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Biotechnology Policy Development:

Volume I

By CIELAP

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BIOTECHNOLOGY POLICY DEVELOPMENT: VOLUME I

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BIOTECHNOLOGY POLICY DEVELOPMENT

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EXECUTIVE SUMMARY

Purpose of Project: to provide the Ontario Ministry of the Environment with a foundation for development of its regulatory policy governing environmental release of experimental and commercial biotechnology products

more specifically to provide:

- a report, based on research and discussion with relevant authorities, on potential environmental effects associated with the biotechnology industry
- a report, based on research and discussion with relevant authorities, on policy issues which must be addressed during biotechnology policy development
- recommendations for initial steps to be taken by MOE

Project Findings: commercial biotechnology applications most likely to be developed in the near future are:

- vaccinia vaccines
- microbial fertilizers
- microbial pesticides
- genetically engineered plants
- microbial waste treatment
- microbial ore leaching

accurate prediction of environmental effects associated with any of the applications listed above can only be made for a specific product; scientific authorities consulted during the project were not willing to posit environmental effects in the abstract

research done during the project has identified, in general terms, the following potential environmental effects:

- competition with or replacement of an established species
- unrestrained species growth due to lack of natural enemies
- unexpected infectivity, pathogenicity, or toxicity
- infectivity, pathogenicity, or toxicity to non-target organisms
- transfer of genetic traits to unintended recipients
- deleterious effects caused by escape into an unintended environment
- modification of natural cycling processes
- unanticipated modification of the physical environment
- secondary effects

since potential environmental effects exist but can only be predicted with accuracy for a specific product, regulation should be done on a case-by-case basis

policy issues which must be addressed, are:

- purpose of regulation
- subject of regulation
- adequacy of existing legislation
- public participation in regulation
- political commitment to regulation
- information issues
- compliance
- liability and insurance
- jurisdiction
- need for co-ordination of policy development

consideration of applications for experimental release of genetically altered organisms is likely to be the first regulatory challenge faced by MOE; such applications can be expected in the near future, possibly before the end of 1987

given the inherent complexity of the task, it is unlikely that the federal and provincial governments will have developed and implemented a national regulatory policy before such applications are received

legislation presently administered by MOE does not provide a secure basis for regulation of experimental or commercial releases to the environment

Recommendations:

it is recommended that MOE immediately begin development of the Ministry's biotechnology regulatory policy

it is recommended that this be done by issuing for public comment, as soon as possible, a discussion paper setting forth MOE regulatory objectives and means of achieving them

it is recommended that MOE adopt the following policy objectives:

- protection of the Ontario environment
- clarification of Ontario regulation to facilitate development of the biotechnology industry in this province
- enactment of measures to ensure that no experimental field releases are made in Ontario without prior consideration and approval by MOE
- provision of both interim and permanent approvals procedures, both of which provide for adequate public consultation, for consideration of experimental field-releases
- in conjunction with the federal and other provincial governments, establishment of national regulatory procedures, which ensure adequate public consultation, for regulation of commercial biotechnology products released to the environment

it is recommended that MOE use the Environmental Assessment Act, with some modifications, as the vehicle for consideration of any applications for experimental field-releases which may be received in the immediate future

it is recommended that MOE amend the Environmental Protection Act to provide a secure legislative basis for regulation of experimental and commercial biotechnology releases to the environment

it is recommended that MOE ensure that adequate financial and staffing resources are in place to allow MOE to fulfill its regulatory responsibilities

it is recommended that MOE work with the federal and provincial governments to develop and implement a national regulatory policy

1. INTRODUCTION

The regulation of biotechnology poses a new and unique challenge to the Canadian environmental policy process, insofar as government must establish regulatory procedures before the industry begins to market products and before the regulator has a complete understanding of the potential environmental harm which regulation is intended to prevent. Not surprisingly, governments in this country and elsewhere are experiencing difficulty in putting in place a regulatory regime which will meet the twin objectives of ensuring environmental protection and providing the clarity and predictability which is required to foster the growth of the biotechnology industry.

This report is intended to assist the Ontario Ministry of the Environment in developing and implementing its own policies for the regulation of biotechnology. Terms of reference for the study are as follows:

> By means of literature reviews and interviews, relevant biotechnology activities in Canada will be identified, especially recombinant DNA work, environmental facts will be postulated and policy issues and approaches will be determined. Seminars will be held to obtain a tentative consensus and, possibly, a priority listing about environmental effects and policy issues.
>
> Study findings will provide a foundation for development of policies to regulate and ensure the safety of biotechnology activities, primarily those related to recombinant DNA techniques.

Initial planning of the project was done in conjunction with MOE staff in the spring of 1986. It was decided that the project would include the following components:

- preparation of a paper on potential environmental effects associated with biotechnology
- discussion of the paper at a one-day seminar in Toronto, to which would be invited Canadian scientific authorities
- preparation of a paper on policy issues which must be addressed during development of biotechnology regulatory policy
- discussion of the paper at a one-day seminar in Toronto, to which would be invited representatives of the Canadian public and private sectors involved with development of biotechnology regulatory policy
- submission of a report to MOE setting forth findings and recommendations of the project

The project commenced in the early summer of 1986, under the direction of Marcia Valiante, Director of Research, Canadian Environmental Law Research Foundation. Yvonne Skof was employed on a contract basis to do research and assist in drafting both the environmental effects and policy papers. Bernard Glick and Irene Courage were employed on a contract basis to prepare, respectively, the papers on environmental effects and policy issues. Marcia Valiante left the employ of the Foundation effective August 31, 1986, and the duties of project director were assumed at that time by Doug Macdonald.

The paper titled "Environmental Implications of Biotechnology" was discussed at a seminar on September 15, 1986. The paper titled "Policy Issues Raised by the Application of Biotechnology" was discussed at a seminar on October 15, 1986.

Copies of the papers, seminar agendas and lists of participants are provided in Volume II of this report.

Seminar participants were informed that their discussion was public and that a transcript would be made of discussion at each seminar, although specific remarks would not be attributed to individual participants in the final project report.

Volume I of this report is divided into four major chapters, as follows:

Chapter 2 . a summary of the paper on environmental effects, in lay language, a summary of discussion at the seminar held in Toronto on September 15, 1986, and listing, based on research done in conjunction with the project, of potential environmental effects

Chapter 3 . a summary of the paper on policy issues and summary of discussion at the seminar held in Toronto on October 15, 1986

Chapter 4 . a brief overview of approaches to regulation of biotechnology being taken in jurisdictions outside Canada and at the federal level

Chapter 5 . recommendations for development of MOE biotechnology policy

In addition to the work outlined above, the Research Foundation was asked by MOE to provide comment upon the extent to which existing legislation administered by the Ministry could be used to regulate the biotechnology industry and to provide information upon testing procedures which might be used in considering an application for approval of a field test of an organism which has been altered using modern genetic engineering techniques. Discussion of both issues is contained in Chapter 5.

2. ENVIRONMENTAL EFFECTS

2.1 Summary of Paper

What follows is a summary of the paper titled "Environmental Implications of Biotechnology".[1] The paper was written to provide background information and raise issues for discussion at the seminar which was held on September 15, 1986. The complete paper is included as Chapter 1, Volume II of this report. The term "biotechnology" as defined therein is limited to the enabling technologies of recombinant DNA and cell fusion. This discussion is intended for the lay reader. A more detailed scientific discussion can be found in the original paper.

2.1.1 The Enabling Technologies

2.1.1.1 Introduction

Deoxyribonucleic acid (DNA) is a molecule that contains the hereditary information of an organism. A DNA molecule contains many defined segments, or genes. Each gene determines or affects a specific structure or function of the organism. (Ribonucleic acid or RNA takes the place of DNA in some viruses).

2.1.1.2 Recombinant DNA

In 1973, Boyer and Cohen carried out the first recombinant DNA experiment, beginning a new era in biotechnology. In recombinant DNA, DNA from two different sources is cut into

pieces. These cut DNA fragments are then spliced together to form a new DNA molecule containing genetic material from both organisms.

2.1.1.3 Vectors Used in Recombinant DNA

A vector is an agent used to carry DNA into a new cell. Recombinant DNA techniques can be used to insert foreign DNA (representing one or more genes) into a vector. The vector is then used to carry the foreign DNA into a host organism. Vectors are composed of either DNA or RNA, and include: plasmids, bacteriophages, cosmids, retroviruses and transposons. They usually contain a DNA segment known as an origin of replication, which ensures that the vector (and the foreign DNA it contains) will be duplicated inside the host cell.

1. Plasmids

Plasmids are small, circular, double-stranded molecules of DNA. When they are inserted into a bacterial host cell, they exist separately from the hereditary information of the bacterium (which is found in the bacterial chromosome). Plasmids may, however, exchange their genetic material with that contained in the host chromosome, thereby changing the composition of the genetic material they carry. Plasmids are classified as either conjugative or non-conjugative, on the basis of their ability to move from one organism to another. Conjugative plasmids are more likely to be transferred into a new organism.

2. Bacteriophages

Bacteriophages are viruses which infect bacteria. This type of vector can insert itself directly into the chromosome of the host bacterium. In this integrated state the bacteriophage, (including the foreign DNA it carries), replicates along with the host chromosome.

3. Cosmids

The cosmid vector is a special type of plasmid, which can be packaged to resemble a virus. The resulting 'virus' particle, can then be used to infect a host cell. Cosmids are able to carry relatively large amounts of foreign DNA into a cell. Once inside the cell cosmids behave in the same manner as plasmids.

4. Retroviruses

Retroviruses contain RNA as their genetic material, and therefore code for an enzyme which enables DNA to be formed from the RNA. The DNA which is produced reflects the same hereditary information that was contained in the original RNA. This complementary DNA strand can integrate into various sites of the host chromosome, and affect the expression of nearby genes. Prior to their use as vectors, retroviruses must be 'disarmed' by removing their ability to transform the host cell into a cancerous cell. Another concern is that retroviruses contain potentially unstable DNA sequences, that facilitate the transfer or deletion of DNA.

5. Transposons

A transposon is a discrete segment of DNA which can duplicate itself and 'jump' to another position on an organism's DNA or to another DNA molecule. Since a transposon cannot exist independently, it must be integrated into either plasmid, bacteriophage, or chromosomal DNA. Transposons have a repeating sequence at each end of the molecule, which may contribute to the structural instability of DNA molecules into which they are integrated. (That is, these sequences increase the probability that genetic information will be deleted or exchanged). Before being used as vectors, some DNA is usually deleted from the transposons in order to severely restrict their ability to move from one position to another.

2.1.1.4 Cell Fusion

The other major technology of interest is that of cell fusion. Cell fusion is the joining of two different types of cells to form a single, new cell containing genetic information from both cells.

1. Animal Cell Fusion

Animal cell fusion is used in the production of monoclonal antibodies, which are important tools in the diagnosis of certain diseases. Monoclonal antibodies are antibodies which recognize only one specific portion, or site, of a particular invading

foreign substance. That particular site has a unique chemical signature. Generally when a foreign protein enters an organism, the organism's immune system responds by creating antibodies to fight the invader. Many different types of antibodies are formed, each kind capable of attacking the invader at a different site. Serum removed from the attacked organism will contain a mixture of all of these antibodies. However, it is now possible to obtain a culture of highly specific, purified antibodies, known as monoclonal antibodies. To create these antibodies, a mouse is injected with a foreign protein, causing it to have an antibody response. Many different lines of cells develop, each one secreting a particular type of antibody. These antibody-producing cells are then removed from the mouse's spleen and fused to mouse tumour cells. The fused cells, known as hybridomas, continue to produce antibodies indefinitely. A culture developed from one of these hybridoma cells will produce many highly specific, purified antibodies.

Since these purified antibodies bind only to a certain specific site they can be used as diagnostic tools to identify the presence of that site. Different lines of monoclonal antibodies will each recognize a special 'chemical signature', or binding site. Special lines of monoclonal antibodies have been developed to recognize the presence of various illicit drugs, and to diagnose several diseases.

2. Plant Cell Fusion

Plant cell fusion involves the joining of two plant protoplasts (i.e. cells which have had their cell walls removed), to obtain a single cell which contains a combination of genes from both parents. Although this technique allows the combination of sexually incompatible plants, the resultant hybrids are often genetically unstable (i.e., the content of the hereditary information is likely to change as the cell population grows and multiplies). This technique is further limited by the inability to grow whole plants from the fused cells of some plant species.

2.1.2 Environmental Effects

As with any technology, there are risks associated with the development of biotechnology and the use of the resulting products, both from an occupational health aspect and from a wider environmental perspective. The background paper focuses on the environmental problems which could result from deliberate or accidental releases of living genetically-engineered organisms.

Given the differing views of scientists and the general lack of experience with large-scale introductions of live, altered organisms into the environment, it is difficult to predict the effects of a particular environmental release.

Martin Alexander has suggested a conceptual framework for this assessment process.[2] He states that the probability of a

deleterious effect from the release of a modified organism is a function of five factors: P_1, P_2, P_3, P_4 and P_5, where:

P_1 is the probability the organism will survive

P_2 is the probability that the surviving organism will be able to multiply

P_3 is the probability that the organism will be transported to a site where it might have an effect

P_4 is the probability that genetic information coding for a deleterious trait will be transferred to another species

P_5 is the probability that the engineered organism, or an organism to which it transfers its DNA, will harm the ecosystem

Although Alexander's framework was developed with genetically engineered organisms in mind, the same principles apply to the selective application of large numbers of naturally occurring organisms (for example, in microbial mining, bacterial fertilization, pest control, and waste management). However, in the case of naturally occurring organisms, there is usually some information available concerning their survival requirements and patterns, their behaviour, and possibly their environmental interactions. This historical information considerably simplifies the calculation of the crucial probabilities identified by Alexander.

