear power technology" for potential insight into potential societal reponse, and imoproving approaches for technological risk management.

Since then, various risk issues of specific types of experiments beyond the small scale of experiments in laboratory and on the environmental release of the bio-products of genetically altered organisms have been debated. The debates inevitably include ethical and cultural problems for the life sciences and for the public perceptions on potential biohazards. In addition, the debates also affect the economical and political dimensions of industrial competitions in world market, as well as foods and energy problems in the developing countries.

- Risks from Traditional Technology -

A typical modern production system of phermaseutical bio-products consists of fermentation process in which genetic engineering techniques are applied, and other processes of chemical modification, refinement, and sterilization. These processes use a variety of chemical solvents, gases and water particularly in refine, purifying and recycling processes. Such processes are subject to fire and explosion hazards, of runway reactions, and of exposure to toxic solvents. Accidents or unsteady operations with less human control can be always happened in emergency situations.

The primal group at risk is operators who have not been trained as scientists or technicians. Spills, leaks, and exhaust gases containing engineered microorganisms or their components are the potential sources of occupational health and risks. The secondary impacts of the escaped materials of various toxic chemicals out of normal operation would be long-term or chronic pollution to residents or ecosystems in neighborhood through underground contamination or air transportation. A typical example is found in Silicon Valley of California where industries disposed variety of toxic chemicals and metals to the environment emerging from refining and washing semiconductor wafer and integrated circuits (Siegel & Markoff 1985).

- Risks from the Combination of New and Traditional Technologies -

Most serious biohazards involved in commercial application of biotechnology are likely to arise from the combined technology. This stage of technological development includes not only risk issues from new technology under large scale operation but also, more importantly, risks from system and institutional failures.

Can management or control of future bio-reactors or bio-breeders in commercial use be safe enough not to produce unintentional new organisms or not to disperse new organisms accidentally? Or can a system of purification, recycling or waste treatment processes be operated without significant failures of emitting their by-products or wastes out of their containment boundary ? Can a current system of occupational regulation adequately protect workers in future biotech-factory from invisible toxic, allergenic or infectious health impacts ? Finally, can a current industrial policy of maintaining strong competitive position in the world market be fairly compromised with long-term objectives of safety, health and global environmental preservation ? Those are some of the questions which we have to cope with in integrating new genetic engineering into the traditional engineering technology as well as in managing a system of large scale process involving human judgment.

In addition, in the phases of mass-consumption and recycle of wasted products, we might face much more complex issues of societal management of supply and demand in terms of the socio-economic distribution of benefits and

damages. Agricultural and environmental applications of commercial biotechnology raise very complicate issues of beneficiaries and losers in terms of resource conservation unless adequate institutional and regulatory frameworks exist at the national and international levels.

- Risk Characteristics of Commercial Biotechnology -

The commercialization of biotechnology consists of following phases:

i) research and experiments in laboratory,
ii) large-scale-experiments in quasi-open system or controlled natural environments,
iii) commercial production in large scale and distribution in markets,
iv) mass consumption and recycle of wasted bio-products.

Table 2 shows a summary of discussion to characterize the important factors of risk sources associated with our definition of commercial applications of biotechnology at each development stage of commercialization. Thus, we can define the nature of risks from the combination of three types of technologies as follows:

(1) scientific and disciplinary failures
(2) engineering and occupational health failures
(3) systems and institutional failures.

Each stage is related to the risks characterized in the former section. For example, the stages of i) and ii) may have "scientific and disciplinary failures" in regulating scientific ethics and social responsibility, and stages of iii) and iv) may produce catastrophic accidents via "a systems failure" where main causes could arise from human failure of management in the integration of new and conventional technology.

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3. Biotechnology Risk Debates

Debates on Scientific and Disciplinary Risks

Prior to the NIH guidelines (1976). Assisted by a relatively small academic community at an early stage of development, the mainstream of the life sciences succeeded in attaining an early consensus over risks within their disciplines (the NIH guidelines, 1976). There was also a political objective of defending their interests of protecting molecular and bio-medical researches by adopting a cautious self-regulation, or moratorium, on certain types of risky experiments (Wright 1985).

