

*Ethical*  
*Aspects of*  
*Agricultural*  
*Biotechnology*



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## Foreword

Ethics, as this report begins by explaining, is concerned with how we may decide what is morally right or wrong. It is a specific discipline which attempts to analyse the concepts and principles used to justify our moral choices and actions in particular situations. Because the applications of modern biotechnology impinge upon some of the most fundamental of human situations - our health, our food, our environment, even our very nature - they raise serious questions in our minds.

It is important to remember that such questioning is not new - 1998 commemorates the 25th anniversary of the discoveries which made modern biotechnology possible and some of the early scientists were so concerned then that for a time they imposed a moratorium on their own research. It is also important to remember, as they did when they recommenced their research after assessing the potential risks, that to decide whether it is ethically justifiable *not* to do something is equally as crucial as to decide whether it is not ethically justifiable to do it.

The ethical argument for modern biotechnology, of course, is that it enables desired aims in healthcare, food production or environmental protection to be met as soon as possible. Proponents of modern biotechnology maintain that these could not be met without modern biotechnology or can be met more easily, cheaply, safely, reasonably rapidly, or with less harm to the environment with it. Following from this are the hopes that future generations may benefit from the present developments. Then there are the fears that, should these developments be inhibited in certain countries, jobs, wealth creation (which determines living standards) and tax revenues (which pay for social systems) would be forsaken because of the globally competitive nature of biotechnology and of trade. Ethical arguments against modern biotechnology, now as 25 years ago, need to be evaluated therefore both in their own right and against these aims, hopes and fears.

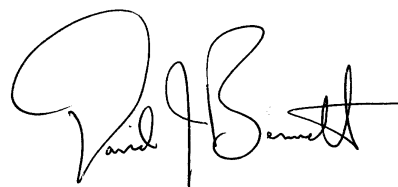
What *is* new is the public interest in biotechnology and the way in which these issues, especially to do with its applications in agriculture and foods, have hit the headlines. Until relatively recently, say a decade or so ago, general public concern hardly existed in Europe. The vast majority of people were virtually unaware of biotechnology and content to remain so. The only real antagonism was from activists in the USA and in isolated incidents in Europe. With its continued growth and commercialisation, however, resonating with other issues in society and taken up by public interest and political activist groupings together with the media, each with their own agendas, biotechnology has been brought to the forefront of public attention.

In 1993, recognising this growing public attention, the Parliamentary Assembly of the Council of Europe issued its Recommendation 1213 that its Committee of Ministers should extend its work on bioethics to include issues related to the application of biotechnology in the agrofood sector and the European harmonisation of legislation in this field. It further

recommended the holding of a pan-European conference of all interested parties and the drawing up of a European Convention covering bioethical aspects of biotechnology in the agrofood sector. Such a Convention would go beyond the "*Draft convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Bioethics Convention*" issued in 1994 by the Steering Committee on Bioethics (CDBI) and ratified as the "*Convention on human rights and biomedicine*" in early 1998. This Convention excludes animal and plant biology insofar as they do not concern human medicine or biology. In 1995 the Committee of Ministers agreed on the convening of the European conference which could prepare the way for determining the desirability of a European Convention covering bioethical aspects of biotechnology applied to the agricultural and food sector since it could be based on studies dealing with the various issues involved. The conference will be held on 16-19 May 1999 in Oviedo, Spain and this report is a compilation in concise form of independent studies, funded by the European Commission under its Agriculture and Fisheries 1994-1998 programme.

The report is the work of leading scientists, ethicists and experts in the patenting and regulatory fields concerned with applications of biotechnology in the agricultural and food areas from throughout Europe. It commenced with a workshop in January 1996 to plan the studies and the main body of the work was carried out between March 1997 and August 1998. The studies were carried out by five Working Groups encompassing the food, industry, medicine, environment and developing countries areas with ethics, patenting, regulation (safety) and economic/political issues integrated across the five areas. Sections drafted by each Working Group based on their studies are combined in this report.

The intention in the report has been to produce a clear, concise and balanced distillation of these studies in non-technical language for ease of understanding and use. The full studies on which it is based are available separately. It begins with an introductory discussion of ethical and legal questions followed by more detailed analysis of the ethical implications of biotechnological applications in the various areas. It makes no attempt to pass judgements. Whether it achieves these intentions is of course for the reader to decide. Please let us know what you feel.



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## Keypoints

<p><b>1 Ethics</b></p> <p>.1 Ethics can usefully be defined as the branch of philosophy concerned with how we should decide what is morally wrong and what is morally right.</p> <p>.2 Ethical conclusions need to be based on reason, take into account historically well established ethical principles, be based on consensus, take account of minority interests and be open to the possibility of change.</p> <p>.3 A useful tradition of ethical reasoning in the European Union and elsewhere is beginning to accumulate about moral questions concerning biotechnology.</p> <p>.4 The simplest approach to deciding whether an action would be right or wrong is to look at what its consequences would be. Controversy exists as to whether that is all which is needed.</p> <p>.5 Traditionally, ethics has concentrated mainly upon actions that take place between people at one point in time. In recent decades, however, moral philosophy has widened its scope by taking into account interspecific and intergenerational issues.</p> <p>.6 Ethical decisions can be taken at a number of levels from the individual to the international.</p> <p>.7 Some general ethical questions which relate to all applications of modern biotechnology include:</p> <p>.1 How to weigh the potential benefits against the possible costs?</p> <p>.2 Do the processes themselves constitute an “unnatural” interference with Nature, particularly in breaching natural species boundaries and violating the integrity of species?</p> <p>.3 What is ethically wrong with interfering with Nature?</p> <p>.4 Do the processes involve the taking of ethically unjustifiable risks?</p> <p>.5 From a religious viewpoint, is modern biotechnology to be interpreted as “playing God” or as collaborating in the on-going work of creation?</p> <p>.6 Do these questions suggest any significant ethical differences between modern biotechnology and more traditional techniques?</p> <p><b>2 Food</b></p> <p>.1 Agriculture has always depended on plant and animal breeding and modern biotechnology provides new possibilities.</p>	<p>.2 Public perceptions of agro-food biotechnology are more critical than of its applications in healthcare. This probably results from the cultural and symbolic functions of food together with most people’s relative ignorance about modern agriculture and food production.</p> <p>.3 The most important areas where biotechnology can provide benefits for European consumers can be in improved price, quality and nutritional value of foods.</p> <p>.4 Regulation has been mostly directed to the safety of foods. Labelling is still a controversial issue at the international level. The EC regulation on novel foods and novel food ingredients (258/97) includes a labelling requirement for a material not present in conventional equivalent foods which “gives rise to ethical concerns” to inform population groups with “well established” food practices. In the USA the Food and Drug Administration considers that no special labelling is required.</p> <p>.5 Ethical considerations of agrofood biotechnology relate to the environment, biodiversity, sustainability, animal welfare and its socio-economic impacts.</p> <p>.6 Consumers rights concerning biotechnological food products relate to the rights to health from safe foods, to be informed and to choose genetically engineered products or not.</p> <p>.7 It is crucial that balanced information is provided to the public. Communication strategies should bring together the scientific, industrial and general communities to promote openness, dialogue and mutual understanding.</p> <p><b>3 Environment</b></p> <p>.1 The current environmental problems that arise from agriculture stem from modern, intensive agricultural practices and not from the use of genetically modified crops, as the latter are only currently being introduced into European agriculture. The use of biotechnology may either exacerbate or ameliorate these effects depending on how it is applied.</p> <p>.2 It is therefore important, before applying new biotechnology, to consider the precautionary principle, the need for sustainable development and the need to maintain and possibly enhance agriculturally-important biodiversity.</p> <p>.3 The latter is emphasised in the two case studies, one on the introduction of GMO crops into their centres of origin (frost tolerant potato) and the other on the importance of mediterranean biodiversity, taking the case of Greece.</p>
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**4 Medicine**