Numerous factors affecting the survival of a released organism have been identified, including: the season of the release, the pH of the environment, the extent of adsorption of a microorganism to the soil, the water content of the soil, the

soil type, and the presence of nutrients. Death of microorganisms could be caused by toxins, solar radiation, acidity, viruses, predators, or lack of essential nutrients.[3] Survival may also be hampered if an organism, such as a bacterium, carries extra plasmids as a result of genetic engineering, since the cell expends extra energy replicating this additional DNA. Unrestrained species growth could cause the death of individual members of the population as a result of the depletion of their food supply.[4]

Alexander is of the view that an organism will not have a significant ecosystem impact unless it is capable of growth and multiplication. Generally, organisms which are good competitors and tolerant of environmental stresses will proliferate.

For an organism to have an adverse environmental effect it must be brought into contact with organisms or environments which could be harmed by it. All organisms have the potential for dispersal. Animals can travel using their own locomotive capabilities and plant seeds and pollen can travel considerable distances. Microorganisms, however, have the greatest capacity for dispersal, often being able to travel hundreds or thousands of miles. Dispersal may occur by air, water, animal carriers, or direct human contact. Successful aerial dispersal depends upon the amount of time the organism can survive in the air, and the size and shape of the organism or any particle to which it adheres. Properties of the water, including current and wave

action, are major factors in water dispersal. Popular animal vectors are earthworms and burrowing mammals (for soil bacteria), bees and other insects. Direct contact is a common dispersal mechanism in infectious diseases.

The probability of an adverse environmental effect may increase if certain genetic traits are transferred to unintended recipients. Thus one must consider both the probability that the organism will transfer some of its genetic material, and the likelihood that the engineered organism will obtain undesirable traits from organisms indigenous to the site in which it will be released. Most of the literature focuses on the former question. Deletions of certain DNA sections can limit the mobility of vectors used in recombinant DNA experiments and thereby decrease the chance that the organism will transfer its new trait to an unintended recipient. Furthermore, some repeating DNA sequences have been identified as potentially unstable segments, because they may facilitate either the exchange or deletion of genetic information.

Deleterious environmental impacts will generally fall into one of the following categories:

1. **Competition with or Replacement of an Established Species.**

2. **Unrestrained Species Growth Due to Lack of Natural Enemies:** Unrestrained population growth could deplete the flora and fauna which make up the food supply of the growing population.

3. **Unexpected Infectivity, Pathogenicity, or Toxicity[5]:** For example, an experiment by Giles and Whitehead demonstrated that the combination of two non-pathogenic organisms could result in a fused organism exhibiting pathogenicity. In

that experiment cell fusion changed a normally non-pathogenic, symbiotic fungus into one which was lethal to tree seedlings.

4. **Infectivity, Pathogenicity, or Toxicity to Non-Target Organisms:** For example, a microbial pesticide developed to control insect pests may indirectly poison the birds which prey upon those insects.

5. **Transfer of Genetic Traits to Unintended Recipients:** For example, herbicide resistance may be transferred from a crop plant to a weed.

6. **Deleterious Effects Caused by Escape into an Unintended Environment:** For example, it has been suggested that ice-minus bacteria may migrate north, harming plants which require a freezing season in order to grow[6].

7. **Modification of Natural Cycling Processes:** For example, microorganisms which have been engineered to enhance their nitrogen-fixing abilities may affect the nitrogen cycle if they are released into the environment in large quantities.

8. **Unanticipated Modification of the Physical Environment:** For example, the displacement of naturally occurring bacteria by 'ice-minus' recombinants could interfere with rainfall. The ice-crystallization protein found in the naturally occurring bacteria is thought to play an important role in the formation of snow and rainfall, and therefore a shortage of this protein could result in lower levels of precipitation[7].

9. **Secondary Effects:** Secondary effects caused by an extensive use of biotechnology products could exert new pressures on the environment. For example, one could expect an increase in the use of herbicides as a result of the presence of herbicide-resistant plants.

2.2 Summary of Seminar Discussion, September 15, 1986

2.2.1 Purpose of Seminar

The scientists participating in the seminar discussion were drawn from industry, academe and the federal and provincial governments. They were invited on the basis of their expertise in biotechnology, microbial ecology, or the regulation of scientific endeavours.

The purpose of the seminar was to identify the imminent applications of biotechnology and the environmental effects which might be associated with these applications. The discussion at the seminar quickly focussed on living organisms intended for deliberate release into the environment, since they pose the greatest environmental risks.

2.2.2 Applications

In attempting to forecast the most likely applications for the future, it was recognized that predictions could not be made based upon scientific advances alone. It was pointed out that the economic incentives (or disincentives) relative to the introduction of a particular product, as well as the social and regulatory context for that product, would be important factors in deciding whether an application for field testing of the product would be made.

The most likely applications for field testing within the next five years were identified as follows:

1. **Vaccinia Vaccine.** An application to test an orally administered rabies vaccine could be expected.

2. **Microbial Fertilizers.** Microbial fertilizers would most likely be genetically engineered forms of Rhizobia.

3. **Microbial Pesticides.** There are many microbial pesticides currently in use within Canada and all are likely to be subject to genetic manipulation and improvement. A host-pathogen system of particular interest for the application of genetic engineering is the spruce budworm/Bacillus thuringiensis (B.t.), nuclear polyhedrosis virus system.

4. **Genetically Engineered Plants.**

5. **Microbial Waste Treatment.**

6. Microbial Ore Leaching.

2.2.3 Environmental Effects

The participants concluded that environmental effects could not be discussed in general terms. It was stated that the risk of a potential adverse effect could not be examined in a meaningful manner without reference to a particular case and a particular fact situation.

Flowing from this was discussion of the need to expand the existing knowledge base. It was concluded that further research in microbial ecology is required to understand the behaviour of microorganisms in the natural environment. It was recognized that while there were background data which one could look to to assess the potential deleterious effects of a regular biological organism released to the environment, there was no data base available in making the same assessment for a genetically engineered organism. A suggestion was made to devote considerable effort to the gathering and sharing of this type of information with other countries. Finally, it was suggested that a meaningful risk/benefit assessment procedure applicable to genetically engineered organisms should be developed.

In a debate over whether genetically engineered organisms were any different from naturally occuring organisms, the general consensus was that there were no major differences between the potential effects associated with genetically engineered

organisms and those derived by conventional means. However, it was recognized that some products obtained by genetic engineering were not likely to be obtained using traditional methods. For example, conventional mutation and selection would be unlikely to produce an E. coli which carried a human insulin gene. It was also noted that products obtained by recombinant DNA techniques could exhibit different or enhanced properties if they were subjected to mutation and selection pressures following genetic engineering. That is, after a product is created using recombinant DNA techniques, it may be subjected to conventional mutation and selection techniques. One could induce mutations within a population of recombinant organisms and then select those individuals which exhibited the desired properties. In this manner, a population of organisms could be developed which would be even more efficient at performing their designed function than were the original recombinant organisms.

2.3 Potential Environmental Impacts

The following discussion of potential environmental concerns is drawn primarily from the background paper titled, "Environmental Implications of Biotechnology", included in Volume II and only in part from discussion at the September 15 seminar. References are included for any supplementary sources of information used in the discussion.

2.3.1 Vaccinia Virus

A vaccine is a preparation that contains the whole or parts of a disease causing organism, and is intended to enhance an individual's immunity to a disease. Recombinant DNA techniques have been used to create a live vaccine, which elicits a better immune response than conventional vaccines. This vaccine was developed from the vaccinia virus - the same virus used to protect people from smallpox. The vaccinia virus has turned out to be an ideal host for the insertion of genes useful in the immunization of animals against various diseases, such as rabies.

The use of a recombinant vaccinia virus as a live vaccine is considered an environmental release, because when an animal or human is inoculated with a live virus the possibility of further transmission of that virus within the community exists.[8] Even though the vaccinia virus has been used safely in the eradication of smallpox, there are some concerns about using it as a live recombinant vaccine. The virus functions as a weakened virus. (That is, the vaccinia virus used in the vaccine preparation is alive, but it has been weakened so that it can no longer cause disease.) However, since little is known about the mechanism used to weaken the virus, a recombinant DNA vaccine may prove more virulent than anticipated. Notwithstanding the fact that virulence is determined by many different genes, the degree of virulence can be significantly altered by a single point mutation.[9] It is also possible that the insertion of new genes

into the vaccinia virus may alter the range of hosts or tissues it affects.[10] Although the virus has a broad host range, its effects differ from species to species, suggesting a potential danger should the vaccine be transferred between species. A vaccine tested and proven safe for one type of organism could cause unfavourable reactions in another. Since a recombinant vaccinia vaccine for rabies may be administered orally, it is important to identify any non-target organisms which could take up this vaccine.[11] Furthermore, the effects of a transfer of the inserted gene to another organism should be considered, since the recombinant virus could recombine with related viruses.[12] In addition, past experience has shown that the vaccinia virus itself may result in undesirable side effects, including skin eruptions and central nervous system disorders.

2.3.2. Microbial Fertilizers

Nitrogen is an essential plant nutrient, often supplied by fertilizers. Some plants can form symbiotic relationships with nitrogen-fixing microorganisms which have the ability to supply them with nitrogen-containing compounds. (A symbiotic relationship is one in which two dissimilar organisms live in close association for their mutual benefit.)

Since microbial fertilizers (i.e., nitrogen-fixing microorganisms) would likely affect the rate of nitrogen fixation, their effect on the nitrogen cycle must be considered

if they are to be released into the environment in large quantities. Past experience has also demonstrated that one must be careful when applying modern enabling technologies to an organism involved in a symbiotic relationship. One such relationship exists between the fungus Rhizopogon and a certain pine tree species. In 1975, Giles and Whitehead carried out an experiment designed to introduce nitrogen-fixing ability into the Rhizopogon fungus.[13] To accomplish this goal, they fused cells of a nitrogen-fixing bacteria with Rhizopogon cells, both populations of cells being non-pathogenic. Unexpectedly, one strain of the fused cells killed tree seedlings to which it was applied. It appears that the modified fungus interacted with the pine tree seedlings in a new and dangerous manner. The delicate balance required for the symbiotic relationship had been destroyed. In this instance, cell fusion had turned a normally non-pathogenic, symbiotic fungus into one which was lethal to tree seedlings. However, this type of deleterious effect could easily be detected by laboratory and greenhouse testing.

2.3.3 Microbial Pesticides

Microbial pesticides present a number of concerns, which are best discussed in reference to particular proposed applications. Certain precautions may be taken in the case of microbial pesticides in order to reduce environmental risks. Two genetically-engineered microbial pesticides are modified strains

of Pseudomonas syringae and Pseudomonas fluorescens, described below.

Natural strains of Pseudomonas syringae make a protein which is responsible for ice formation, whereas genetically engineered 'ice-minus' strains do not. It is therefore hoped that crop plants sprayed with the modified 'ice-minus' bacteria will be resistant to frost damage. 'Ice-minus' bacteria are classified as pesticides because they are intended to displace the natural strains of P. syringae which currently inhabit the crop plants.

Environmental precautions were taken in the development of this mutant strain. A deletion of genetic material was used to create the desired 'ice minus' characteristic, since a deletion prevents any reversion to the natural bacteria and ensures that no uncharacterized DNA is inserted. Although most strains of P. syringae are natural pathogens for several major crops, the strains used in this experiment were isolated from healthy plants and failed to exhibit pathogenicity in their isolated or modified form.

Environmental concerns raised by opponents of this experiment include: the possibility that these bacteria will migrate north proving harmful to northern plants which require a frost season in order to grow; the possibility that the ice-minus gene will be transferred to insects thereby increasing their host range; and the concern that rainfall may be inhibited by displacement of the wild-type bacteria by the ice-minus strain

(because the ice-crystallization protein is considered to play an important role in the formation of snow and rainfall).

A second pesticide is a strain of bacteria, Pseudomonas fluorescens, which has been engineered to carry a toxin-producing gene removed from Bacillus thuringiensis. The modified P. fluorescens now expresses the B.t. toxin which is lethal to certain soil insects. In commercial application, the altered bacteria would be used to coat seeds at the time of planting with the expectation that, as the plant develops, its roots would be free from invasion by soil insects.

Environmental concerns are the same as those related to chemical pesticides: human and non-human health effects, and damage to the ecosystem. It is possible that this living, multiplying pesticide may prove harmful to earthworms or other beneficial soil organisms, because the genetic engineering designed to enhance its commercial success may unexpectedly increase its host range or virulence. Birds and other predators of the target organisms may be poisoned indirectly as a result of consuming the treated insects. A recent study has established that certain insects can develop insecticide resistance to the B.t. toxin in circumstances where the toxin is not rapidly degraded. Normally the B.t. toxin is broken down quite rapidly when it is applied to crop plants.[14] However, engineering living organisms produce the toxin over an extended period of time,

may ultimately lead to the rise of insect populations which are resistant to this natural pesticide.