When they faced public disputes on the r-DNA researches at academic communities, such as Cambridge, Massachusetts, San Diego, California, Ann Arbor, Michigan (Krimsky 1979, Jackson & Stich 1979), the disputes never spread out of the control of the NIH guidelines. Since biotechnology research and development has required a high degree of public research funds, this voluntary self-regulation has maintained a strong discipline in the whole life science arena, including research at private firms. The inclusion of the conflict within the biological disciplines in the Recombinant DNA Advisory Committee (RAC) under the NIH also seems to have succeeded in maintaining trustworthy character.

Worst-case-scenarios. One of difficulties that the early disputants faced was estimating the likelihood of events that leading to a serious epidemic. The key events would be:

1) pathogenic bacteria must be synthesized : P_1
2) the engineered bacteria must escape from the laboratory : P_2,
3) the strain must be viable in nature : P_3,
4) the strain must compete with other micro-organisms: P_4.

If the total likelihood of the potential epidemic is the products of each independent likelihood (frequency) $P_t=P_1P_2P_3P_4$, the problem is a typical case of the "very low probability/high catastrophic hazard". A British genetic scientist R. Holliday (New Scientist, 1977) estimated the probability that led to epidemics such as death by infection (C_1) or an epidemic (C_2) based on a worst-case-scenario in which one careless spilling of genetically engineered bacteria in a laboratory, that had latent virus genomes of causing oncogenic, on hands or clothes and that would lead up to a cancer would be: C_1 (death by infection) = 10^{-11} and C_2 (epidemic) = 10^{-13}. These figures are extremely low in terms of an incident per numbers of experiments. It should be stressed, however, that there are no adequate data for the r-DNA experiments from which we can draw legitimate estimates for either objective or subjective probability. And, of course, the estimates did not address "intentional release scenarios or sabotage".

The great uncertainties remaining in estimating these frequencies of worst events initiated a kind of risk assessment by the NIH in the early 1980s to confirm the adequacy of biological and physical containment. The outcomes of the worst-case-scenarios (cloning tumor virus DNA into the strain of E. coli K12 by means of the so-called "shot gun" technique and introduction of the organisms into mice cells) were reported to prove that disarmed or domesticated E. coli K12 is safety enough under the current system of containment, but "may be somewhat more ecological fit than had been anticipated" (Levin, 1984). These empirical studies of risk assessment based on worst-case-scenarios and given the fact that no apparent infectious and epidemic episode has occurred since 1976, resulted in a series of relaxation

epidemic episode has occurred since 1976, resulted in a series of relaxation of biological and physical containments (R-DNA Bull).

Risk Assessment for Environmental Release. As far as the risk assessment of the environmental release of genetically engineered organisms is concerned, deeper gaps of risks perception are found between mainstream of the life sciences, and the microbial and ecological sciences. The OTA model of risk assessment (1984) consists of the following five phases:

1) formation: creation of a novel genetically altered micro-organism.
2) release: deliberate or accidental release into the environment.
3) proliferation: multiplication, growth, transport, modification, and die-off with possible transfer of genes to other organisms.
4) establishment: survival, formation of niche with possible colonization of humans or other biota.
5) effect: human or ecological impacts due to ecological interaction with some host or environmental factors.

Recent scientific disputes have shown a polarization of expert judgments between molecular scientists and ecological scientists on these matters (Science 1987). During the period between 1984 and 1986, the U.S. regulatory agencies of the NIH (RAC), USDA and EPA approved at least eight applications of the experimental release of the genetically altered microorganisms. Most were microbial pesticides for mitigating frost damage or insect damage. When one of environmental critics, the Foundation of Economic Trend (Mr. Jeremy Rifkin) challenged some of the approvals by the NIH and EPA, the District of Columbia Court ruled that an environmental impact assessment was needed for approval, and granted a temporary injunction to stop the experiment until the environmental impact assessment was completed (Science 1984).

Although the experiments were eventually conducted later in 1986 or 1987, the court decisions (the District of Columbia Court in 1984, and the Appeal Court in 1985) shook the cautious EPA's attitude toward development of the regulatory policy and procedures on the environmental release of the genetically engineered microorganisms. The current EPA attitude for screening environmental applications is to concentrate on environmental effects, including methodology for estimating fate and effects of engineered microbes, and to adopt a case-by-case approach for evaluating the environmental release of the genetically engineered organisms (Levin et al 1987). There has been several suggestions with respect to the applicability of existing risk assessment techniques developed for toxic chemical materials to the assessment of genetically altered microorganisms, most reports have acknowledged the lack of suitable methodologies to address the environmental release problems (OTA forthcoming, OECD 1986). Table 3 displays the important differences of disciplinary judgment between molecular scientists and ecological scientists that appeared in major scientific journals.