- .1 Biotechnology offers many opportunities for the production of medicines, vaccines and other medical products using agricultural sources for further improvement of human and animal health.
- .2 New products can be developed using this technology, or the production of already existing products made more cost-effective.
- .3 The disadvantages of the use of biotechnology must not be overlooked: although safety regulations do exist unforeseen and unwanted consequences may still occur.
- .4 The continued development of biotechnology in relation to the use of agriculture for medicine will undoubtedly raise new ethical questions and controversies. However, there is good reason to expect that the very considerable body of expertise that exists in relation to medical and other areas of ethics will help to give rise to some degree of consensus in many of these novel areas, though it must be recognised that ethical debate is characterised by conflicting arguments and viewpoints.

**5 Developing Countries**

- .1 The issues that are identified need to be addressed regardless of the technology used to manufacture or market a product; these need to be within the context of (agricultural) need and/or food resources.
- .2 The view in countries where there is enough to eat, and where choice of what to eat is assumed may be significantly different from that pertaining in other countries. Choices need to be made by those who have to live with their consequences.
- .3 Many of the issues identified which are of ethical concern are not specific to developing countries, but occur within parts of countries considered to be developed. The developing world is much too diverse to be treated as a whole. The issues which result from moving from "traditional" agriculture to industrialised agriculture are those which need consideration.
- .4 Biotechnology *per se* does not lead to a loss of biodiversity; all modern agricultural techniques contribute both positively and negatively.
- .5 Technology has the capacity to contribute to the empowerment of rural communities.
- .6 The increase in the world population will mainly occur in the developing countries and therefore food increase needs to occur in those countries. The developed world is supplying food to the developing world. Furthermore, governmental agencies control access to the staple crops that form the major starch, oil and protein sources. It is important to provide a mechanism for sustainable food production where and when needed.
- .7 Developing countries contribute significantly to the

added value made in agriculture. In this respect it could therefore be beneficial for these to set up a balanced system of intellectual property rights.

- .8 There are five major players that contribute to agricultural research: governmental and public institutions, international institutions, non-governmental organisations and industry.
- .9 Developing countries should be free to use their land according to their own view. The prejudices and views on industrialised agriculture which colour the "Northern" approach to agricultural produce should not be imposed on those not getting enough to eat.
- .10 Developing countries should be helped to have access to biotechnology based on their genetic resources (Convention on Biological Diversity).
- .11 All parties to the Convention on Biological Diversity have an obligation "to provide for the effective participation in biotechnological research activities by those Contracting Parties, especially developing countries which provide the genetic resources for such research, and where feasible in such Contracting Parties". There will be costs associated with maintaining biodiversity within a centre of origin, which should be borne by the international community.

**6 Industry**

- .1 Industrial development of biotechnology in Europe varies both between different sectors of biotechnology and different areas within Europe. Environmental and food-related issues are more important in northern European countries, whereas production and employment tend to prevail in southern and eastern countries.
- .2 The conclusions from public opinion surveys concerning applications of biotechnology are that:
  - 1 Usefulness is a precondition of support, in no case is a "not useful" application given support.
  - 2 People will accept some risk if the application is (a) useful and (b) morally acceptable.
  - 3 Moral concerns act as a veto regardless of views on risk and use.
  - 4 If risk is less significant than moral acceptability in shaping public perceptions, then public concerns are unlikely to be alleviated by technically based reassurances and other policy initiatives dealing solely with risks.
- .3 Employment is in itself an ethical issue where biotechnology in Europe is concerned.

## Chapter 1

### Ethical and legal introduction

#### 1.1 How can we make ethical decisions about biotechnology?

Ethics can usually be defined as the branch of philosophy concerned with how we should decide what is morally wrong or morally right. It may be useful to distinguish at the outset between ethics and morals, as the two are frequently confused, mainly because both terms can be used in a number of different though related senses. We all have to make moral decisions daily on matters great or (more often) small about what is the right thing to do, and we may give much thought, little thought or practically no thought at all to these choices. Ethics, however, is a specific discipline which tries to probe the reasoning behind our moral life, particularly by critically examining and analysing the concepts and principles which are or could be used to justify our moral choices and actions in particular situations. Ethics, then, in this sense does not tell us what to do, but tries to clarify the range of arguments which might be used to support or criticise what we do.

Despite this rather purist definition of ethics, however, the term “ethical” is used in a number of looser senses, sometimes simply as an equivalent for “moral”, but also to refer to concerns, debates, decisions and conclusions about practical moral questions which take into account or are based upon the discipline of ethics and its critical analysis of concepts and principles. It is in this wider sense that we shall be using the terms “ethical decisions” and “ethical conclusions” in what follows. It must be emphasised, however, that ethics as a discipline does not provide automatic moral expertise or authoritative answers to moral problems. Consequently, its function in this report is not to offer substantive solutions but to illustrate and examine the moral issues at stake and their underlying arguments.

The aim of this chapter, then, is to provide an introduction to how ethical decisions may be made. An attempt will be made to put forward a number of ethical principles that need to be considered when trying to decide whether or not particular instances of biotechnology are morally acceptable or unacceptable. In the light of these principles, the practice of biotechnology in the agrofood sector will be examined in later chapters.