2.3.4. Genetically Engineered Plants

Genetically engineered plants were considered by seminar participants to be less of a threat than similarly modified microorganisms. As was stated, "You can always go over that (a macroorganism) with a chain saw or a lawn mower and wipe out the macroorganism quite rapidly. The microorganism is a little more difficult in that case." Problems in controlling the plant populations may occur, however, if the plant is allowed to seed or to pollinate. It was also stated that it is very difficult to control the spread of aquatic plants. Therefore, consideration should be given to developing contingency plans to prevent the spread of genetically engineered plants, should they exhibit undesirable traits.

Since portions of the DNA of a weed species may be quite similar to DNA sequences of a related crop species, there is a risk that a trait conferring a selective advantage on a plant (e.g. herbicide resistance) may be transferred to a closely related weed. In this light, the potentially unstable 'direct repeat' segments on vectors used in the genetic engineering of plants are a concern, because these sequences increase the possibility that the new genetic trait will be transferred. There is also some concern that plants which have been

genetically engineered by inserting DNA sequences which were not fully identified, could produce a toxic product or by-product. Such plants should therefore be tested for toxicity.

2.3.5. Microbial Waste Treatment

Microorganisms could be developed to break down a compound known as lignin. The degradation of lignin is one of the slowest reactions in decomposition of organic matter. Therefore, if organisms were engineered to rapidly break down this material, the nutrient cycling process would occur at a faster rate. These organisms would also have the potential to attack live trees (largely composed of lignocellulose). However, since untreated plant material has proved difficult to degrade in the past, it is most likely that the digestion of trees would only occur under specially controlled conditions.

Microorganisms used to degrade oil and industrial chemicals could have unintended consequences. For example, they could leave their intended environment and begin degrading other related compounds, or break down the original chemical into a new, toxic compound. Small-scale experiments would be useful in more accurately assessing the nature of these risks.

2.3.6. Microbial Ore Leaching

Bacteria modified to leach minerals and then released into a mine could cause harm if they subsequently invaded a different

environment. For example, plants require iron in an unoxidized state as a nutrient. Therefore, the invasion of the environment by large numbers of bacteria which oxidize iron could detrimentally affect plant populations.

2.3.7. Organic Waste Or Debris From Contained Applications

Seminar participants noted that the waste produced by biotechnology industries is different from traditional forms of industrial waste. By-products from the biotechnology industry contain much higher concentrations of organic substances. This type of waste may impact on the environment in a new manner. For example, the release of large quantities of these waste materials will alter the character of the environment, and may thereby favour the growth of certain populations of microorganisms whose population size had been restricted in the past.

The difficulties in dealing with the old forms of industrial waste suggest that methods of disposing of these new waste products should be carefully considered. New pollution control devices may be needed, as well as monitoring systems that identify and allow the assessment of the hazards of this organic waste.

2.3.8. Genetically Engineered Organisms VS. Naturally Occurring Organisms

A great deal of discussion was concentrated upon determining whether the potential for harm caused by genetically engineered

organisms was greater than that posed by naturally occurring organisms. Although the range of potential combinations and the speed with which they can be created is enhanced by genetic engineering, the general consensus was that the modified organisms were not intrinsically any more dangerous than their naturally occurring counterparts.

2.4. Conclusion

There are potential, though low probability, risks to the environment as a result of new biotechnological applications. No adequate methodology is in place to assess these risks since existing risk assessment methodologies for chemicals cannot be applied to the assessment of living biotechnology products, without extensive modifications. The questions posed by Martin Alexander's model for risk management provide a good starting point for development of such a methodology. It is concluded that environmental effects must be assessed on a case-by-case basis.

There is a pressing need for additional research on the behaviour of genetically engineered organisms in the environment. As knowledge is gained about the nature, survival, and stability of various vectors, hosts and host-vector systems, and as scientific expertise in predictive models develops, the ability to predict potential effects will improve.

Perhaps the primary conclusion which can be drawn is that regulation of biotechnology is characterized by a higher degree of uncertainty than is found in other areas of environmental regulation.

Martin Alexander has stated the problem this way:

> For the ecologist and the environmental scientist attempting to predict the risk of introducing new organisms into our environment, there is a high degree of uncertainty in anticipating the consequences of genetic engineering. Such an uncertainty apparently does not characterize many laboratory-based geneticists and representatives of industry, who rarely have an adequate base of information in ecology or other environmental sciences. This uncertainty, however, is found among many scientists whose daily concern is the behaviour of organisms in natural environments, as well as in those man-controlled environments that we use for food and fibre production. The degree of uncertainty surely is not reduced by specialists in other disciplines who maintain that, even in the absence of data or convincing theoretical arguments, no problems exist.[15]

Martin has pointed out that the potential for environmental disruption increases as industry moves from initial tests to full-scale commercial activity:

> Indeed, a review of other technologies indicates that there was little or no hazard in their early stages. For example, during the initial development of the chemical industry or at the time when the use of pesticides was just beginning, little or no hazard existed for society at large and no threat was posed to major natural ecosystems, but as those technologies became more widely used and moved in new directions, the environmental and health problems became quite apparent.[16]

Given this high degree of uncertainty, it can be concluded that agencies charged with the mandate of environmental protection are warranted in adopting a conservative approach, erring on the side of caution, in development of regulatory policy.

FOOTNOTES - PART 2

1. Bernard Glick and Yvonne Skof, Environmental Applications of Biotechnology (Toronto: Canadian Environmental Law Research Foundation, August 1986).

2. Martin Alexander, "Ecological Consequences: Reducing the Uncertainties" (Spring 1985), 1 Issues in Science and Technology 57-68, at 63-64.

3. Martin Alexander, "Part 1: Survival and Growth of Bacteria" (July 1986), 10 Environmental Management 464-469, at 465-66.

4. Unrestrained species growth could lead to a depletion of the nutrient supply, resulting in a population decline.

   For example see:

   Charles J. Krebs, Ecology (New York: Harpers & Row, 1972) at 196. In this text, a description is provided of a herd of 15 reindeer introduced into St. Paul Island in 1922. The population grew continuously until it reached a peak of 2,000 reindeer in 1938. However, the land became overgrazed and the population declined to 8 reindeer in 1950.

5. (i) U.S., Congress, Subcommittee on Investigations and Oversight, Committee of Science and Technology, The Environmental Implications of Genetic Engineering, (Washington: U.S. Government Printing Office, Feb. 1984), at 19 and 63-75.

   (ii) K.L. Giles and H.C.M. Whitehead, "The transfer or nitrogen fixing ability to a eukaryote cell" 14 Cytobios 49-61.

6. Judith Miller, "Harmful Environmental Effects of Biotechnology: Consequences of a Deliberate Release," in The Regulation of Biotechnology, a one day conference presented by the Canadian Environmental Law Research Foundation (Toronto: CELRF, October 9, 1984) 1-21, at 5.

7. Reginal Rhein, Jr., "'Ice-minus' May End Killer Frosts - and Stop the Rain," November 25, 1985, Business Week 42.

8. Edwin Dennis Kilbourne, Epidemiology of Viruses Genetically Altered by Man - Predictive Principles," in Bernard Fields, Malcolm A. Martin, and Daphne Kamely, eds., Bradbury Report 22: Genetically Altered Viruses and the Environment (Cold Spring Harbour, New York: Cold Spring Harbour Laboratory, 1985), 103-117, at 104.

9. Ibid, at 103.

10. Bernard Moss, "Use of Vaccinia Virus Vectors for the Development of Live Vaccines," in Bernard Fields, Malcolm A. Martin and Daphne Kamely, eds. Bradbury Report 22: Genetically Altered Viruses and the Environment (Cold Spring Harbour New York: Cold Spring Harbour Laboratory, 1985), 291-300, at 293-295.

11. Statement of a science seminar participant.

12. Bernard Moss, supra footnote 10, at 296.

13. (i) U.S. Congress, Subcommitte on Investigations and Oversight, Committee on Science and Technology, The Environmental Implications of Genetic Engineering, (Washington: U.S. Government Printing Office, Feb 1984), at 19 and 63-75.

(ii) K.L. Giles and H.C.M. Whitehead, "The transfer of nitrogen fixing ability to a eukaryote cell" 14 Cytobios 49-61.

14. William H. McGaughey, "Insect Resistance to the Biological Insecticide Bacillus thuringiensis" (July 1985), 229 Science 193-195.

15. Martin Alexander, "Environmental Consequences of Genetic Engineering," in U.S. Senate, Subcommitte on Toxic Substances and Environmental Oversight, Committee on Environment and Public Works, The Potential Environmental Consequences of Genetic Engineering (Washington: U.S. Government Printing Office, 1984), 64-76, at 65.

16. Ibid, at 66-67.

3. POLICY ISSUES

3.1 Summary of Paper

The scope of the paper titled "Policy Issues Raised by the Application of Biotechnology,"[1] which was the background document distributed to participants prior to the seminar discussion on October 15, 1986 and which is reproduced in Chapter 3, Volume II of this report, is limited to environmental releases of the products of modern biotechnology. A release to the environment may take the form of an intentional release, an accidental escape, or a discharge of wastes or by-products from the manufacturing process. Once again, modern biotechnology refers to the technologies of recombinant DNA and cell fusion. The products of these technologies could be living organisms (e.g. microbial pesticides), killed organisms (e.g. single cell protein products formed from dried cells), or inanimate products derived from a biological system (e.g. human insulin produced by genetically engineered E. coli).

Present legislation, that could apply to biotechnology regulation, is grouped in the paper into four broad categories: environmental legislation, agricultural protection legislation, product-oriented legislation, and workers' protection legislation. Because the focus of the paper is environmental protection, an analysis of the issues involved in occupational health legislation is not included in the paper, although it is

recognized that stringent occupational health and safety controls would contribute to environmental protection.

Because the paper was intended to provide background information and to stimulate discussion, it raises issues and poses questions, rather than providing definitive recommendations for the regulation of biotechnology. Chapter one addresses the question of societal goals served by a regulatory scheme for biotechnology, and asks how various goals should be ranked. Such goals could include: the protection of human health and the environment, quality control of products, the protection of agricultural resources, consumer protection, and the facilitation of industrial development.

The second chapter examines the subject of regulation. What is it that needs to be regulated? Is it only products of modern biotechnology that should be regulated, or should the same regulations apply to all potentially dangerous biological or biologically derived products regardless of the technique by which they were developed? Should regulation apply to only certain products of the new biotechnology, such as living organisms (as opposed to killed organisms or inanimate products) or to all? Should the regulatory focus be the biotechnology process or the product (recognizing that a product-based regulatory approach may still require regulation of some aspects of the manufacturing process)?

The paper advances the argument that modern biotechnology, as such, is not adequately regulated by existing legislation.[2] However, provisions are in place which might be applied to certain modern biotechnology products or wastes. Regulatory gaps must be identified and then filled by either the development of a comprehensive new system or by amendments to existing legislation. Finally the need to harmonize legislation, or to centralize the administration and enforcement of such legislation should be examined.

The third chapter lists the various activities which may be regulated during the life-cycle of the product. They include:

1. Production
2. Storage
3. Use
4. Sale
5. Import and Export
6. Waste management and disposal
7. Spills, and
8. Transportation.

Chapter four deals with information issues. Not enough is known about the products and the wastes of biotechnology and their potential environmental impacts. Government needs additional information in order to regulate. Since a case-by-case analysis is the preferred method of regulation, government will need information about both the products and

their effects prior to issuing a permit or a licence. A monitoring program would assist in tracking the effects of these substances in the open environment.

Closely related to the issue of providing information to government, is the concern of industry and researchers that any trade secrets disclosed to government remain confidential.

The public must have access to adequate, detailed information to allow it to participate in the regulatory process. But the need to maintain confidentiality of trade secrets makes the provision of public information a difficult process.

The paper suggests that consideration be given to the development of a biotechnology data bank. A mechanism might be developed whereby information is shared, not only within government, but also with research scientists and industry.

Liability and compensation are dealt with in the fifth chapter. Generally, the common law appears inadequate to compensate victims of a biotechnology field release that has caused unintended harm. This is because some biotechnology products are alive and may multiply, spread, and exchange genetic material with other living organisms, making it difficult or impossible to prove a causal connection between a release and an adverse effect that may be discovered at a later date.

Compensation for victims of this technology may be provided by creating a statutory cause of action or compensation scheme.

A strict liability offence may be created. Alternatively, the victim may be entitled to compensation from the Crown, combined with some form of subrogation of the plaintiff's action to the Crown. Another possibility is the creation of a compensation fund. Mandatory insurance or the posting of a bond may be required to ensure that companies will have funds available to compensate victims and repair environmental damage.

On the other hand, government could consider limiting the liability of biotechnology companies as a means of fostering industrial development, especially for companies involved in producing products with a great potential benefit to society.

Compliance and enforcement are the subjects of the sixth chapter. Since unauthorized, small scale environmental releases would be very difficult to detect, ensuring compliance with biotechnology regulation may be difficult.

Sanctions imposed for a failure to comply with regulatory requirements could take a number of forms. Benefits could be denied the offender by withdrawing financial support or refusing to issue further licences or permits. Administrative authorities could be given the power to inspect premises and seize products which violate regulatory provisions and to issue orders to refrain from potentially harmful actions or to take remedial action. Further sanctions, such as fines, jail terms, and injunctions could be imposed by the courts. Imprisonment of the person responsible for an unauthorized release would be most

effective if officers, directors, or agents of a corporation, who authorized, acquiesced in, or participated in the commission of the relevant offence could be held liable.