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Containment System The principal way of controlling the "biohazard potentials" from r-DNA experiments has been "a system of biological and physical containment" which limits the risk of genetically engineered organisms escaping to the environment. The objectives of biological containment are to minimize survival of host organisms outside laboratory and to minimize the transfer of the genetic materials in the laboratory hosts to non-laboratory hosts. In another words, "domesticated" or "disarmed" bacteria and plasmids (DNA moleculars) are used that are unlikely to perform essential biological functions of growth or transfer DNA to other cells outside laboratory conditions. Escherichia Coli (E. Coli. K12) is most commonly used for that biological containment. For example, for a biological containment of "host-vector" system, the guidelines defined three levels of containment: EK1, EK2, and EK3 refereeing to the biological nature of the E. Coli K12. The physical containment defines a level of equipments and practices that provide physical barriers to preventing the escape of the microorganisms from the experimental facility. This containment is classified into four levels: P1, P2, P3 and P4, ranging from the use of standard good microbial practices (P1) to requirement of the highest containment facility (P4) which exists at only a few facilities in the U.S. and only one in Japan by the end of 1986. For example, some risky experiment ("shot gun") would be allowed under the "EK2 - P4" containment level. A decade of regulatory experience shows that about eighty per cent of the proposed experiments to the NIH is now covered by Class I, which are exempt for pre-approval under current guidelines.

Safety Requirements for Industrial Applications. The applicability of this "system of containment" to the commercialization of biotechnology has been questioned on a number of grounds. McGrarity points out four major reasons for different risk considerations to be taken into consideration with regard to "large-scale-release" biotechnology versus "small-scale" biotechnology in laboratory (1985):

a) less human control
b) less effective power of biological containment in the environment
c) difficulties in assessing human and environmental risks
d) conflicting benefits and damages in distributional levels

Safety requirements for commercial biotechnology, thus, needs a different perspective of potential biohazards, according to laboratory or process scale, as well as to the levels of combination of new and traditional technologies. The 1986 OECD report on "Recombinant DNA Safety Considerations", after a two-year controversy in an ad hoc expert committee, summarizes a range of scientific considerations to be taken into account for large scale applications of r-DNA techniques such as i) safe handling of bulk quantity of the microorganisms and ii) safety of biologically active products.

The fundamental controlling way of handling these safety considerations in industrial applications uses the same method of "a system of biological and physical containment" as is used in laboratory research, but in a different context. They propose the concept of "Good Industrial Large Scale Practice (GILSP)" for organisms that may be handled at a minimal level of containment, together with the established safe operation practices used in the traditional fermentation processes. The concept of "GILSP" reflects industry's view on "least and no additional cost" for the majority of industrial applications that use the authorized non-pathogenic microorganisms.

Japanese regulation on industrial application, it might be noted, relies heavily on this concept of "GILSP". At the end of 1986, the Japanese Ministry of International Trade and Industry (MITI) gave the prior approvals to over fifty applications by "GILSP" for production of diagnostic medicals or "amino acids", and one application for production of ensyme with requirement of a bit more severe physical containment of the closed production process than of a semi-closed production processes for "GILSP" (Japan EA 1987).

An early attempt to address the occupational risk problems was made by the National Institute for Occupational Safety and Health (NIOSH). It identified potential occupational hazards from different sources: microbial, products, and reagents (Landrigan, R-DNA Bull.,1982). As the major defense against the first two hazards, the report relied primarily on the "system of biological and physical containment", but did not elaborate the reagent (solvent, waste waters, etc.) hazards simply because of the applicability of occupational standards for pharmaceutical and fermentation industries. It, however, strongly recommended the medical surveillance of workers in biotech-firms in view of the currently lack of data and information concerning long-term or chronic "allergenic" or "oncogenic" impacts by genetically engineered microorganisms.