##### 1.1.1 The way ethics is done

Ethics is a branch of knowledge just as other disciplines, such as science, mathematics and history, are. Ethical thinking is not wholly distinct from thinking in other disciplines but it cannot simply be reduced to them. In particular, most people agree that ethical conclusions cannot be unambiguously provided in the way that a mathematical theorem can. However, this does not mean that all ethical conclusions are equally valid. As in branches of knowledge such as science and history some conclusions are more likely to be valid than others. One can be most confident about an ethical conclusion if three criteria are

realised; first, if the arguments that lead to the particular conclusion are supported by reason, secondly, if the arguments have been conducted within a well established ethical framework and thirdly, if a reasonable degree of consensus exists about the validity of the conclusions, arising from a process of democratic debate.

It might be supposed that reason alone is sufficient for one to be confident about an ethical conclusion. However, there are problems in relying on reason alone when thinking ethically. In particular, there still does not exist a single universally accepted framework within which ethical questions can be decided by reason. Indeed, it is unlikely that such a single universally accepted framework will exist in the foreseeable future, if ever. This is not to say that reason is unnecessary but to acknowledge that reason alone is insufficient. For instance, reason cannot decide between an ethical system which looks only at the consequences of actions and one which considers whether certain actions are right or wrong in themselves, whatever their consequences.

The insufficiency of reason is a strong argument for conducting debates within well established ethical frameworks. Traditionally, the ethical frameworks most widely accepted arose within systems of religious belief. Consider, for example, the questions “*Is it wrong to steal? If so, why?*”. There was a time when the great majority of people would have accepted the answer “*Yes. Because scripture forbids it*”. Nowadays, though, not everyone accepts scripture as a source of authority. Another problem, of particular relevance when considering the ethics of biotechnology, is that while the various scriptures of the world’s religions have a great deal to say about such issues as telling lies, killing people and sexual behaviour, they are less directly applicable to the debates that surround today’s biotechnology. A further issue is that we live in an increasingly pluralistic society. Within Europe there is no longer a single shared set of moral values. Even the various religions disagree on ethical matters and many people no longer accept any religious teaching.

Nevertheless, there is still great value in taking seriously the various traditions - religious and otherwise - that have given rise to ethical conclusions. People do not live their lives in isolation: they grow up within particular moral traditions. Even if we end up departing somewhat from the values we received from our families and those around us as we grew up, none of us derives our moral beliefs from first principles, *ex nihilo*, as it were. In the particular case of moral questions concerning biotechnology, a tradition of ethical reasoning is already beginning to accumulate. Most member states of the European Union have official committees or other bodies looking into the ethical issues that surround at least some instances of biotechnology while the European Commission has a group of advisors on the ethical implications of biotechnology. The tradition surrounding ethical reasoning in this field is nothing like as long established as, for example, the traditions surrounding such questions as abortion, euthanasia, war and trade protectionism. Nevertheless, there is the beginning of such

a tradition and similar questions are being debated in many other countries across the globe.

Given, then, the difficulties in relying solely on either reason or any one particular ethical tradition, we are forced to consider the approach of consensus. It is true that consensus does not solve everything. After all, what does one do when consensus cannot be arrived at? Nor can one be certain that consensus always arrives at the right answer - a consensus once existed that women should not have the vote. Nonetheless, there are good reasons both in principle and in practice in searching for consensus. Such a consensus should be based on reason and democratic debate and take into account long established practices of ethical reasoning. At the same time, it should be open to criticism and refutation and the possibility of change. Finally, consensus should not be equated with majority voting. Consideration needs to be given to the interests of minorities, particularly if they are especially affected by the outcomes, and to those - such as young children, the mentally infirm and non-humans - unable to participate in the decision-making process.

### 1.1.2 Is it enough to look at consequences?

The simplest approach to deciding whether an action would be right or wrong is to look at what its consequences would be. No-one supposes that we can ignore the consequences of an action before deciding whether or not it is right. This is obvious when we try to consider, for example, whether imprisonment is the appropriate punishment for certain traffic offences - *eg* reckless driving. We would need to look at the consequences of imprisonment, as opposed to alternative courses of action such as imposing a fine or banning the offender from driving. Even when complete agreement exists about a moral question, consequences may still have been taken into account. Consider the extreme example of the torture of children for pleasure. Clearly there is overwhelming agreement that this is wrong and no debate about this conclusion is normally needed. However, at least part of the reason why such a behaviour would be wrong is that practically everyone can immediately see that the consequences in terms of the suffering of the children involved, not to mention their families and the rest of us, far outweighs any perverted pleasure or other benefit the torturers might receive.

The deeper question is not whether we need to take consequences into account when making ethical decisions but whether that is all that we need to do. Are there certain actions that are morally required - such as telling the truth - whatever their consequences? Are there other actions - such as betraying confidences - that are wrong whatever their consequences? This is about the most basic question that can be asked in ethics and it might be expected by anyone who is not an ethicist that agreement as to the answer would have arisen. Unfortunately this is not the case. There still exists genuine academic disagreement amongst moral philosophers as to whether or not one needs only to know about the consequences of an action to decide whether it is morally right or wrong.

Those who believe that consequences alone are sufficient to let one decide the rightness or otherwise of a course of action are called consequentialists. The most widespread form of consequentialism is known as utilitarianism. Utilitarianism itself exists in various forms, but it begins with the assumption that most actions lead to pleasure and/or displeasure. In a

situation in which there are alternative courses of action, the desirable (*ie* right) action is the one which leads to the greatest net increase in pleasure.

Consider the question as to whether or not we should tell the truth. A utilitarian would hesitate to provide a unqualified "yes" as a universal answer. Utilitarians have no moral absolutes beyond the maximisation of pleasure principle. Instead, it would be necessary for a utilitarian to look in some detail at particular cases and see in each of them whether telling the truth would indeed lead to the greatest net increase in pleasure.

There are two great strengths of utilitarianism. First, it provides a single ethical framework in which, in principle, any moral question may be answered. It doesn't matter whether we are talking about the legislation of cannabis, divorce or the patenting of DNA; a utilitarian perspective exists. Secondly, utilitarianism takes pleasure seriously. The general public may sometimes suspect that ethics is all about telling people what not to do. Utilitarians simply say that people should do what maximises the total amount of pleasure in the world.

However, there are difficulties with utilitarianism as the sole arbiter in ethical decision making. For one thing, an extreme form of utilitarianism in which every possible course of action would have to be analysed consciously in terms of its countless consequences would quickly bring all human activity to a stop. Then there is the question as to how precisely can pleasure be measured. For a start, is pleasure to be equated with well-being or happiness? And, anyway, what are its units? How can we compare different types of pleasure, for example sexual and aesthetic? Then, is it always the case that two units of pleasure should outweigh one unit of displeasure? Suppose two people each need a single kidney. Should one person (with two kidneys) be killed so that two may live (each with one kidney)?