Chapter seven deals with jurisdiction. In Canada, the federal and provincial government both have powers to regulate certain aspects of biotechnology. Jurisdiction will depend on the choice of the subject of regulation.

In order to establish one all-inclusive scheme dealing with environmental protection, quality control, workers' protection, and health protection, the ideal situation would be one of cooperation between the federal and provincial governments. Where legislation is limited to regulation of local industries and allocation of risks, the provinces would have jurisdiction. The paper suggests that potential risks associated with biotechnology, or the need for a national strategy for development of the biotechnology industry, might take this matter beyond the realm of the provinces. The federal government might regulate certain aspects to ensure "peace, order and good government" and Parliament could declare that modern biotechnology industries are undertakings for the general advantage of Canada and therefore come under federal jurisdiction.

The concluding chapter sets forth, in the order of priority seen by the authors, the policy issues which must be addressed. The major ones are listed as follows:

- subject/activities to be regulated
- adequacy of existing legislation
- information issues
- prevention of unauthorized release
- remediation
- jurisdiction
- compliance
- compensation

3.2 Summary of Seminar Discussion

Discussion at the seminar held October 15, 1986, is summarized in the following paragraphs. At the conclusion of the seminar, consensus was reached on the major policy issues which must be addressed.

There was no attempt to reach consensus on the priority ordering of these issues.

3.2.1 Purpose of Regulation

Different goals of biotechnology regulation, such as protection of human health and the environment, quality control of the products of modern biotechnology, protection of agricultural resources, consumer protection, and the promotion of research and industrial development were discussed.

3.2.2 Subject of Regulation

A biotechnology product may be regulated using a process-based approach or a product-based approach. If the process is regulated, the applicable regulations are chosen solely on the basis of the process used, without regard for the product. If the product is regulated, regulation is based upon the inherent risks posed by that product, regardless of the method by which it was produced. A product-based regulatory approach may still require regulation of some or all aspects of the production process.

Some concern was expressed that the public perceives products of recombinant DNA and cell fusion techniques to be hazardous and will therefore ask for regulation of all biotechnology processes. However, it may not be scientifically supportable to single out genetically engineered organisms for special treatment, since many scientists feel that recombinant organisms are not substantially different from naturally-occurring organisms. From this perspective, the new technology is only a continuum of what was done in the past using traditional methods. In fact, it was argued the newer technologies allow more specific mutations, resulting in a product organism that is better characterized than one created by conventional mutation and selection and therefore poses a more easily manageable risk.

The consensus was reached that any regulatory scheme must be scientifically supportable, rather than developed solely to assuage public fears. It was further felt that a regulatory scheme centered around the techniques of modern biotechnology could result in inequities. For example, chemicals produced in biological systems could be subject to more stringent controls than similar products produced in a chemistry laboratory. Many felt that product regulation is a better basis for regulation than one which assumes that genetically engineered organisms are intrinsically more dangerous than organisms produced by other methods.

Finally, a discussion was entered into relating to the industrial activities which should be regulated when a potentially dangerous product is manufactured. Some participants argued for a "cradle to grave" approach in which regulation would begin at the research and development stage and carry through to the final disposal of waste products. Required technology could be specified by a variety of methods, such as orders or approvals. Those participants pointed out that creation of waste, which could be an environmental problem, is an inevitable part of the manufacturing process. Others disagreed, suggesting that regulation could begin at the product stage, setting out safety, efficacy, and purity standards for the product as well as regulating its use.

3.2.3 Adequacy of Existing Legislation

It was pointed out that environmental legislation was not designed to address the problems of biological contamination of the environment. In Canada, an inventory of legislation which could apply to biotechnology has been prepared by federal officials.[3] Determination of the applicability and adequacy of that legislation has not yet been made.

For product regulation there are certain regulatory structures in place. For example, as one participant stated, if a product "has any claims as a pesticide, it's irrelevant whether it's genetically engineered or not. It's controlled."

3.2.4 Regulation and Public Participation

The public participation issue was broken down into four areas: public confidence, public participation in the regulatory process, access to information, and the need for public education.

It was stated that public mistrust may lead to pressure for increased regulation.

American experience, it was pointed out, has demonstrated that it is difficult to convince the public that existing regulations will ensure protection of health and the environment.

One participant stated that public participation in the review or licensing process is necessary, "so that the public can see that, yes, government is doing the job they said they were

going to do". This right to participate will only be meaningful to the extent that the public has access to the necessary information to reach its own conclusions about the potential risks of an environmental release.

Provision of detailed information to the public concerning field releases of genetically engineered organisms was identified as one method of preventing unwarranted adverse public reaction. However, this is complicated by the need to protect the proprietary nature of certain industrial secrets.

Participants were of the opinion that the Canadian public has exhibited apathy, rather than concern, about the possibility of environmental releases of genetically modified organisms. Nonetheless, it was suggested, a latent public concern exists which would likely manifest itself if an open air testing of a biotechnology product occurred 'next door'. A number of participants suggested that, to prevent public doubts, industry and government should develop an effective educational program. People must be made aware of both the potential benefits and the risks of this technology. They should be informed that, "these things aren't viruses from outer space that are going to decimate the entire population". It was suggested that the thrust of such a program should be disemmination of general information about recombinant DNA, rather than specific, complicated, technical details of a proprietary nature.

3.2.5 Political Commitment to Regulation

One participant stated that biotechnology would have to be moved up on the "political agenda", before steps can be taken toward the creation or amendment of relevant legislation.

A regulatory scheme might be developed by consultation involving the various stakeholders but it was pointed out that elected officials must be committed to the process at the outset if such a consultative approach is to be successful.

3.2.6 Information Issues

The topic of information encompasses many issues, but two were identified by seminar participants as being of particular importance - the information needs of regulators and the issue of access to information.

The types of information regulators might seek could be subdivided into a number of areas: an inventory of current biotechnology activities, background information on the organisms involved, testing protocols and the burden of proof a company must meet in establishing the safety of a product.

It was stated that notification of the regulatory body should be the minimum requirement for a company that is about to undertake field tests of a product. It is difficult to define the point at which a product leaves the laboratory and enters the environment. For example, would testing inside a greenhouse be

considered field testing? Two reasons were given for the notification requirement. First, it ensures that government is aware of current biotechnology developments, the parties concerned, and the types of products involved. Secondly, public confidence is inspired if government is monitoring the activity.

If notification requirements were introduced they would have to specify the content of the notice and the parties to be notified. For example, should notification of the regulatory agency alone be required or should affected members of the public, such as those living in close proximity to the proposed testing site, also receive notice?

The necessary background information might include tests to determine how a genetically modified organism behaves in the environment. For example, scientists could develop tests to determine whether these new organisms behave differently from their naturally-occurring counterparts. If new recombinant organisms behave in substantially the same manner as those produced by traditional methods, then their future behaviour can be predicted more accurately. Past experience can then be used to increase predictive capabilities.

It was stated that risk management should proceed on a case-by-case basis, since more experience with genetically manipulated organisms is required in order to set general standards. This case-by-case process does not necessarily mean that a de novo assessment will take place for each product;

rather, general questions will have to be addressed, which will then be tailored and perhaps expanded in application to the particular product under study.

It was felt that the types of tests which will be required must be developed by scientists that are knowledgeable in the area. These tests would certainly differ from those used to evaluate the safety of chemicals, although those tests could provide a useful starting point. One suggested testing procedure was the creation of an environmental chamber which could be used to test the behaviour of 'released' recombinant DNA organisms in a controlled manner.

The regulator would also need to establish the burden of proof a company must overcome in order to establish the safety of a product.

It was recognized that it is difficult to both provide public information and protect trade secrets.

3.2.7 Compliance

Some seminar participants felt that there was a greater chance to obtain voluntary compliance with regulations from the biotechnology industry than from other commercial endeavours, since, as one participant stated:

> [The biotechnology industry] is small. It's new. It builds on natural processes. It's been subject to a degree of self-regulation that doesn't describe other industries, other developments.

Debate developed respecting the ability to monitor released genetically modified organisms. It was pointed out that it is possible to determine whether or not an organism carries particular genetic information. One such method is known as southern hybridization.[4]

3.2.8 Liability and Insurance

It was felt that issues relating to liability for damage by genetically engineered organisms are similar to those created by other forms of pollution, such as chemical contamination. This is because, as one participant stated,

> You're dealing with causation, scientific uncertainty; the fact that you may have a latency period between the event and the damages.

In other words, it is difficult to prove that a particular release of a contaminant resulted in damage which was only discovered much later, because scientific controversy often exists with respect to the probable cause of the damage. It is difficult to prove that an incidence of cancer was caused by exposure to a particular chemical at some time in the past. This difficulty is compounded when living organisms are the contaminants, because the onset of damage may occur many generations following the original release of organisms to the environment.

Another liability issue arises when government decides to approve a proposed field release. As one participant asked, "[O]nce there have been established protocols for testing and the

company complies with those protocols, who's liable?" By approving an industrial trial, the regulatory body is accepting responsibility for the risk assessment, and the concomitant liability.

The general difficulties in obtaining adequate liability insurance have affected the biotechnology industry, along with all other commercial endeavours. A company that is unable to obtain insurance coverage at a reasonable price may be precluded from engaging in activities that may be of great potential benefit to society. An illustrative example is the development of human vaccines:

> In the vaccine field, because of this discrepancy now with existing vaccines between the potential benefits for the public of vaccination and the potential liability, which is a deterrent to people who are in the business of producing, there is a very strong move to try and establish either some limitation of liability or some public insurance mechanism. The public good as opposed to the individual good is very strongly in support of vaccination but the liability from class action suits as well as of individuals just is totally out of keeping with the profit potential of the vaccines. So, it's one of those situations where there really is a call for some kind of fund or limitation.

A similar case for limitation of liability might be made for certain applications of biotechnology products.

3.2.9 Jursidiction

It was pointed out that potential applications of biotechnology span many areas of activity, including agriculture, mining, waste disposal, and production of food and drugs, and

therefore fall within a number of jurisdictional domains. Areas of responsibility of different government agencies must be clearly established. It was recognized that significant resources would be required to establish federal/provincial jurisdictions with respect to biotechnology.

It was stated that a coordinated national approach to regulation is desirable for two reasons. First, the fact that genetically engineered organisms, and most certainly microorganisms, can spread across provincial boundaries, makes environmental control a national problem. Furthermore, industrial development would be aided by requiring the same set of tests for an environmental release, regardless of the province chosen as a testing site.

3.2.10 Need for Coordinating Agency

Many federal and provincial governmental agencies are involved with biotechnology regulation. Therefore, it was stated, some sort of coordinating mechanism is necessary. Interprovincial consistency in regulation is also desired. Finally, Canada should attempt as far as possible to coordinate its policies with those in existence in other countries, since biological compounds can easily cross international boundaries.

One method of ensuring coordination is the development of a new regulatory scheme. This approach was rejected by some seminar participants as unrealistic. Since departments would

give some portion of their responsibilities to a new body while retaining residual duties, there may be a duplication of activities. Another problem pointed to was the time required to establish a new body.

An alternative suggestion was the creation of a coordinating body to foster the development of a comprehensive strategy. This body would facilitate information sharing, and coordination among the various government agencies. It might be endowed with some regulatory authority. This coordinating body could also be charged with the task of developing a guide or 'road map' that industry might use in determining the proper government agency or agencies to approach in order to obtain approval for a field release.

FOOTNOTES - PART 3

1. Irene Courage and Yvonne Skof, Policy Issues Raised by the Application of Biotechnology (Toronto: Canadian Environmental Law Research Foundation, October 1986).

2. Ibid., Chapter 2, pp 7-19.

3. Canada, A Report in Two Volumes to the Interdepartmental Committee on Biotechnology, Co-ordinated Study on Government Processes in Safety and Regulation of Modern Biotechnology (Ottawa: Ministry of State for Science and Technology, January 1986) Draft Report.

4. 'Southern hybridization,' (also referred to as 'Southern blotting') is a technique used to locate a specific DNA sequence in an organism. In Southern hybridization, a radioactively labelled piece of (single-stranded) DNA, called a DNA probe, is used to track down and locate the particular sequence of interest. The DNA probe is constructed in such a way that it will bind only to the specific DNA sequence being sought. In the testing procedure, the hereditary material (i.e. DNA) of the tested organism is broken down into fragments. This material is then exposed to the DNA probes. After testing, the tested material is washed. If the tested material contains the DNA sequence of interest, DNA probes will remain bound to it following the washing. (The binding of a probe is signalled by the presence of radioactivity).

   See: R.W. Old and S.B. Primrose, Principles of Gene Manipulation (Cambridge: Blackwell Scientific Publications, 1985), 8-9.