Table 4 lists regulatory options in terms of our three categories of biotechnology risks. As far as the scientific and disciplinary risks are concerned, some of the options such as "partial moratorium", "voluntary self-regulation" have been partly used, and some haven't. So far, the U.S. is the first country that has initiated and pioneered most regulatory options in disciplinary risk issues. However, regulatory options for the other risk areas of "engineering and occupational" and "systems and institutional" issues have not been fully addressed yet, since industrial development is still at a very early stage.

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Debates on Systems and Institutional Risks"

Given the current scientific knowledge of potential risk factors in commercial biotechnology and the regulatory options that exist for mitigating these risks, are we really able to cope with the three types of biotechnology risk issues by regulatory options currently identified in Table 4 ? Or do we have to wait for the infant industry to grow into larger industrial conglomerates in order to obtain enough data and informations on potential biohazards ? And if delay is chosen, have we taken the same route as the risk management of hazardous chemicals produced by the "petro-chemical industry", missing a rare opportunity to implement effective preventive options (Commoner 1987) before they occur. These questions lead to a set of important risk issues of relating to "systems and institutional failures".

Scientists Views on Commercial Biotechnology A disciplinary safety consensus, that the r-DNA research imposes no risks to the public greater than those arising from traditional microbiology researches (unless the NIH guidelines are to be challenged), has now been disseminated throughout the wider academic communities and in public administration. The potentials of promising benefits from commercial application of biotechnology, widely recognized over recent years, has accelerated the credibility of the "disciplinary consensus"

and "voluntary but quasi-public regulation" of the NIH guidelines. Discussing the health, safety, and environmental regulation of commercial biotechnology, the U.S. OTA (1984) acknowledged this "safety consensus" in the U.S., and admitted that the U.S. guidelines and regulation on r-DNA research are the least restrictive in any of the competitor countries. So far Japan has been reluctant to approve the environmental release of genetically engineered microorganisms unless a number of uncertainties are resolved (Ito 1985), and West Germany is preparing further strict regulation for the environmental release issue (Nature, v.325, 474, 1987).

Recent study on risk perception among the U.S. leadership groups in science policy revealed that "the majority of leaders in science policy favor the encouragement of r-DNA work" (see Table 5, Miller 1985). However, a more important conclusion drawn from the report was that, despite a broad acceptance of the present regulatory structure (the NIH guidelines), most leaders did not feel very well informed about r-DNA and its principal terms other than the professional people in biological sciences. Nearly half of the leaders of either social science or environmental groups responded that they were not very well informed about the conduct of experiments involving genetic engineering. The positive responses in science policy, environmental, and religious leaders of "well informed" were 24 %, 6 %, and 21 %, respectivel.

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Regulators Views on Process versus Product Hazards. The institutional structure of the U.S. regulation for approval of biotechnology products is now defined by the so-called "Coordinate Framework". There are three major federal agencies involved in regulating biotechnology products: The Food and Drug Administration (FDA), The Department of Agriculture (USDA), and The Environmental Protection Agency (EPA). The NIH and the NSF are also included in research policy problems.

The most remarkable difference in approach among regulatory agencies is apparent in the issue of "product-based" control versus "process-based" control of biotechnology products. It highlights the different view of risk perception relating to the content of risk nature of genetically engineered organisms in our natural environment. The FDA and USDA have a strong position that the regulation of genetically engineered organisms does not present significant and unusual problems and should be addressed by traditional scientific and regulatory principle, whereby the products are evaluated on their own merit and not by the method by which they are produced.

By contrast, EPA has taken the position that the genetically engineered organisms would be "pesticides" or "new chemical substances" that are regulated under the "Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) or "Toxic Substances Control Act (TSCA). The former (FIFRA) requires a premarketing clearance procedure under which the EPA review the pesticide's safety. The latter (TSCA) authorizes the EPA not only to acquire information on "chemical substances" in order to identify potential hazards, but also to regulate "production, distribution, use, and disposal" of the chemical substances if they can present an unreasonable risk of injury to health or the environment or could result in substantial human or environmental exposure.

Which of these views on regulating biotechnology products should prevail was one of the important policy issue at the Coordinate Framework. The EPA's

view of designation of genetically engineered microorganism as "pesticides" or "toxic chemical substances" has been criticized by the main stream of life sciences, primarily because of the restrictive and heavy burden on the young industry and life science researchers.