Utilitarians claim to provide answers to all such objections. For example, rule-based utilitarianism accepts that the best course of action is often served by following certain rules - such as "*Tell the truth*", for example. Then, a deeper analysis of the kidney example suggests that if society really did allow one person to be killed so that two others could live, many of us might spend so much of our time going around fearful that the sum total of human happiness would be less than if we outlawed such practices.

For our purposes it is sufficient to note that utilitarianism is an important way of looking at ethical questions. It needs to be taken seriously into account even if not everyone unquestioningly accepts it.

The major alternative to utilitarianism is a form of ethical thinking in which certain actions are considered right and others wrong in themselves, *ie* intrinsically, regardless of the consequences. Consider, for example, the question as to whether a society should introduce capital punishment. A utilitarian would decide whether or not capital punishment was morally right by attempting to quantify the effects it would have on the society. Large amounts of empirical data could need to be collected comparing societies with capital punishment and those without it with regard to such things as crime rates, the level of fear experienced by people worried about crime and the use to which money saved by the introduction of capital

punishment might be put. On the other hand, someone could argue that regardless of the consequences of introducing capital punishment, it is simply wrong to take a person's life, whatever the circumstances. Equally, someone could argue that certain crimes, for example first degree murder, should result in the death penalty - that this is simply the right way to punish such a crime.

There are a number of possible intrinsic ethical principles and because these are normally concerned with rights and obligations of various kinds, this approach to ethics is often labelled "deontological". Perhaps the most important are often thought to be those of autonomy and justice. People act autonomously if they are able to make their own informed decisions and then put them into practice. At a common sense level, the principle of autonomy is why people need to have access to relevant information, for example before consenting to a medical procedure. Autonomy is concerned with an individual's rights. Justice is construed more broadly. Essentially, justice is about fair treatment and the fair distribution of resources or opportunities. Considerable disagreement exists about what precisely counts as fair treatment and a fair distribution of resources. For example, some people accept that an unequal distribution of certain resources (*eg* educational opportunities) may be fair provided certain other criteria are satisfied (*eg* the educational opportunities are purchased with money earned or inherited).

Much energy can be wasted when utilitarians and deontologists argue between themselves. There is little if any common ground on which the argument can take place though some modern philosophers argue that there can be no theory of rights and obligations without responsibility for consequences, and no evaluation of consequences without reference to rights and obligations. For our purposes we can conclude that we need to look both at the consequences of any proposed course of action and at relevant intrinsic considerations before reaching an ethical conclusion.

### 1.1.3 Widening the moral community

Traditionally, ethics has concentrated mainly upon actions that take place between people at one point in time. In recent decades, however, moral philosophy has widened its scope in two important ways. First, interspecific issues are now increasingly taken into account. Secondly, intergenerational issues are recognised as being of importance.

Interspecific issues are of obvious importance when considering biotechnology. Put at its starkest, is it sufficient only to consider humans or do other species need also to be taken into account? Consider, for example, the use of new practices (such as the use of growth promoters or embryo transfer) to increase the productivity of farm animals. An increasing number of people feel that the effects of such new practices on the farm animals would need to be considered as at least part of the ethical equation before reaching a conclusion. This is not, of course, necessarily to accept that the interests of non-humans are equal to those of humans. While some people do argue that this is the case, others accept that while non-humans have interests these are generally less morally significant than those of humans.

Accepting that interspecific issues need to be considered leads one to ask "*How?*". Need we only consider animal suffering? For example, would it be right to produce, whether by conventional breeding or modern biotechnology, a pig unable to detect pain and unresponsive to other pigs? Such a pig would not be able to suffer and its use might well lead to significant productivity gains: it might, for example, be possible to keep it at very high stocking densities. Someone arguing that such a course of action would be wrong would not be able to argue thus on the grounds of animal suffering. Other criteria would have to be invoked. It might be argued that such a course of action would be disrespectful to pigs or that it would involve treating them only as means to human ends and not, even to a limited extent, as ends in themselves. This example again illustrates the distinction between utilitarian and deontological forms of ethical reasoning, as the issue of pain can be separated from that of rights and obligations in this case.

Intergenerational as well as interspecific considerations may need to be taken into account. Nowadays we are more aware of the possibility that our actions may affect not only those a long way away from us in space (*eg* acid rain produced in one country falling in another) but also those a long way away from us in time (*eg* increasing atmospheric carbon dioxide levels may alter the climate for generations to come). Human nature being what it is, it is all too easy to forget the interests of those a long way away from ourselves. Accordingly, a conscious effort needs to be made so that we think about the consequences of our actions not only for those alive today, about whom it is easiest to be most concerned.

### 1.1.4 The level at which ethical decisions are made

Finally, it needs to be recognised that ethical decisions can be taken at a number of levels. Ponder, for instance, the production of organic vegetables - *ie* vegetables grown without the use of artificial fertilisers and pesticides. As an individual I have to choose whether to buy organic produce in preference to non-organic produce. Some of the factors that affect my choice will have little to do with morality, being instead to do with such things as convenience (Does the shop at which I buy my vegetables sell both types of produce, so that I can choose between them?), upbringing (Was I used to both sorts of produce as a child?) and aesthetics (Do I prefer the look or smell of one of these types of produce?). However, ethical factors may also affect my choice. For example, do I feel that pollution is a moral issue and that more organic vegetables should be grown in order that fewer pesticides should be used? Or, on the other hand, do I feel that there is a moral argument for maximising agricultural yields through the use of artificial fertilisers and pesticides, perhaps so that less farm land is needed for production, so reducing pressures on existing wild areas?

Ethical decisions are taken at levels other than that of the individual. Shops need to decide whether or not to stock organic produce. Again, many factors - especially, of course, commercial ones - will affect such a decision but ethical factors may enter too. At a still higher level, regional and national governments and international bodies decide which sorts of agriculture to subsidise or support in other ways. Again, ethical considerations may enter. Then there are further subtleties. I may choose only to purchase organic vegetables - thus

forbidding myself non-organic ones. However, I may not be in favour of the sale of non-organic vegetables being prohibited altogether. This might be because I consider that the gains from the prohibition of the sale of non-organic goods would not be worth the loss of others' autonomy. On the other hand, I may be in favour of slavery being prohibited, considering that the gains from the prohibition of slavery (principally those to do with justice and the rights of all people) are sufficient to be worth the loss of autonomy of those who would still like to have slaves.

### 1.1.5 Conclusions

There is no single way in which ethical debates about biotechnology or almost any other matter can unambiguously be resolved. However, that does not mean that all ethical arguments are equally valid. Ethical conclusions need to be based on reason, take into account historically well established ethical principles, be based, so far as possible on consensus, take account of minority interests and be open to the possibility of change. Education and debate play an important role, helping to enable people to clarify their own thinking, express their views and participate in the democratic process.