4. APPROACHES TO REGULATION IN OTHER JURISDICTIONS

4.1 International Developments in Biotechnology Regulation

Coordination of biotechnology policy at the international level has commenced. On December 2-3, 1985, the initial meeting of the Ad Hoc Group on Safety and Regulation of the Organization for Economic Cooperation and Development (OECD) was held in Paris to discuss with safety considerations arising from the application of recombinant DNA technology in industry, agriculture, and the environment. The mandate of the committee includes examination of approaches to be used in the risk management of recombinant DNA technology. The eventual goal of the OECD is to conclude an international agreement on protection of health and the environment, as well as enhance international trade in biotechnology. The committee has recommended that a case-by-case assessment be carried out prior to the use of biotechnology products in agriculture and the environment.[1]

Biotechnology policy development is being done in a coordinated manner within Europe. The Commission of the European Communities has developed six "action priorities" for biotechnology. These are: research programmes, funded pilot projects in beneficial areas of biotechnology application, policies to ensure the availability of agricultural product resources for industrial conversion, development of a European approach to biotechnology regulation, development of a European

approach to intellectual property, and the management and concertation of policies related to biotechnology. Community regulations either exist or are in draft form for: medicaments and veterinary medicines, chemicals and fertilizers, foodstuffs, worker protection, seeds, animal feedstuffs, plant protection products, animal reproductive technologies, hormones, toxic and dangerous waste, major accident hazards, cosmetics, and the registration of recombinant DNA research. An important issue in regulation is the ability of existing legislation to handle new biotechnology applications.[2]

In June, 1985, the European Biotechnology Co-ordination Group was formed. A subgroup, the European Committee on Aspects of Biotechnology (ECRAB) was formed to develop an industry position paper on safety and regulation in biotechnology. This paper was presented to the Commission of European Communities in April, 1986.

The major regulatory concern was identified to be release of live genetically engineered organisms into the environment. A suggested risk assessment scheme for these releases identified five developmental steps requiring risk evaluation:

1. project initiation;
2. contained laboratory testing;
3. small scale, non-contained experiments;
4. field applications; and
5. commercial applications.

A structure for risk assessment was presented in the paper. As a first step the donor, vector and host organisms are used in order to determine the proper level of containment necessary for research. This is followed by design of experimental and monitoring systems, establishment safety measures, evaluation of potential risks and planning of emergency response procedures.[3]

Another international development is the formation of an International Centre for Genetic Engineering and Biotechnology (ICGEB) by the United Nations International Development Organization, in order to promote biotechnology research and development in developing countries. The ICGEB aims to become an international centre for research projects of interest to developing countries, to provide state-of-the-art training in biotechnology to scientists from developing countries, and to collect information on biotechnology and biosafety for use by developing countries.[4]

4.2 Development of Regulatory Policy In The United States

During the 1970's the National Institutes of Health (NIH) developed guidelines for recombinant research done in laboratories with funding supplied by NIH. In 1983 NIH approved an application to field-test the "ice-minus" biotechnology product, which is intended to prolong agricultural growing seasons, but the experiment was halted by a court injunction, granted on the basis that environmental assessment of the test had not been done.

The Environmental Protection Agency has assumed regulatory authority on the legislative basis of the Toxic Substances Control Act. EPA approved an application for an experiment release in Monterey County, California, which provoked local opposition to the test. This approval was then revoked in 1986 after it was learned that the company in question had conducted unauthorized tests.

In a similar manner the United States Department of Agriculture has granted and then subsequently withdrawn approval for field testing of a livestock vaccine.

During recent years the U.S. administration has worked to develop an approach to biotechnology regulation and bills have been introduced into Congress. Bodies have been created with mandates to coordinate scientific policy and regulation.

At a conference in April, 1986, a number of speakers described the regulatory process in the United States as being in a "state of disarray."[5]

4.3 Federal Developments in Biotechnology Regulation

In 1983 the Canadian government introduced the National Biotechnology Strategy, administered by the Ministry of State for Science and Technology (MOSST). The main thrust of the National Strategy is to encourage industrial biotechnology development.

Certain biotechnology product areas are identified as priorities for commercial development. These are: health care,

mining and mineral leaching, plant strain development, nitrogen fixation, cellulose utilization, and waste treatment. As part of the National strategy, a National Biotechnology Advisory Committee was formed to advise the Minister of State for Science and Technology. The Committee is chaired by Dr. John Evans and is composed of 25 members drawn from universities, industry, and the federal government.[6]

MOSST oversees the Network Chairman Working Group on Biotechnology, which unites the chairmen of various biotechnology networks, such as BioNet (human and animal health care products), BioMinet (mineral leaching and metal recovery), and BioFor (forest-based industries).

The various networks are designed to bring together representatives from science, industry, and government in order to increase the flow of information amongst these different sectors. Each biotechnology area identified as a priority area for industrial development has its own network. The networks are intended to ensure that scientific research meets industry's needs and to foster the formation of cooperative ventures among network members. Every network conducts meetings at least once per year.[7]

Although the National Biotechnology Strategy has started to address the issue of clarification of a regulatory framework the main thrust of the Strategy is still the development of the biotechnology industry in Canada.[8]

An Interdepartmental committee of assistant deputy ministers has been functioning for several years. In 1986 the committee commissioned the report titled "Regulatory Issues Concerning Biotechnology in Canada", done by Beak Consultants Limited. This study, which recommends establishment of a coordinating agency for biotechnology, was discussed at a meeting of federal and provincial agencies on December 3, 1986. No decisions were made at that meeting which will affect the development of a national policy in the immediate future.[9] It is not known if MSST intends to proceed itself with establishment of such a coordinating body.

Establishment of such a coordinating agency was recommended by Dr. Evans in a speech given in Montreal on December 5, 1986.

Reporting to the Interdepartmental Committee, is a working group on Safety and Regulation, composed of representatives from Environment Canada, Health and Welfare Canada, the Medical Research Council, MOSST, and Agriculture Canada. This group produced the study titled "Coordinated Study on Government Processes in Safety and Regulation of Modern Biotechnology". The study provides a survey of potentially applicable legislation but no analysis or recommendations are contained in the study.

Environment Canada is presently developing a consolidated Environmental Protection Act which will include provisions of the Clean Air Act, the Environmental Contaminants Act, and parts of the Canada Water Act. It is possible that some provisions aimed at biotechnology regulation will be included in this initiative,

since the following reference to biotechnology appears in The Final Report of the Environmental Contaminants Act Amendments Consultative Committee, dated October, 1986:

> Although proposals dealing with biotechnology have not been formally addressed by this Committee, members recommend that the Ministers should ensure that the Environmental Contaminants Act in its amended version covers such issues.[10]

Thus the Environmental Contaminants Act, which will be consolidated with other legislation to form the federal Environmental Protection Act, may be amended to provide for regulation of biotechnology in some fashion. The recent Environment Canada report titled, From Cradle to Grave: A Management Approach to Chemicals advocates a systematic, preventative approach to the regulation of chemicals. The activities of concern include research and development, marketplace introduction, manufacture, transportation, distribution, use, and disposal. It is possible that a similar approach will be applied to the products of modern biotechnology. [11]

Agriculture Canada has recently prepared a memorandum, dated May 5, 1986, titled "Guidelines for the Registration of Microbial/Biological Pesticides." These guidelines, however, are intended to apply only to naturally occurring organisms. The memorandum specifically excludes genetically engineered or modified organisms:

> These guidelines do not apply to biochemical pest control agents nor to genetically engineered organisms. These latter groups will be addressed in a separate memorandum.[12]

The National Research Council biotechnology program is directed toward meeting the research needs of the modern biotechnology industry. Major projected areas of activity have been identified as: biochemical engineering, genetic engineering, protein engineering, cell biology, molecular immunology, applied microbiology, plant biotechnology, and marine biotechnology.[13]

4.4 Conclusion

This review of regulatory policy development in other jurisdictions, most notably in the United States and at the federal level in Canada, has demonstrated the inherent complexities of the task. This is hardly surprising, given the lack of information about potential effects, the fact that potential commercial applications cut across a number of jurisdictional boundaries and the growing public mistrust of new technologies, coupled with a demand for increasingly higher levels of environmental protection.

In the face of these difficulties, MOE can expect to receive applications for approval of field tests in the near future. Allelix has stated that it hopes to conduct field tests "within the next year or so".[14] The recommendations advanced in the following chapter are intended to assist the Ministry in developing regulatory procedures for both experimental tests and commercial activity.

FOOTNOTES - PART 4

1. OECD, "Safety in Biotechnology", (press release, Paris, December 9, 1985), 1-56.

2. Mark Cantley, "Concertation in Biotechnology: Getting Europe's Act Together" in The 1986 Washington International Conference on Biotechnology, April 21-22 1986, (Alexandria, Virginia: Inside EPA Weekly Report and the Center for Energy and Environmental Management, 1986), 1-14.

3. Europe, European Biotechnology Co-ordination Group, Subgroup European Committee on Regulatory Aspects of Biotechnology, "Safety and Regulation in Biotechnology" 4 (no.5) Swiss Biotech, 15-20.

4. Wafa Kamel, "1986 Washington International Conference on Biotechnology" in the 1986 Washington International Conference on Biotechnology, April 21-22, 1986 (Alexandria, Virginia: Inside EPA Weekly and CEEM, 1986), 1-6.

5. The 1986 Washington International Conference on Biotechnology, April 21-22, Virginia Alexandria.

6. Canada, Ministry of State, Science and Technology, 1984 Annual Report: National Biotechnology Advisory Committee (Ottawa: Minister of Supply and Services, 1985), at 10, 12, and 29-32.

7. Ibid., at 10 and 25.

8. Ibid., at pp 10 and 25.

9. Personal communication, Dr. Martin Boddington, December 1986.

10. Canada, Environment Canada and Health and Welfare Canada, Final Report of the Environmental Contaminants Act Amendments Consultative Committee (Ottawa: Minister of Supply and Services, 1986), at 69.

11. Canada, Environment Canada, From Cradle to Grave: A Management Approach to Chemicals (Ottawa: Minister of Supply and Services, 1986).

12. Canada, Agriculture Canada, "Guidelines for the Registration of Microbial/Biological Pesticides" (Memorandum, Ottawa, May 5, 1986), 1-24, at 1.

13. Maurice Brossard, "The Biotechnology Program" (November, 1986), 1 Biotechnology Bulletin, 1-2 at 2.

14. Allelix plans to field test two types of living, genetically engineered organisms "within the next year or so:"

1. a genetically engineered plant;
2. genetically engineered bacteria formed by inserting a pesticidal gene into non-pathogenic soil bacteria.

(Personal Communication, Mr. Michael Henry, Allelix, December 16, 1986.)

5. RECOMMENDATIONS

5.1 Introduction and Summary of Recommendations

The preceding chapters indicate the following salient points which must be recognized during development of MOE policy:

- biotechnology offers both potential benefits and the potential for environmental damage
- biotechnology regulation must be clarified
- the first regulatory task faced by MOE will be application for approval of an experimental release, quite possibly in 1987
- it is highly unlikely that a national biotechnology regulatory system will be in place before such an application is received.

Given the inherently slow pace of development of a national regulatory strategy, in conjunction with the rapid pace of industrial development, it is inevitable that the Ontario government and, more specifically, the Ministry of the Environment will be asked to consider potential environmental damage associated with an experimental field release of genetically altered organisms before a national regulatory strategy is in place.

It is for this reason that the Ministry must begin immediately to develop its own biotechnology regulatory policy, without waiting for action at the federal level. It is essential

that an Ontario policy be developed and put in place in order that Ontario citizens may receive the benefits offered by biotechnology without harm caused to the Ontario environment.

Any regulatory policy must include the four elements listed below:

- an adequate data-base
- clearly defined and realistic policy objectives
- legislative and administrative mechanisms for achieving those objectives
- adequate human and financial resources

This chapter sets out recommendations for action to be taken under each of the four headings listed above. Before turning to these specifics, however, it is useful to look forward to the probable developments of the biotechnology industry over the next few years and the ways in which the Ministry must respond to those events.

Applications for the release of genetically altered organisms to the environment have already been received by the Ministry[1]. As is indicated in Chapter 4, Allelix has announced that it hopes to conduct field tests in 1987.

At the present time, the Ministry does not have an adequate legislative basis upon which to evaluate such applications nor is it likely that legislative amendments and associated regulations can be put in place before the end of the year. For this reason an interim means of evaluating such applications for experimental field releases must be put in place immediately.

At the same time the process, including full public discussion, for considering the most appropriate legislative amendments which would provide a permanent, on-going approvals process must be initiated as soon as possible.

Successful field tests will then lead to applications for approval of commercial use of biotechnology products. A regulatory system for consideration of such commercial use applications must be in place by that time. Ideally, this would take the form of a national regulatory strategy with responsibility shared between the federal and provincial governments.

MOE faces, therefore, in order of sequence, the following requirements:

- establishment of an interim system for experimental release approvals
- establishment of a permanent system for experimental release approvals
- establishment of a regulatory system for commercial use, preferably done on a joint federal-provincial basis

Bearing in mind these requirements which must be met in the near-term, the recommendations of this report can be summarized as follows:

1. MOE should immediately begin the biotechnology policy development process without waiting for action at the federal level.

2. The first step in this policy development process should be release of a discussion paper setting forth MOE policy objectives and means of achieving them.

3. Policy objectives should include the following:

   . protection of the Ontario environment

   . clarification of Ontario regulation to allow industrial development in the province

   . enactment of measures which will ensure that no release to the environment of genetically altered organisms will be made without MOE approval

4. A policy decision should be made now to use the Evironmental Assessment Act on an interim basis for considering experimental field-release applications.

5. Following adequate public consultation, the Environmental Protection Act should be amended to provide a legislative basis for experimental field release approvals.

6. In conjunction with other jurisdictions, a system for regulating commercial use of biotechnology products should be put in place as soon as possible.

The remainder of Chapter 5 sets forth the project recommendations in more detail.

5.2 MOE POLICY DEVELOPMENT

5.2.1 Data-Base

It is recommended that MOE establish a data-base adequate for biotechnology regulation.