Developers Views on Liability versus Regulation Cost. The liability problem facing by the start-up genetic engineering companies is possibly far larger problem than that had faced by nuclear utility companies when they started for commercial power plant. Recent move of the court decisions toward "strict liability" for the failure of products safety could impose a tremendous insurance cost to the young industries unless some remedy measures are given by public regulation (Nature v.310, 527, 1984). Any accidents due to the r-DNA research and genetically engineered products are likely to be covered by this concept (Dworkin 1979). Despite the strong advocate by biotechnology industry claiming that "these genetic processes should be seen as alternative manufacturing methods" and "risk analysis should focus on the end products rather than on the processes" (Hardy and Glass 1985), many small biotechnology companies have got troubles to obtain insurance at reasonable cost (Nature, v.324, 295, 1986).

Conversely, it might be noted, the young start-up companies need a kind of public intervention in regulating possible risks in terms both of capital and of products failures. Any governmental decision to regulate biotechnology products or production process by genetic engineering techniques would include a decision how far the public has to shoulder some of this liability issue (Robbins, geneWATCH, 1984). As is claimed by the young industry for keeping a strategic position in world market, it would be a matter of public policy decision that whether the society should bear the costs for the unique risk regulation (management) that there has been no proven hazards or accidents so far in the start-up industry for the sake of avoiding "extremely low but catastrophic hazards" (Hardy and Grass 1986).

Public Views on Environmental release of "Frostban". In April, 1987, the first experimental release of a genetically engineered microorganism was conducted after long disputes among various public organizations and environmental groups at a strawberry patch in northern Salinas Valley, Monterey county of California. It provides the first example of how regulatory agencies have actually dealt with the various uncertain risk issues, and how local community responded to the experiment of the environmental release of new organisms.

In 1984, the experiment was first proposed by the Advanced Genetic Sciences (AGS), a venture firm based on Connecticut, to produce and market a "Ice Nucleation Inactive (INA -)" bacteria by genetic engineering techniques to reduce frost damage to agricultural products. The biotechnology product, called "Frostban", is a mixture of two variants of "pseudononas" that has uncertain pathogenicity to certain types of plants. After initial approval by the EPA in November, 1985, a series of complicated disputes were occurred among various federal regulatory agencies (EPA, FDA, and NIH or RAC), state agency (California Department of Food and Agriculture (CDFA), local government of Monterey County (MC), environmental interest groups (e. g. the Foundation of Economic Trend (FET)), the local community.

Four distinct types of risk that each regulatory agency and concerned group looked for in the problem identification phase : plant pathogenicity by the CDFA, weather alternation by the EPA, ecosystem disruption by the MC, and interference to natural evolution by the FET. Their assessments were conducted separately, lacking consensus among organizations, and ended up by

each writing the worst-case-scenario of its principal concern. The response of the local community was fairly reflected by the MC's concerns on ecosystem disruption. However, many public opponents of the Monterey County did not share the environmental group's view (FET) of opposing human interference to natural evolution and selection. Rather, the general public acted to assure that "due process was taken in regard to the evaluation of risks from the first test in the U.S." (Nimon 1987). The developer, AGS, was not viewed as trustworthy because of its reluctance to disclose information. In fact, the AGS did conduct indoor greenhouse experiments without compliance with legal requirement, and was fined by the EPA for "falsification of data".

The final decision by the local community (the MC) was a "one year moratorium" on the planned experiment to seek a further safety evidence. But, eventually, public opposition eased by that time, since they have no legal power to prevent such authorized experiment by federal and state regulatory agencies. This case, however, indicates that, despite of long disputes over the environmental release of novel organisms, actual public concerns and risk communication among concerned groups in local level may be still at a low stage of development.

4. Concluding Notes : A Comparison of Biotechnology and Nuclear Power Technology

Past scientific and technological debates over these risk issues are examined to explore the current state of risk perceptions, assessment, and regulation to cope with a set of important but uncertain risk issues of "low probability/catastrophic hazard". A number of observers have noted parallels between the risk management issues posed by "nuclear power" and "biotechnology" (Slovic et al 1985, Edward and Von Winterfeldt 1984, Morone and Woodhouse 1986). Here, we discuss this question, exploring both the similarities and dissimilarities and their broader societal implications.