## 1.2 General ethical questions about biotechnology

Many of the ethical questions posed by modern biotechnology are concerned with specific applications of that technology, and so will need to be examined on a case-by-case basis in the following sections of this report. To do this will require a detailed technical analysis of the particular application and in most cases an assessment of the likely outcomes, for most of the ethical questions here will focus upon the possible consequences of various biotechnological innovations, where ethical judgements have to be made about the value or priority to be placed upon different possible costs and benefits and indeed about what is to be counted as a cost or a benefit. So, for example, an examination of the ethical issues surrounding genetically engineered herbicide-tolerant crops will need to consider such factors as possible environmental risks and benefits and possible socio-economic effects; judgments can then be made about what is to be counted as a cost and a benefit in this case and how these are to be weighed and compared against each other, and these judgments will be specific to that particular example.

There can also, however, be identified a number of more general ethical questions which relate to all applications of modern biotechnology, and as it would be repetitive and cumbersome to refer to them in each of the specific sections of this report, they are best dealt with here in a separate brief review.

It is, of course, the case that while modern biotechnology may raise moral concerns, there are moral arguments in its favour too. Arguments in favour of specific instances of modern biotechnology will be considered in later sections as and when they arise. Broadly speaking, though, the overarching argument in favour of modern biotechnology is that it enables certain desired ends to be met either for the first time or more easily, more cheaply or more safely. These desired ends include the betterment of human health, the production of more food and the generation of new products, and many hope that future generations may benefit incrementally from research and

development initiated now. Arguments against the use of modern biotechnology, then, need to be evaluated both in themselves and against these intended benefits.

Moral concern can and does exist, however, not only about the possible consequences of modern biotechnology but also about the nature of the process itself. If the technology itself is thought to be morally wrong for some reason, then all of its applications will be affected by what some have called a "moral taint". These general moral concerns are of considerable importance for this study, partly because of their wide-ranging nature and partly because they appear to be felt by significant proportions of the general public in EU countries. In the following summary of these concerns there will, for reasons given in the introduction, be no attempt to pass judgment on their validity. Instead, the ethical basis of some of the possible moral positions will be analysed and a number of key questions identified.

### 1.2.1 Tampering with Nature

There is evidence from studies in several EU countries that people's beliefs about Nature play a role in their evaluation of the products of modern biotechnology. Though it is by no means the only moral concern that can be identified, the belief that, for example, genetic engineering is "unnatural" and thereby wrong lies at the root of many people's unease, and several studies have found that "unnaturalness" is an important determinant of people's underlying concern.

This in turn helps to explain the wide disparity of views and attitudes concerning genetic engineering and other instances of modern biotechnology, for conceptions of Nature and of what counts as "natural" and "unnatural" are never merely descriptive. They embody values and prescriptions about what it is morally right and wrong to do to the natural world and consequently are open to diverse interpretations. These conceptions and interpretations may be for many people (other than philosophers and theologians) implicit rather than explicit, but this does not lessen their influence upon people's attitudes, choices and behaviour.

What is the basis of this concern and what ethical principles does it imply? Reduced to its simplest form, the argument seems to be as follows: "*Nature and all that is natural is valuable and good in itself; all forms of biotechnology are unnatural in that they go against and interfere with Nature, particularly in the crossing of natural species boundaries; all forms of modern biotechnology are therefore intrinsically wrong*".

The ethical issues at stake here centre around the moral status of Nature. Various possible positions can be distinguished. Nature can, for example, be conceived of as benevolent and intrinsically good, or as hostile and intrinsically bad or as morally neutral. Each of these positions will have implications for one's attitude towards modern biotechnology, for each represents a set of fundamental principles and assumptions which may be held in some cases consciously and explicitly, or perhaps more often unconsciously and implicitly.

If Nature is seen as intrinsically good and so deserving of moral respect, modern biotechnology becomes morally questionable because it can be interpreted as tampering at a very basic level

with the structure of Nature. If Nature is seen as hostile and intrinsically bad, then the moral implications are reversed if it is our duty to try to reform that which is bad or imperfect and to attempt to impose order upon chaos. If Nature is seen as morally neutral, simply as a factual situation which confronts us, then modern biotechnology per se also becomes morally neutral as a technique or set of techniques which can be used for good or ill to modify living organisms.

Whichever of these positions is held, further ethical analysis will be needed to clarify the concepts and principles involved and to examine the structure of the arguments.

### 1.2.2 Naturalness and Unnaturalness

Before any of the above arguments can get off the ground, we have to be able to identify and agree about what is to count as “natural” and “unnatural”. This is no easy task.

Depending on the context in which it is used, the word “natural” may mean “usual”, “normal”, “right”, “fitting”, “appropriate”, “uncultivated”, “innate”, “spontaneous”, and no doubt many other things as well. Perhaps most commonly, “natural” is contrasted with “artificial” or “man-made”, but on the basis of that distinction practically every element of our modern Western life-style is “unnatural”. Nor can more traditional products and processes avoid such a charge of “unnaturalness”, for the progress of civilisation has been largely dependent upon our “interference” with Nature. Yet if every domestic or farm animal, every garden plant or agricultural crop, every item of food or clothing is thought of as unnatural because it interferes with Nature, as logically it must, then the concept of “unnaturalness” may become so broad as to be meaningless.

The more specific and serious charge of “unnaturalness” that has been levelled against genetic engineering, however, is that it breaches natural species boundaries and violates the natural integrity of species. A biologist might try to refute the argument that it is unnatural to breach the genetic boundaries between species on a number of grounds. For a start, such a view fails to realise that the theory of evolution, on which all our understanding of the nature of species is based, requires that species change over time. Every species alive today is believed to be the direct descendant of the early single-celled species that existed over three billion years ago. Species that currently exist have passed through many, possibly hundreds, of separate speciation (formation of a new biological species) events. In other words, species are not static; their genetic composition naturally changes over time.

Further, a view of evolution that assumes that species remain genetically isolated from one another is out of date. We now realise that a number of distinct processes allow the movement of genetic material from one species to another. Certain viruses, for example, carry genetic material between species. Equally, many bacteria have mechanisms that allow them to take up genetic material from other species and then integrate it into their own. In other words, for many species, their very nature, *ie* their telos, includes the ability to cross species barriers. So it is possible to argue that genetic engineering is not fundamentally unnatural: it uses techniques which either exist in Nature (*eg* the transfer of genetic material between species via viruses) or have been used by humans for millennia (*eg*

selective breeding). Similarly, other techniques of modern biotechnology such as tissue culture, cloning and embryo transfer have their origins either in Nature or in long-established human practices. However, to argue thus may be to push the similarities between modern biotechnology, on the one hand, and Nature and traditional biotechnology, on the other, too far. In any useful sense modern biotechnology does involve a significant departure from what has gone before. It therefore lays itself open to the charge that it is “unnatural”.