Information required falls into the categories listed below:

1. Biotechnology industry activity in Ontario
2. Biotechnology industry activity in other jurisdictions
3. Regulatory approaches being implemented or considered in other jurisdictions
4. Data sufficient to allow an assessment of potential environmental impacts (see 5.4 below)
5. Data needed to achieve compliance with regulatory requirements.

5.2.2 Policy Objectives

It is recommended that MOE develop and release for public comment a statement of policy objectives for regulation of the biotechnology industry.

Given the mandate of the Ministry to protect the environment of Ontario, it is recommended that such objectives be as follows:

1. **to ensure that no release of a genetically engineered organism to the Ontario environment is made without prior approval of the Ministry**
2. **to ensure that Ontario has an interim regulatory procedure for experimental release approvals in place as soon as possible, regardless of action taken by other Canadian jurisdictions**
3. **to ensure that a permanent procedure for experimental release approvals, resting upon an adequate legislative base, is in place as soon as possible**

4. **to work with other jurisdictions to establish a national regulatory system for commercial use of biotechnology products**

5.2.3 Legislation

The statutory basis for environmental protection is found primarily in the Environmental Assessment Act[2], the Environmental Protection Act[3], the Pesticides Act[4], and the Ontario Water Resources Act[5].

All of this legislation was enacted prior to development of the biotechnology industry and it is not, for that reason, designed specifically to protect against environmental effects associated with that industry.

The Environmental Assessment Act does not apply at this time to private-sector activity. Other than the interim use of the Act, recommended below, it is not suggested that the Act be used to regulate the biotechnology industry in the absence of comparable regulation of other private-sector activity.

Under the terms of the Environmental Protection Act it is illegal to release a harmful contaminant to the environment[6]. A "contaminant" is defined as:

> any solid, liquid, gas, odour, heat, sound, vibration, radiation, or combination of any of them resulting directly or indirectly from the activities of man that may,
> (i) impair the quality of the natural environment for any use that can be made of it,
> (ii) cause injury or damage to property or to plant or animal life,
> (iii) cause harm or material discomfort to any person,
> (iv) adversely affect the health or impair the safety of any person,
> (v) render any property or plant or animal unfit for use by man,
> (vi) cause loss of enjoyment or normal use of property, or
> (vii) interfere with the normal conduct of business.[7]

It is not certain that a genetically altered organism would fall within the definition of "contaminant". Regulation based upon this uncertain legislative authority would be open to court challenge.

Given the broad definition of pesticide contained in the Pesticides Act, it is believed that genetically engineered pesticides, either of an experimental or commercial nature, could be successfully regulated under the Pesticides Act, (in conjunction with the federal Pest Control Products Act[8]). A 'pesticide' is defined as,

> any organism, substance or thing that is manufactured, represented, sold or used as a means of directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest or of altering the growth, development or characteristics of any plant life that is not a pest and includes any organism, substance or thing registered under the Pest Control Products Act (Canada)[9];

Therefore, it seems that MOE could apply the Act to modern biotechnology products. It is suggested that a review committee (the Ontario Pesticides Advisory Committee or another external committee) begin now to review current interpretations, practices and procedures under the Act, in order to identify any modifications that might have to be made in their application to genetically engineered pesticides.

It does not appear that the Ontario Water Resources Act provides a basis for regulation of the biotechnology industry.

As is set out below in section 5.3, it is recommended that the Environmental Protection Act be amended and that the amended Act provide the primary basis for biotechnology regulation in Ontario.

5.2.4 Resources

It is recommended that MOE assess present financial, staffing and equipment resources and determine additional resources required to implement its biotechnology regulation policy.

Internal policy development will require an assessment of MOE's ability to implement that policy. Therefore, an inventory and analysis of MOE resources which could be applied to biotechnology regulation should be undertaken. A report of manpower expertise should be prepared, along with an estimate of the educational upgrading which would be required for both professional and technical staff. The presently used testing protocols, equipment, and monitoring devices, which could be applied to biotechnology should be identified. An accounting of available or potentially available financial resources must also be made.

It is recommended that MOE develop its internal and external expertise in biotechnology matters.

It is likely that MOE will have to expand existing resources in terms of personnel and equipment.

The acquisition of appropriate human resources is probably best achieved by creating an external advisory committee, similar in structure to the Ontario Pesticides Advisory Committee. Mechanisms would have to be developed to ensure confidentiality of trade secrets.

In addition to external experts, internal expertise should also be developed. Knowledge in the field of biotechnology will

increased once experience is gained with environmental releases and new testing procedures. Staff at MOE must be able to interpret the impact of this new information, and respond with the appropriate modifications to the regulatory scheme or its implementation.

Internal expertise should be acquired by upgrading the education of employees already familiar with one or more of the scientific disciplines encompassed by biotechnology, so that they are aware of the role played by related disciplines. Scientific experts should be familiar with many of the following areas of knowledge: the basic and applied sciences, biochemistry, ecology (especially microbial ecology), genetics, microbiology, molecular biology, toxicology.[10] Technical staff will also have to be trained to administer tests for biological contamination, and to use monitoring procedures designed to track modified organisms and particular introduced genes. Finally, current regulatory staff will need to undergo educational programs to familiarize themselves with the concepts and terminology of biotechnology.

It is recommended that MOE upgrade facilities and equipment so that it is capable of testing for harmful effects of released organisms and able to monitor biotechnology products in the environment.

Secondly, facilities and equipment may have to be upgraded. Most model ecosystem or microcosm testing systems presently in use are not subject to high levels of physical containment. It may be necessary to establish contained ecosystem test sites, either at universities or at government or private research institutes. The use of high containment facilities may be

minimized by basing certain predictions on the behaviour of 'safe' organisms. Tests with these 'safe' organisms could be used to develop data about the efficacy of various test systems or to establish criteria against which to evaluate test results. However, eventually these 'safe' organisms would have to be tested against their genetically engineered counterparts, in order to compare their survival capabilities and environmental impacts. At this point, properly contained facilities would be required.[11]

Furthermore, new monitoring equipment will be needed to trace microorganisms and their inserted genes. Monitoring of the released organism, and the foreign genetic material it contains is important. Monitoring ensures that industry is complying with the regulatory process, and provides information on the activity of modified organisms which can be used to modify and improve the regulatory scheme. The predictive capabilities of the required tests can be analyzed by comparing the anticipated and the actual behaviour of the released organisms. Ecological cycles should also be monitored, so that potential problems will be recognized before they get out of hand.

There are existing mechanisms, such as the Southern hybridization technique, for testing an organism to determine whether it contains a particular gene. This technique, however, is a laboratory technique that may have to be adapted for mass field monitoring. It is based on the concept of using a

complementary DNA 'gene probe' to determine if the organism in question contains the DNA segment of interest. There are several limitations to such a technique. One must predetermine the DNA sequence that is being sought, so that monitoring is effectively limited to experiments the government knows are being carried out. Furthermore, since the technique is not selective, every organism in a given sample must be tested. Finally, difficulties may be encountered in separating microorganisms from environmental contaminants, such as soil. If an uncontaminated sample is not obtained, the technique may not work. Therefore, more refined monitoring techniques should be developed.

5.3 EXPERIMENTAL RELEASE APPROVALS

5.3.1 Interim Measures

It is recommended above that MOE ensure that no release of a genetically altered organism is made to the Ontario environment without prior Ministry approval. At the present time, however, there is no legislative basis to prohibit such a release. It is recommended below that the Environmental Protection Act be amended in such a manner as to provide this legislative authority. It is recognized, however, that such a legislative amendment process will take time and it is suggested that there is need for an interim approvals procedure which can be used prior to amendment of the EPA.

It is recommended that MOE use the Environmental Assessment Act to regulate experimental releases of genetically altered organisms to the environment, until an approval procedure under the Environmental Protection Act is implemented.

The Environmental Assessment Act is an existing statute which could be used immediately for consideration of experimental releases of genetically modified organisms. This is only an interim solution, since the Act was not designed with biotechnology applications in mind. Nonetheless, it is preferable to a total lack of jurisdiction over experimental releases.

The Environmental Assessment Act does not apply to private undertakings unless they are 'major' and are designated by regulation as subject to the Act.[12] Since most biotechnology companies are small enterprises, there is a good possibility that

the companies or their proposed releases are not 'major' private undertakings. Furthermore, the Environmental Assessment Regulation states that research undertakings are exempt from the provisions of the Environmental Assessment Act. A 'research undertaking' is defined as "an undertaking that is carried out for the purpose of or that consists of research", which is in turn defined to include measuring, monitoring and testing.[13] Most currently anticipated environmental releases of genetically altered organisms will be for measuring, monitoring, and testing purposes.

For the Environmental Assessment Act to apply, any environmental release of organisms created using modern biotechnological techniques must be designated as "a major commercial or business enterprise or activity" under section 40(a). Then a regulation must be passed under section 40(d) of the Act, stating that these activities are undertakings to which the Environmental Assessment Act applies. Finally, the exemption for research must be amended to state that a research undertaking does not include environmental releases of (living) organisms modified by modern genetic manipulations.

It is recommended that special procedures be implemented to make the Act more suitable for regulation of biotechnology experimental releases.

The problem of the extensive time and resources required by environmental assessments could be addressed in part by the development of special procedural guidelines for the assessment

of biotechnology releases, which would be designed to limit the length of the assessment.

The necessary power is found in section 18(2), which states:

> The Board may determine its own practice and procedure in relation to hearings and may, subject to section 28 of the Statutory Powers Procedure Act and the approval of the Lieutenant Governor in Council, make rules governing such practice and procedure and the exercise of its powers in relation thereto and prescribe such forms as are considered advisable.

Pre-hearing conferences, the preparation and exchange of witness statements, the use of interrogatories, the appointment of a class representative under section 18(15) could all be considered as streamlining procedures.[14]

5.3.2 Permanent Measures

5.3.2.1 Amendments to the Environmental Protection Act

It is recommended that the definition of "contaminant" in the Environmental Protection Act be amended so as to specifically include organisms created by modern biotechnology techniques.

In addition to the general prohibition against releasing a harmful 'contaminant' into the environment, there are a few preventative measures which may be useful if genetically engineered organisms are subject to the Environmental Protection Act. By virtue of section 17 a Director under the Act may order a person in control of an undertaking to take preventative measures or to have emergency equipment on hand, if it is likely that a discharge of a contaminant from the facilities would cause environmental harm. Section 8 requires certificates of approval for certain industrial activities, such as the construction of a plant that may discharge a contaminant into the environment. It reads:

> 8.(1) No person shall,
> (a) construct, alter, extend or replace any plant, structure, equipment, apparatus, mechanism, or thing that may emit or discharge or from which may be emitted or discharged a contaminant into any part of the natural environment other than water; or
> (b) alter a process or rate of production with the result that a contaminant may be emitted or discharged into any part of the natural environment other than water or the rate or manner of emission or discharge of a contaminant into any part of the natural environment other than water may be altered,
> unless he has first obtained a certificate of approval issued by the Director for the methods or devices or both to be employed to control or prevent the emission or discharge of any contaminant into any part of the natural environment other than water.

Although one may require such a certificate for the construction of new facilities to produce modern biotechnology products, the section does not appear to apply to environmental releases.

Section 27 requires a certificate of approval for a waste management or waste disposal site. Presumably these certificates would be required to operate waste disposal systems which process waste from biotechnology companies or which use genetically engineered microorganisms to treat waste. However, it is not certain that an approval would be required for the testing of waste-treating organisms in the open environment. Section 27 does not refer to research per se:

> 27. No person shall use, operate, establish, alter, enlarge or extend,
>
> (a) a waste management system; or
> (b) a waste disposal site,
>
> unless a certificate of approval or provisional certificate of approval therefore has been issued by the Director and except in accordance with any conditions set out in such certificate.

Waste is defined to include "industrial waste".[15] Waste disposal and waste management sites are also defined in section 24:

> 'waste disposal site' means any land or land covered by water upon, into, in or through which, or building or structure in which, waste is deposited or processed and any machinery or equipment or operation required for the treatment or disposal of waste;
>
> 'waste management system' means all facilities, equipment and operations for the complete management of waste, including the collection, handling, transportation, storage, processing an disposal thereof, and may include one or more disposal sites.

It appears that research concerning the activities of genetically engineered microorganisms may constitute a "use" of an "operation required for the treatment and disposal of waste", and thus fall within the purview of the Act. Another complication arises if the waste is a commercially useful product. It has been held that waste PCB fluids which have been treated and processed to form a fuel are not "waste" within the meaning of the Act.[16] Finally section 50 enables certain wastes, waste management systems, and waste disposal sites to be exempted from the application of this Part, by regulation. Therefore it is unclear whether all waste treatment processes using genetically engineered microorganisms or processing waste from biotechnology companies would be subject to the approval process.

Furthermore, none of these approvals processes were designed with the objective of regulating biological contaminants. For this reason it is preferable to replace them with a new approvals process, specifically intended to achieve the task at hand.

It is recommended that a section be added to the Environmental Protection Act, establishing an approval system for environmental releases of genetically altered organisms.

As noted above, authorities consulted during the course of this project were not able to predict, in general terms, environmental effects which might be associated with biotechnology releases and were of the opinion that such prediction could only be one with respect to a particular situation.

It is recommended that, at least initially, all approvals be done on a case-by-case basis.

It is recommended that regulation under the amended Environmental Protection Act be done on the basis of product rather than process, recognizing that regulation of some or all aspects of the industrial process may still require regulation.