Nature of the Risks.

In the early stages of commercialization of these technologies, several similar characteristics of risks are quite striking. First, although a variety of hazards is present, it is the potential of low probability/catastrophic hazards (uncontrollable epidemic or radiation) that is global in scope that concerns both risk assessors and the public. The extraordinary actions taken disciplinary by the scientific community at the Asilomar Conference, and in the subsequent NIH guidelines. It is instructive to recall that nuclear power, in light of its enormous destructive uses at Hiroshima and Nagasaki, also produced extraordinary actions by the scientists involved in the origins of nuclear energy. Thus, there were early concerns in the late 1940s to bring nuclear energy under international control and to ensure that the technology would be used for peaceful purposes.

Over time, it has become apparent that the very rare quality of major nuclear power plant accidents, and international diversion of nuclear materials, makes definition of the probabilities intrinsically impossible to estimate, or to gain scientific consensus on the numbers. It is already apparent that, despite the very low probabilities estimated for a catastrophic accident at the scientific stage of biotechnology research, that biotechnology is likely to experience the same continuing debate over the likelihood of catastrophic risk scenarios. This is the case, in part, because of the impossibility of achieving, and assuring, completeness (i.e., that all accident scenarios have been identified and considered).

Both biotechnology and nuclear power, despite the global hazard potential, entered the commercialization phase while the technology was still at the forefront of scientific knowledge. This reality ensures that large scientific uncertainties will be present -- it could not be otherwise. In such setting, disagreement among scientists are likely, in particular, life scientists in much broader disciplines. Both technologies have shown, in their early stages, attempts to eliminate the risk issue by achieving consensus among the scientists most intimately involved. This has led to optimistic estimations of risk by sponsoring scientists (e.g., survival of a novel genetically engineered microorganism, that could lead to an unknown epidemic, or melt-down of nuclear power plant were judged "incredible" for much of the the early history by molecular scientists or by nuclear power engineers). In the case of nuclear power, these estimates tend to be buttressed by an initial period of accident-free operation. Then, after all, when faced accidents or environmental problems, the scientific consensus unravels. This happened with nuclear power and there is no reason to deny that it could be likely for biotechnology.

Institutional Structure and Risk Management.

The nature of nuclear power as a complex and expensive technology, and its links with power politics of nuclear weapons, has made it a difficult technology in which to manage risks in an well defined institutional setting. In the U.S., the institutional convergence of technology sponsorship, policy-making, destructive and peaceful uses, and regulation led to basic reforms during 1970s. Biotechnology may well prove equally difficult for risk management, for both similar and different reasons. In its early stages, biotechnology has shown an extraordinary degree of institutional convergence, joining disparate institutions -- industry, government, universities, science -- who share common powerful economic and academic incentives. This convergence has been facilitated and reinforced by a growing concerns over economic competitiveness for development of high technologies. Like nuclear power in its first stages of scientific research and technological development, genetic engineering has successfully secured a high degree of risk self-regulation.

On the other hand, unlike nuclear power, biotechnology has an industrial structure characterized by decentralization, small companies, venture capital, and short planning horizons. It is exactly the type of industrial structure that led to new types of occupational health and environmental pollution problems at Silicon Valley of high technology industry. Despite a great potential of innovation, where companies are small, return on investment quick, and profits of the high-risk type, risk assessment tends to be undervalued and investment in risk management meager. Many of these companies either go out of business or reap large profits before risk failures catch up with them. Product liability at the stage of mass consumption or non-fault liability for wastes management could lead to another difficult issues in risk management.

Public Concerns.

Both nuclear power and biotechnology touch deep public concerns over the nature of the universe, the role of human intervention, and potential harm to future generations. The splitting of the atom involved changes in a fundamental building block of physical world; genetic engineering manipulates a basic building block of the biological world. Properly, the public, while recognizing the enormous benefit, inevitably has a great unease about the hazard. The early establishment of safety consensus within life sciences has successfully mitigated public fears of unknown epidemic or creation of novel pathogenic organisms, at least, at the research and development stages in laboratory, but not at the stages of large-scale-production or release of the organisms in natural environment and ecosystem. As far as "engineering and occupational" and "systems and institutional" risk issues are concerned, there exit a broad array of risk sources and large scientific uncertainties that surround these risks. In this context, it is almost certain that the concerns will prove difficult to remove and, should serious risk events occur (such as Chernobyl and TMI, or a intentional release of harmful organism) or problems remain unsolved (wastes), the concerns may threaten continued deployment of the technology.