Apart from these conceptual issues we also need to take account of certain methodological considerations in making moral judgments about how we should behave towards Nature, however defined. To assume that we can simply deduce what is morally right and wrong from certain facts about the world and about Nature is to commit what philosophers have called the “*naturalistic fallacy*”, often translated as “*You can’t get an ought from an is!*” The logical point at issue here is really a very simple one: simply because something happens in Nature does not mean that it is right or good, that it should be preserved or protected. A specific example of the naturalistic fallacy can be found in the argument about breaching natural species barriers. Even if these barriers unequivocally can be identified (which appears unlikely), their mere existence provides no clear ethical directives about what ought to be done about them. The English Channel is a “natural” barrier between England and France, but that geographical fact tells us nothing about whether it is morally right or wrong to cross from England to France.

Questions about the ethical status of Nature, therefore, are fundamental to any analysis of general moral concerns about modern biotechnology. However, while it is possible as we have seen to hold that the technology is intrinsically wrong because of the ways in which it tampers with Nature, this moral concern is often related to the more pragmatic issue of safety. For some, then, “unnaturalness” may not be an intrinsic concern but rather another way of expressing fears about possible risky consequences. The argument here would be that “*Nature knows best*” and that the natural world as we know it is the result of a long evolutionary process with a well-established track record, whereas genetic engineers are gambling with their unproven introductions.

Critics of modern biotechnology may argue that we simply have not had sufficient time to evaluate fully the risks it poses, and at one extreme apocalyptic scenarios may be painted in which genetically engineered species cause ecological devastation or novel vaccines lead to terrible loss of human life. At the other extreme, some of those in favour of modern biotechnology may dismiss such fears assuring the public that they have nothing to fear and that modern biotechnology does not pose new risks but promises countless benefits.

Again, the specifics of such arguments need to be examined for particular cases. In general, though, a few points can be made. First of all, nothing in life is totally safe. Indeed, the equation between what is safe and what is morally right is not always straightforward. Perhaps the world would be safer if no one went skiing or drove their cars at speeds in excess of 40 kph. Does that mean that we should ban skiing or set speed limits of 40 kph? Secondly, and in opposition, it should be remembered that history tells us that new technologies sometimes have a habit of proving problematic in ways that were not, and

sometimes could not have been, envisaged when first introduced. On the other hand, new technologies sometimes have unforeseen benefits. Arguments about safety, then, are rarely so conclusive as to lead to a complete ban on, or unconditional acceptance of, a radically new technology in advance of careful, long-term empirical research and monitoring as to its actual consequences.

We do not need to say more about this subject at this point, however, partly because technical questions of risk and safety will be examined in many (if not all) of the particular applications of the technology to be described in this report, and also partly because it can be argued that risk and safety are empirical matters rather than moral or ethical issues, though they raise such issues when further questions about responsibility, accountability and justifiability enter in.

### 1.2.3 Blasphemy

The general moral concerns outlined above can in some cases include a religious dimension, when they are accompanied by an underlying set of religious beliefs and principles concerning the relationships between God, Nature and human beings.

It is, for example, quite possible to hold religious views to the effect that modern biotechnology is blasphemous. These views rest upon the assumption that God has created a perfect, natural order; for humans to attempt to “improve” that order by manipulating DNA, the basic ingredient of all life, thereby crossing species boundaries instituted by God, is not merely presumptuous but actually contemptuous of God. Such beliefs reflect conceptions of God and Nature in which, since God is thought of as having a moral and rational character, humans in the end must submit to “*things as they are*” as the revelation of that goodness and wisdom.

The essence of this concern, then, is that modern biotechnology is trying to “*displace the first Creator*” or to “*play God*”.

By no means all religious believers would make these claims. Different religions will have different perspectives upon the nature of God and his creation, but even among Christians there is no unanimous condemnation of modern biotechnology per se. There is, for example, scriptural support for the view that humans have been given by God an approved, privileged position of “dominion” and control over Nature. Another interpretation of how humans relate to the rest of the natural world is that, in some sense, we are co-creators, co-workers or co-explorers with God. The argument here is that our scientific understanding of the universe, in particular cosmology and the biological theory of evolution, shows that creation is an ongoing process. The universe has been in a continual state of development for some fifteen thousand million years. Within just the last few thousand years, humans have begun consciously to influence the course of that continued creation in a way never before attained by any species. In any useful sense of the term, therefore, we are co-creators with God, altering the future of the world year by year, hour by hour, as we cause some species to become extinct and alter the genetic constitution of others by the traditional techniques of artificial selection as well as by the newer approach of genetic engineering. Further, if genetic engineering can help to overcome genetic defects caused by harmful mutations, it may

help to restore creation to a fuller, richer existence and so play an important role without encroaching on the scope of divine activity.

It can perhaps be argued, in this vein, that humans may have a moral and theological responsibility, even a duty, to use genetic engineering to root out imperfections in the natural world, including those found in humans. Viewed in this light, genetic engineering can be seen as a tool with the potential to eliminate harmful genetic mutations, reduce suffering and restore creation to its full glory.

The range of religious viewpoints which can be adopted on these issues is further broadened by the variety of positions held by different world religions. Even within Christianity there is no agreement on which principles are applicable here, while other religions such as Hinduism, Judaism and Buddhism have distinctly different perspectives upon the nature of God and the creation, and consequently upon what our attitude towards creation and its genetic foundations should be. Religious approaches to modern biotechnology, then, may take the form of outright rejection, cautious neutrality or enthusiastic acceptance, thus reflecting the possible positions already noted above in connection with more secular moral concerns about tampering with Nature.

### 1.2.4 Conclusions

Arising from the above brief survey, three key questions can be identified which may help to clarify further the ethical principles underlying the general moral and religious concerns which have been outlined.

- (1) Is there a significant ethical difference between modern biotechnology and other more traditional techniques, which might make this form of tampering with Nature and playing God particularly and distinctively objectionable? If so, what is the precise basis of this difference? One possible answer to this would be that modern biotechnology can, to a greater extent than hitherto, breach natural species boundaries and violate the natural integrity of species, in which case the second question must be:
- (2) What is the ethical status of species and what is it legitimate and illegitimate for human beings to do to them? Does the crossing of species boundaries also introduce a new element of unjustifiable risk?
- (3) Are some species of more ethical importance than others, and if so, does this make the genetic modification of human and animal material more suspect than that of plants and microbes, a view that seems to be borne out in surveys of public opinion?