A regulatory scheme based on product analysis is preferred to a scheme based on the process used to create the product.

A process orientation would require all products created by modern technologies, such as recombinant DNA and cell fusion, to pass through the regulatory scheme. In the report titled "Coordinated Framework for Regulation of Biotechnology," the focus upon process was criticized for the following reasons:

> 1. While certain processes can be used to produce new combinations of traits in microorganisms; their use does not necessarily mean that new combinations of traits have been formed.[17]
> 2. Genetic engineering processes do not necessarily produce organisms that present risks, nor are non-engineered organisms necessarily safe.[18]
> 3. [Since] the process-based approach would single out certain techniques for regulation, it would result in market distortions that favored the more traditional techniques even though the newer techniques could be as safe or safer.[19]

In a product-based approach, regulation would be based upon the risk which the product poses to the environment. This approach is more scientifically supportable. In its discussion of potentially dangerous microorganisms, the report referred to above cited the following factors as signals that a microorganism may present a reviewable risk of harm. Particular attention should be given to:

Microorganisms that
(1) are used in the environment,
(2) are pathogenic or contain genetic material from pathogens,
(3) contain new combinations of traits (e.g. organisms that are genetically modified to contain genetic material from dissimilar source organisms and organisms that are non-indigenous).[20]

These same criteria could be applied to macroorganisms.

The product focus is preferred because it does not penalize the modern biotechnology industry by subjecting it to greater scrutiny than traditional technologies while ensuring environmental protection. It should be clearly understood, however, that even with the product-based approach recommended here, some aspects of the industrial production process must be regulated. Regulation only of the finished product with respect to such things as storage, transportation, use and sale will not provide adequate regulatory protection.

To ensure environmental protection, regulation should start with initial field tests and continue through to disposal of industrial waste. This is because certain concerns cannot be adequately addressed at the production stage. Pre-production notification requirements enhance the monitoring capabilities of a regulatory body. Containment of non-debilitated organisms, during their production, is important from both an environmental and an occupational health aspect. Accidental environmental escapes of microorganisms from the production stage may not be a grave concern when the escaped organism is a debilitated form of E. coli. However, the situation is more serious with respect to microorganisms tailored to survive and multiply in the

environment. Finally, most industrial waste is formed during the production process. Pure product regulation would not allow the government to specify the composition and intermediate handling of industrial wastes.

It is recommended that the Environmental Protection Act be amended to establish an approvals procedure for the release of living biotechnology products by developing methodologies for: hazard identification, exposure assessment, dose-response assessment, and risk characterization.

The release of living biotechnology products into the environment is a unique problem. These products have the ability to reproduce and multiply. They may present more complex problems than the introduction of exotic species into a new environment. In fact many of these products are specifically engineered so as to change their traditional ecological role. Furthermore, one must monitor not only the released organism, but also the fate of the inserted gene (which may be transferred either horizontally or by reproduction). Finally, these new products are often engineered to survive in the environment, presenting new issues with respect to containment.[21]

There are four major components of the assessment procedure: identification of the hazard, exposure assessment, dose-response assessment, and risk characterization.[22]

Hazard identification, or the attribution of adverse effects to a product, is a major problem. Tests to predict the survival, growth, multiplication and dispersal of a modified organism, and its possible deleterious effects, are still in the developmental stage. There is no existing data base against which to compare

and interpret the results of such experiments.[23] Predictive capabilities are especially low where an organism has been modified to overcome limiting factors in the environment, or to affect ecological processes such as nutrient cycling.

Exposure assessment, which defines the conditions for exposure to the identified hazard, requires the development of tests to measure the potential for an organism's multiplication and dissemination. The likelihood of transfer of the introduced genetic material must also be studied.[24]

A dose-response analysis must then be carried out. With chemicals, the primary measure of dose is the concentration of the chemical. For biotechnology products, the operative measure is population density. Studies must be carried out to determine if there is a threshold concentration of organisms which must be surpassed before harmful consequences will result.[25]

A quantitative analysis of the above three factors will lead to a characterization of the risk. In characterizing the risk one must consider the harm that could result from both small-scale research tests of relatively pure products, and the large-scale release of possibly less pure commercial products.[26] Quantitative risk assessment is very difficult at present, because only crude tests are available for assessing the ecological hazards of a product, and the exposure levels it will reach. These problems are compounded by the fact that one must consider not only the single product, but the cumulative effect

of all biotechnology products which are released in the area or its environs.[27]

Finally society must arrive at a set of criteria as to what are acceptable or unacceptable risks. This is perhaps the most difficult task of all.

5.3.2.2 Data Required to Assess a Particular Field Application[28]

A number of questions have to be addressed to assess a proposed field release of a genetically modified organism. These have been set out in Table 1, which follows.

A description of the host and donor organism (or donor organisms, in the case of cell fusion) would be required. In the case of recombinant DNA techniques a description of the vector used would also be necessary. The method used to create the modified organism would have to be explained in detail and the inserted DNA would have to be characterized.

Ecological information about the donor(s), host, and modified organism would also be provided, along with the results of any pre-release assessments.

Finally, a description of the proposed field trial would be required, including a description of the monitoring procedures and emergency response plans.

TABLE 1

DATA REQUIRED TO ASSESS AN APPLICATION FOR A FIELD RELEASE OF A BIOTECHNOLOGY PRODUCT

1. Identification of Host and Donor Organism (or Donor Organisms in Case of Cell Fusion)
   - classification, source, strain & history of behaviour
   - organism's reproductive cycle
   - organism's capacity for genetic transfer
   - extent of genome characterization
2. Vector (for Recombinant DNA)
   - method of construction of vector
   - ability of vector to survive, independent of host
   - genetic composition of vector
   - host range of vector
   - frequency of transfer of vector
   - if vector is 'disarmed', the probability of remobilization of the vector
3. Description of Modified Organism
   - source and function of DNA
   - method of vector introduction (or of cell fusion)
   - amount and nature of donor and/or vector DNA remaining in organism
   - test results re: genetic stability of inserted DNA

- phenotypic expression of introduced DNA in modified organism, under a variety of environmental stresses
- reproductive cycle of organism
- extent of characterization of genome
- characterization of the site of modification in the recipient genome
- rate and level of expression of the introduced genetic material
- procedures used to verify genetic structure of recombinant organism

4. Inserted DNA Sequence

- source of DNA
- characterization of DNA
- function of gene: expression of the gene in the donor and the host
- data available to show that the introduced gene has no long-term deleterious effects

5. Ecological Information about Donor, Host, and Modified Organism

- habitat and geographical distribution
- physical and chemical changes affecting survival, growth, multiplication (such as, temperature, humidity, dessication, and UV radiation)
- host range

- interactions with other organisms in the environment (competition, prey, hosts, symbionts, predators, parasites and pathogens)
- role in biogeochemical or biological cycling processes
- pathogenicity, infectivity, toxicity, virulence, or role as a carrier of pathogens
- chronic effects on ecosystem of a biotechnology product and its derivatives
- ability of organism to form long-term survival forms, such as seeds, spores, etc.
- major phenotypic alterations which may alter community structure (e.g., nutrient production)
- changes which affect an organism's reponse to nutrient limitations

6. Pre-Release Risk Assessment

- results of microcosm, greenhouse, or growth chamber experiments under spectrum of environmental conditions expected within the release area and surrounding environment

  RE: survival, growth, multiplication, dissemination, frequency of transfer of genetic information, adverse effects on non-target organisms, effects on cycles, comparison of ecological behaviour of modified organism with that of the parent strain

- evaluation of whether genetic modification would alter the potential hazard posed by an organism
- list of potential hazards which were evaluated
- precautions taken to minimize risks
- analysis of consequences of the organism remaining in the environment beyond the planned time period
- cumulative risk of multiple introductions of the same or different organisms (where applicable)

7. Field Trial

- aim of proposal
- benefits of using genetic engineering approach, over other approaches
- what will be evaluated
- number of organisms to be released and their reproductive capabilities
- description of test site and immediate surroundings: describe native species and identify environmental characteristics which affect survival and dispersal
- containment measures available
  a) physical: barriers, plastic liners
  b) biological: conditional lethal mutants
- introduction protocols
- facilities available at site
- work method and supervision

- release protocols which have been designed to minimize risk
- on site worker protection
- procedures to be followed at end of experiment
- likelihood of a general commercial release should the field test prove successful

8. Monitoring
   - description of monitoring procedures
     a) frequency of sampling
     b) data sought
     c) sensitivity: limits of detection for survival, dissemination and nontarget interactions
   - rationale for monitoring system chosen
   - characteristics of organism which permit, or aid identification
   - methods for monitoring biological or biogeochemical processes likely to be affected
9. Emergency Response Plans
   - procedures available to control or eliminate the organism in an emergency situation
   - procedures available to deal with extreme environmental conditions (e.g., floods)

It is recommended that tier testing not be implemented until further knowledge is obtained about environmental releases of biotechnology products.

Tier testing implies some level of standard setting; therefore, it is premature at this time. Tier testing suggests that the requisite tests be carried out in succession: the first test being the organism's ability to survive; the second being its ability to multiply; the third being its ability to transfer genetic traits; and the fourth being its ability to cause environmental damage. If, for example, there is no probability that an organism will survive and multiply, it is unnecessary to test for the probabilities of gene transfer or environmental harm.

However, the process is not that simple. Probabilities of survival and multiplication may approach zero but are rarely, if ever, equal to zero. Thus certain standards must be set. For example, what probabilities are close enough to zero to warrant no further testing? What perceived deleterious effects require some data for potential environmental harm notwithstanding that the probability of survival is almost nil? In the absence of such standards, tier testing cannot be done.

It is recommended that testing protocols, specifically designed to test the environmental fate and ecological effects of released biotechnology products, be developed.

Tests developed to measure chemical contamination are not adequate to test for the potential deleterious effects of genetically engineered organisms released to the environment.

While hazard identification and exposure assessment are independent exercises for chemical compounds, the same is not necessarily true for biological contaminants. Environmental factors which affect an organisms's growth, may also affect the traits it exhibits.[29] Also, chemicals will affect related species in a similar manner, so that 'surrogate species' can be used to test for their effects. The same is not true for pathogenic or parasitic microorganisms, which may have severely restricted host ranges.[30] Furthermore, the range of tests required for living organisms is greater. Tests are required to study their environmental fate (i.e., survival, growth, etc.) and their effect on ecosystem cycles.

In addition to standard toxicity tests, model ecosystem tests must be carried out for modified organisms. These test systems, which are designed to simulate the external environment, allow scientists to study the ecosystem effects of an organism under contained conditions.[31] A model ecosystem is judged on the basis of its design, the source of its environmental material, the manner in which that material was introduced into the test system, and the range of environmental conditions under which the organism was tested.[32] In order to make this testing process meaningful in a regulatory context, standardization of the model ecosystems to be used,[33] and the types of tests to be carried out[34] is needed. Furthermore, the test system should be analyzed to determine how accurately it represents the environment it is meant to model.

It must be recognized that these tests are imperfect since the environment tends to become oversimplified. Processes become uncoupled, and not all the flora and fauna are represented within the test system.[35]

It is recommended that mathematical and statistical research be undertaken to support the development of the above-mentioned testing protocols.

The difficulties described above indicate that statistical and mathematical analyses must be used to support test results. The model systems must be calibrated, by measuring to what extent the predicted behaviour of organisms agrees with their actual behaviour in the field.[36] Mathematical models should also be developed to help analyze the experimental data, especially with respect to an analysis of the effects of time or very small ecosystem changes.[37]

Statistical methods must also be developed so that meaningful confidence intervals can be established for these predictions. Standard procedures for extrapolating the results of these tests to predict the behaviour of the organism in the field, and from one site to another, are required.[38]

Tests should also be developed to determine whether genetically engineered organisms behave the same way in the environment as do naturally mutated organisms. If this is the case, then our predictive capabilities are increased.

It is recommended that risk assessment procedures include provisions for adequate public consultation.

Public participation is a necessary component of the approval process. A balance must be reached to enable citizens of this province to provide meaningful input into the regulatory process without unduly hampering industrial development. Public participation makes more information available to the decision-makers, and enables the public to develop confidence in the regulatory system.

Trade secrets of business should be protected, except insofar as they are directly related to the environmental hazard posed by the biotechnology product.

To ensure meaningful public participation, the public must receive adequate notice of pending approvals, have access to the information upon which a determination of safety is made, and have an opportunity to comment on the decision, either before a tribunal or in the form of written submission.[39] Public participation in the process should be encouraged by educating people about biotechnology, and providing intervenor funding. The education component should familiarize the public with the general principles of biotechnology, as well as its potential benefits and risks. People should also be made aware of their right to participate the approval process, and the procedure to be followed to take part in the review.

5.4 COMMERCIAL REGULATION

The recommendations advanced in the preceding sections were intended to provide interim and permanent procedures for the consideration and approval of experimental field releases of living, genetically engineered organisms. The remainder of the chapter deals with regulation of commercial production and use of living biotechnology products.

For a number of reasons, including uniformity of standards and access to increased resources, it is preferable for biotechnology commercial regulation to be done on a national basis. As is described in Chapter 4, the federal government is presently developing a regulatory policy and it is recognized that MOE will assist in that process.