Two theoretical constructs in the risk analysis literature underscore this point, in spite of a vast accumulation of scientific knowledge and regulatory experiences over a decade. The well-known public perception work by Slovic et al. shows that nuclear power and genetic engineering occupy a common location in their four risk quardrants as "dreadful" risks (1985). The

public tends to be highly concerned and to desire strong regulation and control of such risks. The second example is the Edwards/Von Winterfeldt taxonomy of risk controversies which suggests that genetic engineering would fall in the category of "technological mysteries", where societal debates continually oscillate between debates over facts (what are the probabilities and consequences?) and values (what should be the social purposes of biotechnology?) (1985).

Both technologies are likely to be intensely debated and controversial technologies in regard to their risk characteristics (and, of course, benefit). It is still at the very early stage to make any decisive evaluation both on the risk assessment and on risk management processes of the commercial applications of genetic engineering (large-scale production and mass-consumption, and environmental release of genetically altered organisms). However, our study indicates that a decade of disputes on the environmental release of the novel organisms have not mobilized actual public concerns enough to communicate the nature of risks among concerned groups including scientific community, industry, and regulatory agencies. It seems that the public does not prepare to discuss the "systems and institutional" risk management questions on who and how shoulder the burden of regulation in terms both of new technological and economic development, and of preventing a new type of technological hazards.

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Table 1 Technological Character of Commercial Biotechnology

New technology (genetic engineering)	Traditional technology (bio-chemical & process engineering)	Combined technology (systems & computer engineering)
o recombinant DNA	o fermentation	
o cell fusion	o breeding	bio-design and synthsis
o monoclonal antibodies	o purification & recovery process	
o bio-reactor	o chemical reactor	

Table 2 Conceptual classification of technological risks from commercial applications of biotechnology

	New technology	Traditional	Combined
Research & Experiment	risk asses. of biohazards potentials of new organisms to human health and environ. asses. of new organisms in natural ecosystems		
Production		risks from process engineering, and occupational hygiene	risks from integration of new & traditional chemical, fermentation technologies
Consumption		risks from management of public health issues in commerce & trades	risks from societal management of supply & demand for consumer goods and services
Recycle & Waste		risks from management of waste treatment & recycle conservation	risks from resource management for conservation & ecosystem protection
Risk/ Hazards	scientific/ disciplinary risks	engineering/occupational health risks	systems/institutional risks

Table 3 Major disciplinary differences on scientific implications of the environmental release of genetically engineered microoranisms

stage	molecular scientists	ecological scientists
o proliferation: multiplication, transfer of genetic materials to other organisms,	r-DNA (engineered modification) is repeat of natural selection process in 3 to 4 billon years that life has evolved.	simple mutation, rearrange-ment may trigger advantageous changes for proliferation.
o establishment growth, interactions, formation of ecological niche.	added genetical materials are physiological disadvantage to survive.	added handicaps may vary depending on environmental context.
o effects: secondary impacts, interference with natural evolution	similar to intro-duction of new chemicals in environ-ment.	Engineered organisms to overcome natural limiting factors are of significance in ecolo-gical shift.