## 1.3 Biotechnology, intellectual property, and morality

### 1.3.1 Introduction

This section addresses the moral dimension of intellectual property law as touching upon biotechnological innovation, with special reference to agricultural biotechnology. Within the area of intellectual property as a whole, the primary emphasis

will be upon patent law as virtually unique in containing specific moral provisions. However, some reference to plant variety rights will be necessary as ancillary to the main theme. The section will focus on the moral aspects of innovative techniques used in or on behalf of the agricultural industry and the products to which such techniques give rise, these being the proper subject matter of the patents which fall within our purview. It is therefore beyond the scope of this section to attempt to formulate a bioethical perspective on the International Conventions and international policy agreements, as such, which bear upon agricultural biotechnology (UPOV, Convention on Biological Diversity, TRIPS Agreement).

### 1.3.2 Essential preliminary concepts

- (1) A patent is a property right granted by State authority which excludes others from the use or benefit of the patented invention without the consent of the patent-holder. A patent may be considered as a “bargain” made between an inventor and the official authorities whereby an inventor informs the public about the invention (rather than keeping it secret) in return for a limited period of legal protection against unauthorised third parties. Secrecy, when possible, is an alternative protective option for an inventor. Under the patent system in many countries an inventor makes the disclosure available to the public long before it is certain that protection will be granted. The open and informative function of patents is considered to spread knowledge of new technology and to be generally in the public interest. Patenting is an adversarial process in which (a) the examining authority has first to be convinced that the conditions of patentability have been met and protection is appropriate, and (b) the patent, if granted, can then be opposed by third parties.
- (2) The expression “patenting Life” is frequently used as shorthand for patenting in biotechnology as a whole. This is an inaccurate and misleading expression which does not help the general public to form a true perception of patenting activity in this field of technology, and it will not be used here. “Life” cannot be patented but living organisms can be patented if they differ significantly from organisms as naturally-occurring. This principle has been established through legal decisions at highest levels in the major industrially developed countries. In Europe, after ten years of intensive debate on successive drafts proposed by the European Commission, Directive 98/44/EC of the European Parliament and of the Council on the Legal Protection of Biotechnological Inventions (hereafter the “patent Directive”) was issued on 6 July 1998. The European Community having concluded this matter through the public and democratic process, no purpose is served by attempting to re-open this particular question or others related to it, including the circumstances under which DNA and RNA sequences may be patented.
- (3) A patent, though granted by a Patent Office, may be either valid or invalid. This is a matter which can be contested in a court or other appropriate tribunal. A patent cannot be validly granted for a product or process

which is already in the possession of the public. It follows that any biological material already in the public domain cannot be privatised in this way. The traditional microbial, plant or animal materials used by indigenous rural communities, as well as their traditional knowledge and agricultural practices, remain forever available both to them and to their descendants. This should be recalled when reference is made to “patenting seeds” of rural communities. Patent procedure being fallible, mistakes can occur and there have been recent instances of traditional remedies being patented in countries remote from the source of this knowledge. Such mistakes are usually corrected once they have been drawn to the attention of the proper authorities and the full facts are known.

- (4) Patents are territorially limited to the jurisdiction under which they are granted. A patent granted in Europe has no direct effect in countries outside Europe. Consequently if no corresponding patent has been applied for in, say, a particular developing country, the local industry and public are free to put the invention to use within that country. However, they may or may not be free to export the product to the “patent country”, depending on what is covered by the patent (for this, read the “claims” of the patent).
- (5) A patent gives the patent-holder no positive right to do anything except seek from a court a remedy against unauthorised use of the invention by others. This will be explained further below. A patent-holder who takes such action has to face the possibility that the defendant will counter-claim that the patent is invalid and should therefore be revoked. Instead of going to law, a patent-holder will often choose to regulate the situation by licensing the patent to the other party on reasonable terms.
- (6) A patent has a limited duration after which anyone may exploit the invention freely.

### 1.3.3 Patenting and morality

Patent law in many countries excludes certain kinds of invention from patentability. One such exclusion pertains to the question of morality. In Europe the morality provision is contained in the first part of Article 53 of the European Patent Convention (EPC) which reads:

EPC Article 53

European patents shall not be granted in respect of:

- (a) inventions the publication or exploitation of which would be contrary to ordre public or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States:
- (b) plant or animal varieties or essentially biological processes for the production of plants or animals: this provision does not apply to microbiological processes or the products thereof.

The national laws of Member States of the EPC contain a comparable provision, although for the national equivalent to Article 53(a) some variations from the above wording are to be found.

No guidance has been provided by the legislators as to the meaning of the term “*contrary to morality*” in EPC Article 53(a) or the system of ethics by which the European and National patent authorities are to apply this provision. But it is clear that, as far as the patent law itself is concerned, the moral question applies to the act of publication or exploitation (use) of the invention rather than to any other activity (see later).

The patent Directive identifies certain specific types of invention which are to be unpatentable as contrary to morality (see later). This Directive is addressed to EU Member States in respect of their own national patent laws, and not to the EPC directly, but it will undoubtedly affect patent practice under the EPC.

### 1.3.4 The interpretation of European patent law

The European Patent Office (EPO), through its Examining Divisions and Appeal Boards, has primary responsibility for the interpretation of the EPC. However, applicants for patents and opponents of such patents are entitled to present moral arguments in dispute of particular official rulings. Furthermore, patents granted by the EPO can be challenged in national courts on this as well as on other grounds.

The EPO official Guideline on Article 53(a) states that “*This provision is likely to be invoked only in rare and extreme cases. A fair test to apply is to consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable*”. This statement accords with the principle established in EPC jurisprudence of interpreting all exclusionary provisions in the narrowest sense possible.

The EPO is developing its position on this subject in connection with a small number of disputed patent applications and patents some of which are discussed below. Formal opposition proceedings on specific patents provide occasions for the EPO Opposition Division and Appeal Boards to interpret Article 53(a) with reference to biotechnological inventions. It is doubtful whether any generally accepted moral principle is offended by the grant of patents on industrially applicable processes involving biological material or on such material *per se*. As defined in the patent Directive, “*Biological material means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system*”. This must include living organisms, viruses, genes and other forms of DNA and RNA. Recital 15 of the patent Directive notes that “*no prohibition or exclusion exists in national or European law (Munich Convention) which precludes a priori the patentability of biological matter*”.

Opponents of certain patents for transgenic plants and animals have raised objections based on risk to the environment and animal suffering. The currently most important test case is the formal Opposition by certain special interest groups to the Harvard oncomouse patent, in which the primary moral question is whether the potential benefit to cancer research

justifies the use of animals genetically engineered to possess increased sensitivity to carcinogens. As this case may not provide a useful precedent for transgenic farm animals, it is not reported with the case studies given below. A decision of the EPO Opposition Division has been awaited for some time and may now be expedited by the issuance of the patent Directive.