Large-scale commercial use poses potential environmental consequences greater than small-scale experimental releases. The need for an adequate regulatory approvals procedure is greater, therefore, with respect to commercial use than experimental releases. Although recognizing that the matter does not lie within MOE jurisdiction, it is suggested that MOE work to ensure that there is no commercial use of a living genetically engineered organism in the open environment, until a national regulatory strategy is in place. Failing that, commercial use should not be allowed in the absence of approval under the amended provisions of the Ontario Environmental Protection Act. Again recognizing that this is something which lies largely

outside the jurisdiction of the Ministry, it is suggested that MOE work toward implementation, as soon as possible, of a national regulatory system.

It is recommended that consideration be given to amendments to the Environmental Protection Act to allow commercial regulation on a co-ordinated, national basis.

Amendments to the Environmental Protection Act referred to earlier were intended to provide a legislative basis for consideration and approval of experimental releases. It will be necessary to consider possible further amendments to EPA to allow it to be used, in conjunction with legislation administered by other agencies, for national regulation.

It is recommended that a coordinating body or mechanism be established to ensure consistency in the application of environmental criteria to biotechnology products.

MOE's jurisdiction over biotechnology is likely to be shared with various federal, provincial, and municipal agencies. Therefore mechanisms for cooperation amongst these groups must be developed. Considerable resources, in terms of time and money, will be needed to reach accords among the various jurisdictions with respect to their respective areas of responsibility. Furthermore, since provinces may not have access to required resources at the initial stages of biotechnology development, they may agree to have the federal government take the lead regarding approvals for environmental releases, until such time as they are in a position to perform their own assessments.

The large number of ministries with a stake in biotechnology makes a coordinating mechanism necessary. There is a need for uniformity in the treatment of biotechnology products among the provinces. Interdepartmental cooperation and consistency in processing approvals is also desirable. Otherwise two types of problems may occur:

> One is that industry could be forced to run a gamut of agencies and spend a lot of time and effort going through the maze. The other is that industries could get around the regulations of one agency by going to another.[40]

Therefore consistency in the application of environmental protection criteria is required.

It is recommended that the coordinating body develop and maintain an electronic data base, containing scientific information for use in the regulation of biotechnology.

An electronic data base, containing non-proprietary information should be set up at the national level. Any government body involved in the regulation of biotechnology should have free access to such information. Also, members of the public should be able to access this information through the administrator of the data base. Experts should be made available to the regulating bodies to aid them in interpreting this information. Should a data base fail to be set up at the national level, MOE will be responsible for providing this information to those involved in the approval process.

The data base could be divided into various areas:

1. The classification and past history of organisms used in genetic engineering, as an aid in predicting ecological and other environmental effects;
2. The results of experiments comparing the behaviour of genetically engineered organisms and their naturally occurring counterparts in the environment, as a predictive aid;
3. The development of criteria "against which to predict test results or predict environmental consequences" as experience makes this data available.[41] This data might include relationships between genetic structure and the traits exhibited in response to various environmental stresses;[42]
4. A registry of proposed and current field releases, developed as a result of notification requirements; and
5. Results from the monitoring of industrial activities. These data can be used to identify new risks, and assess the efficacy of the regulatory system in preventing environmental harm.

It is recommended that an educational program, directed at industry, municipalities and the public be undertaken.

Industry requires regulatory guidelines, and a guide to the government agencies it must approach in order to obtain approvals. Municipalities should be kept informed of biotechnology related issues which fall within their jurisdiction, such as those affecting sanitary sewers.

Furthermore they should be kept informed of any applications for testing which are planned to take place within their municipal or regional boundaries. By keeping them informed, and allowing them to voice their opinions during the approval process, one is less likely to encounter local opposition to an approved field test. The public should also be educated about biotechnology, in general, and their right to participate in the approval process. This education function could be undertaken by the coordinating body.

It is recommended that the federal government provide resources for biotechnology regulation, that it is in the best position to provide, such as scientific and legal research.

The federal government should be pressed to provide resources that it is in the best position to provide. These could include the preparation of a scientific data base with information useful in environmental assessments, expert biotechnology consultants, and perhaps testing facilities which require a large financial outlay. The federal government could also undertake research, or fund research, to be used in policy development. Resources could be allocated to undertake legal research on methods of regulation and associated issues. Scientific research could include among other things:

1. empirical research on the ecology of organisms used in biotechnology;
2. studies of factors affecting the environmental risk of genetically modified organisms;

3. development of testing protocols designed to reproduce the external environment, including testing to estimate the predictive capabilities of the test system;
4. refinement of monitoring techniques currently used to identify genetically altered organisms;
5. the development of procedures designed to enhance the environmental safety of organisms (e.g., protocols for chromosomal insertion of a genetic trait to minimize the possibility of transfers; the development of conditional lethal mutants that self-destruct after performing their function);
6. the development of standard risk assessment methodologies; and
7. the eventual development of a classification scheme for host and donor organisms and genetically modified organisms, on the basis of their potential risk to human health and the environment.

It is recommended that the national strategy address the question of insurance. However, it is suggested that a limitation of liability for the biotechnology industry should be cautiously considered.

The major liability issue which arises with respect to the biotechnology industry is: Should we limit the liability of companies involved in risky endeavours which are for the public good, such as the development of vaccines? In general, limitations of liability should be avoided since they tend to

remove some of the incentive toward safe industrial practice. However, a case could be made for government insurance or a limitation of liability in special circumstances.

For the most biotechnology applications, it appears that sufficient economic incentives are available to encourage product development.[43] In these cases, the novel approach to insurance, taken by the Association of Biotechnology Companies provides a useful insurance model. The main drawback of the scheme is that the "proposed coverage limits will be $1 million per company."[44]

Two essential features of the scheme are a rigorous risk management program, and an insurance premium linked to the anticipated risk of the endeavour. The compulsory risk management program will enhance environmental safety:

> The risk management program will provide resources to all participating biotechnology companies to minimize current liability exposures, and to develop programs that continuously evaluate new product liability issues.[45]

The method of arriving at premium payments also encourages safety, since it provides an economic stimulus to avoid high risk projects. The premium system is described as follows:

> Initial product liability insurance will separate biotech companies into at least four or more risk categories, depending upon their products: in vivo therapeutic, in vivo diagnostic, in vitro diagnostic and other (e.g., environmental, chemicals, etc.). Products with the greater liability will have the greater premium.[46]

It is submitted that this type of insurance program is preferable to a limitation of liability, since it provides economic incentives for safety programs.

Benefits offered by biotechnology can only be achieved if regulation is clarified and environmental protection ensured. It is hoped that the findings and recommendations of this project will assist in that process.

FOOTNOTES - PART 5

1. Letter from then Minister of the Environment, Mr. Morley Kells, to Doug Macdonald, March 12, 1985.

2. Environmental Assessment Act, RSO 1980, c.140.

3. Environmental Protection Act, RSO 1980, c.141, as am.

4. Pesticides Act, RSO 1980, c.376, as am.

5. Ontario Water Resources Act, RSO 1980, c.361, as am.

6. Environmental Protection Act, RSO 1980, c.361, 3. 13, as am. RSO 1983, c.52, s.4.

7. Ibid., s.1(c), as am. 1983, c.52, s.1(1).

8. Pest Control Products Act, RSC 1970, c P-10, as am.

9. Pesticides Act, RSO 1980, c.376, s.1(f).

10. James W. Gillett, "Risk Assessment Methodologies for Biotechnology Impact Assessment" (July 1986) 10 Environmental Management, 515-532, at 528.

11. Ibid.

12. Environmental Assessment Act, RSO 1980, c.140, s. 3(b), Proclaimed in force January 16, 1977, Proclamation dated December 15, 1976.

13. Regulation Made Under the Environmental Assessment Act, RRO 1980, Reg. 293, section 12, as am. by O. Reg. 841/81, s.5.

14. Barry E. Smith, "Practice and Procedures Before the Environmental Assessment Board" (1981-82) 3 Adv.Q 195-215.

15. Environmental Protection Act, RSO 1980, c.141, s. 24.

16. See: (1) David Estrin, Environmental Law (Toronto: Carswell, 1984), 149.

    (2) Re Can. Env. Law Assn. and Pitura (1979), 26 or (2d) 488, at 498 (Div. Ct.); affirmed on other grounds, (1981), 32 OR (2d) 605 (CA).

17. U.S. Office of Science and Technology Policy "Coordinated Framework for Regulation of Biotechnology," (Washington; 1986), 51 Federal Register, at 23315.

18. Ibid.

19. Ibid.

20. Ibid.

21. James W. Gillett, "Risk Assessment Methodologies for Biotechnology Impact Assessment (July 1986) 10 Environmental Management 515-532, at 527.

22. Jane F. Rissler, "Research Needs for Biotic Environmental Effects of Genetically-Engineered Microorganisms", (March 1984), 7 Rec. DNA Tech Bull., 20-30, at 20.

23. James W. Gillett, Arthur M. Stern, Mark A. Harwell, and Simon A. Levin "Conclusions and Recommendations" (July 1986) 10 Environmental Management 532-535, at 534.

24. Ibid.

25. Ibid.

26. James W. Gillett, supra footnote 10, at 518.

27. James W. Gillett, Arthur M. Stern, Mark A. Harwell, and Simon A. Levin, supra footnote 23, at 534.

28. This data was drawn from the following articles:

    (1) Jane F. Rissler, supra footnote 22, at 23.

    (2) Anonymous, "UK Issues Field Testing Guidelines" (June 1986), 9 Rec. DNA Tech. Bull., 65-69, at 68-69.

    (3) Australia, Recombinant DNA Monitoring Committee, Dept. of Industry Technology and Commerce, The Planned Release of Live Organisms Modified by Recombinant DNA Techniques: Points to Consider in the Preparation of Proposals for Genetic Assessment (Canberra: Department of Industry, Tecnology and Commerce, May 1985), at 9-11.

    (4) Elizabeth Miskew, "Development of Guidelines for Field Testing of Plants Modified by Recombinant DNA Techniques" (Sept. 84), 7 Rec. DNA Tech. Bull. 114-124, at 123.

(5) Elizabeth A. Miskew, "Field Testing of Microorganisms Modified by Recombinant DNA Techniques: Applications, Issues, and Development of 'Points to Consider' Document (Sept. 85), 8 Rec. DNA Tech. Bull. 102-108, at 106-107.

(6) OECD, "Safety in Biotechnology," (press release, Paris, Dec. 9, 1985), 1-56, at 41-44.

(7) James W. Gillett, Arthur M. Stern. Mark A. Harwell, and Simon A. Levins supra footnote 22, at 534.

(8) James W. Gillet, supra footnote 13, at 529.

29. Deborah Dean-Ross, "Applicability of Chemical Risk Assessment Methodologies to Risk Assessment for Genetically Engineered Microorganisms" (Mar. 86), 9 Rec. DNA Tech. Bull. 16-28, at 26.

30. Ibid, at 20-21.

31. Ibid, at 18 and 25.

32. Harlee S. Strauss, Dale Hattis, Guy Page, Kathryn Harrison, Shawna Vogel, and Charles Caldart, "Genetically-Engineered Organisms: II - Survival, Multiplication and Genetic Transfer" (June 1986), 9 Rec. DNA Tech. Bull. 69-88, at 74-75.

33. Deborah Dean-Ross, supra footnote 29, at 25.

34. Harlee S. Strauss et. al., supra footnote 32, at 77.

35. Deborah Dean-Ross, supra footnote 29, at 19.

36. Deborah Dean-Ross, supra footnote 29, at 24.

37. Ibid, at 25.

38. James W. Gillett, supra footnote 10, at 522.

39. See: Toby Vigod, Submissions by the Canadian Environmental Law Association on An Approach to Standard Setting in Ontario with Specific Reference to Mobile PCB Destruction Facilities (Toronto: Canadian Environmental Law Association, 1984).

40. Statement of policy seminar participant.

41. James W. Gillett, Arthur M. Stern, Mark A. Harwell, and Simon A. Levin, "Conclusions and Recommendations" (July 1986), 10 Environmental Management 515-532, at 523.

42. James W. Gillett, "Risk Assessment Methodologies for Biotechnology Assessment" (July 1986), 10 Environmental Management 515-532, at 523.

43. The benefits of genetic engineering are expected to be substantial. New products and technologies will be developed for a wide variety of industries. Although the current market for the products of genetic engineering is relatively small, sales of such products are expected to rise to more than $100 billion in the United States in the year 2025.

    See: Ralph W. Hardy and David J. Glass, "our Investment: What is at stake? (Spring 1985) 1 Issues in Science and Technology 69-82, at 70.

44. Association of Biotechnology Companies, "ABC Forms Captive Insurance Company," (press release, Washington D.C., October 16, 1985).

45. Ibid.

46. Ibid.

APPENDIX A: BIBLIOGRAPHY

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APPENDIX B: GLOSSARY

APPENDIX C: THE 1986 CANADIAN BIOTECHNOLOGY SOURCEBOOK

1986 CANADIAN BIOTECHNOLOGY SOURCEBOOK

The 1986 Canadian Biotechnology Sourcebook lists and describes 110 commercial operations involved in biotechnology research, development or manufacturing during 1985. Biotechnology is broadly defined in the Sourcebook as the provision of goods and services by the use of biological processes. However, an emphasis is placed upon industries using the newer biotechnology techniques such as genetic engineering, monoclonal antibody production, plant cell culture and enzyme technologies. Fermentation process development was also considered a priority area.

The 1986 Canadian Biotechnology Sourcebook was prepared for the National Biotechnology Advisory Committee by:

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