Table 4 Regulatory options for different risk issues in commercial biotechnology

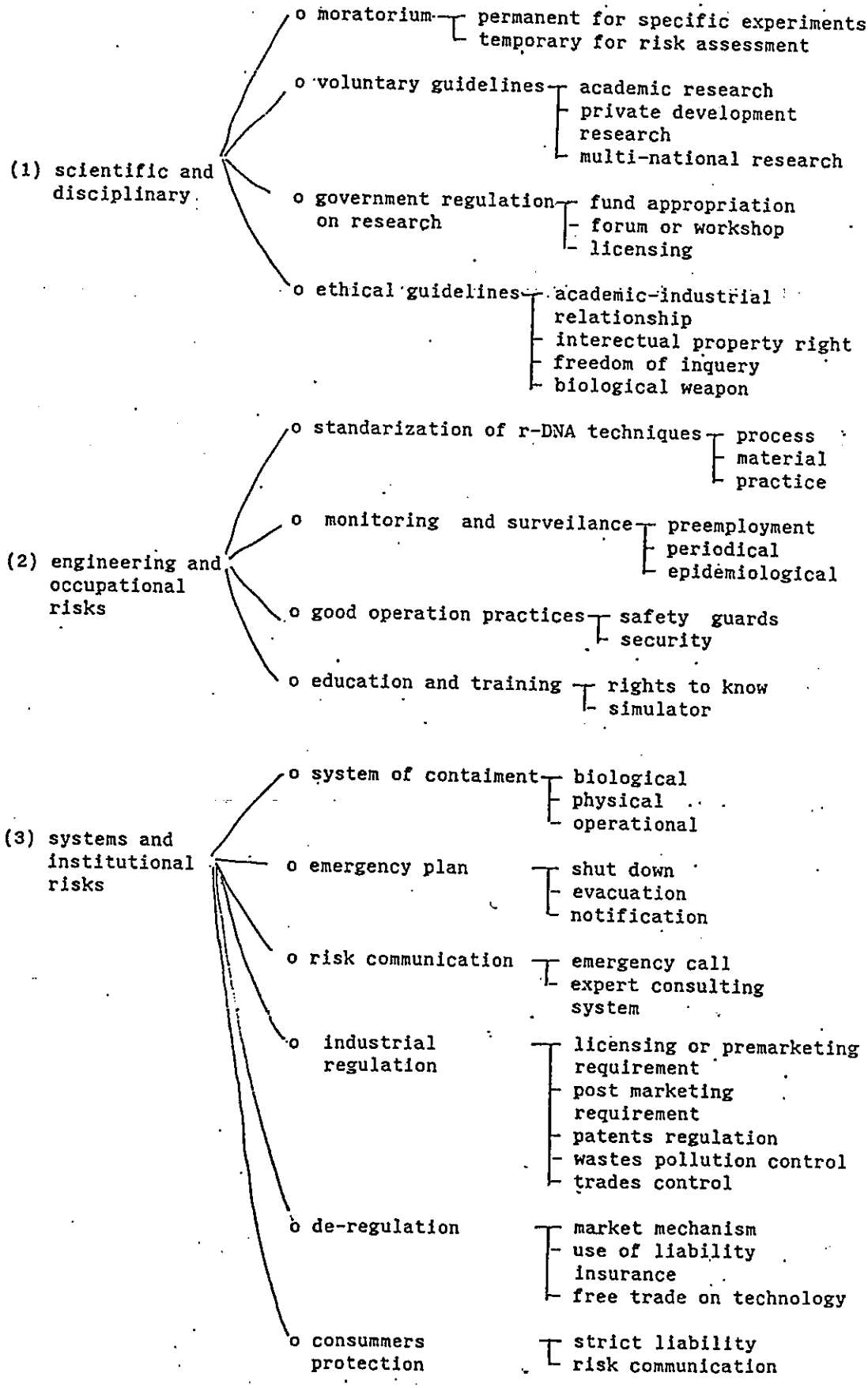

Table 5 Experts perception on the r-DNA technology

	Problem		Informed		
	Major	*Minor*	*Well*	*Moderate*	*N*
Science Policy Leaders	17%	49%	24%	39%	630
Discipline					
Biological Sciences	11	41	59	29	101
Physical Sciences	16	50	17	44	180
Social Sciences	24	51	18	46	109
Engineer-Professional	15	50	21	32	145
Other	22	57	14	41	88
Employer					
For-profit	15	45	22	37	117
University	19	49	30	40	323
Other non-profit	18	52	15	37	155
Environmental Organization Leaders	27	50	6	39	94
Religious Leaders	42	49	21	41	159
All Leadership Groups	23	49	22	39	883

"I'd like for you to indicate if you think the conduct of experiments involving recombinant DNA is a major problem, a problem but not major, or not really a problem."

"I would like for you to tell me if you feel very well informed about the conduct of experiments involving recombinant DNA, moderately well informed, or not very well informed about it."

(Source: R-DNA Tech. Bull.,1986)