The patent Directive, by Article 6.2 (d), denies patents for “*processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.*”

So far there is no comparable test case in the EPO bearing on transgenic farm animals. As to the ethics of novel animal breeding methods, some commentators (from outside the patent official or patent professional community) have suggested that certain types of genetic modification may give rise to “intrinsic objections” which cannot be justified by appeal to potential benefits. For example, modifications which subordinate the life of the animal to human ends and over-ride what is natural to the animal are viewed by some as immoral. It is unlikely to be a straightforward matter for the patent authorities to discriminate between acceptable and unacceptable modifications.

Before outlining some of the matters raised in opposition to certain specific patents it is necessary briefly to consider a question which continually enters the general debate on these issues. This touches on the morality of the very act of patenting certain kinds of invention in biotechnology.

### 1.3.5 The morality of patenting

As indicated above, patent law is explicit in confining the question to whether publication or use of the particular invention is to be judged immoral. But at a deeper level it is considered by some commentators that, over and above the permitted ground of objection under EPC Article 53(a), the very act of patenting certain kinds of invention ranks as a moral issue in itself. This view deserves comment because of the persistence of those who hold it strongly.

Recital (14) of the patent Directive notes that “*a patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial and commercial purposes...*”. This is a cardinal principle of patent law and is relied on by those who hold the view that no moral principle is breached by the acquisition of the legally-permitted rights of inventors to protect their intellectual property against unauthorised use by others.

It is important to emphasise, at this stage of the analysis, that it is the act of seeking and obtaining the legal right that is being considered, not the manner in which a patent-holder might choose to exploit or enforce it.

To hold the contrary position to that advanced above would entail a substantial burden of logical proof. Few commentators would try to extract the intellectual property procurement issue from the context in which it arises, namely, a programme of research, development, and exploitation. Thus, it would seem difficult to divorce this question from that of the morality of the research which precedes the invention. It is the research that

leads to an invention and it is the subsequent patent application that leads to the grant (or refusal) of a patent. As is clear from EPC Article 53(a), the morality of doing the research does not enter into the equation at all. But on general moral reasoning it would be possible to argue that if the research is morally objectionable then to benefit in any way from it, *eg* by the grant of a legally protected position, would also be unacceptable. Biological scientists on the whole might be uncomfortable with the idea of research being immoral. It is also common among the general public to find support for the position that life-science research, though sometimes morally questionable, could be justified if it is likely to generate important scientific knowledge (a utilitarian approach). If so, would it be reasonable to hold that the patenting of its practical application would be morally reprehensible? In practice such a conclusion would probably be rarely encountered.

As indicated above a moral distinction is possible between, on the one hand, the obtaining of legal rights and, on the other, the manner in which such rights are exercised. This distinction is familiar in the patent context from past provisions on Compulsory Licensing which were exercisable in rare cases of abuse of monopoly in some countries and, in others more routinely, to legalise manufacture by the local industry in competition with imported products. In view of the change of attitude towards this issue encouraged by the TRIPS Agreement, and the lack of experience of its implementation so far, it is premature to try to develop this theme here.

### 1.3.6 Case studies

#### 1.3.6.1 The Relaxin case

The Green Party opposed European patent 112.149 granted to the Howard Florey Institute of Experimental Physiology and Medicine for human H-2 relaxin, a hormone involved in reproduction, and a DNA sequence coding for the hormone.

##### *The facts*

A patent for the first relaxin hormone to be discovered (relaxin H-1) had been granted previously but was not in issue in these proceedings. The m-RNA coding for the H-2 relaxin protein had been isolated from ovarian tissue removed in the treatment of an ectopic pregnancy.

##### *The Opponents' Arguments*

The Opponents took objection on a number of grounds. Those concerning morality and *ordre public* are summarised below.

- (i) It was alleged that it is an offence against morals to exploit the pregnancy condition of a woman by removing tissue from her ovary and using it as the basis of a profit-oriented technical process.
- (ii) The use of the ovarian tissue for the purposes of the patent amounted to a form of slavery since it involved dismemberment of women and their piecemeal sale to commercial enterprises. This infringed the human right to self-determination.
- (iii) To patent human genes meant that human life was being patented, which was intrinsically immoral.

- (iv) There was a public consensus that human genes should not be patented.

##### *The Opposition Division decision*

- (i) The patent proprietor had stated that the tissue had been provided with patient consent. This was an instance of a general practice accepted and even welcomed by the public, and approved by the (then) Draft Council of Europe Bioethics Convention, provided the proper information and consent procedures were followed.
- (ii) The slavery argument betrayed a fundamental misunderstanding of the effects of a patent. Gene patents convey no rights to individual human beings. The only stage at which the original human patient was involved was as a voluntary source of relaxin m-RNA.
- (iii) DNA is not "life" but a chemical substance which carries information. A human being cannot be reconstituted from the sum total of human genes. No moral distinction is to be made between the patenting of genes and the patenting of other human substances.
- (iv) The patenting of human genes was a controversial issue on which the opinion of society was not yet definitively formed. It was held that "Only in those very limited cases in which there appears to be an overwhelming consensus that the exploitation or publication of an invention would be immoral may an invention be excluded from patentability under Article 53(a)".

#### 1.3.6.2 The Plant Genetic Systems case (Decision T356/93)

Plant Genetic Systems European patent 242,236 was directed to transgenic plants containing in their cells a gene which conferred resistance to the herbicide *Basta*.

##### *The most important claim:*

*"Plant, non-biologically transformed, which possesses, stably integrated into the genome of its cells, a foreign DNA nucleotide sequence encoding a protein having non-variety-specific enzymatic activity capable of neutralising or inactivating a glutamine synthetase inhibitor under the control of a promoter recognised by the polymerase of said cells"*.

The patent also had claims to the methodology for transforming the plant, vectors, plant cells, and seed. It is important to note that the claims were not limited to particular plant species but referred to "plants" in general. Until this patent was challenged the EPO had been willing to allow patents for plants defined in this generalised way *ie* in non-variety specific terms.

The patent was opposed by Greenpeace under EPC Article 53. The main attack on the patent was based on the morality and *ordre public* provisions of Article 53 (a), the argument being that it was immoral to "own" plants, which were the common heritage of mankind. Greenpeace supported this by producing results of surveys/opinion polls taken in Sweden (only farmers were consulted) and Switzerland.

**The decision of the Technical Board of Appeal:**

The Technical Appeal Board considered the morality objection in depth and rejected it. The Board set out the following principles which they considered relevant to the assessment of such objections:

## (i) The relevance of the human cultural background.

The Board noted that those who drew up the EPC had recognised that “*there was no European definition of morality*”, the same being said for *ordre public*. This was therefore a matter for European Institutions. The Board considered it as generally accepted that *ordre public* covered the protection of public security, the physical integrity of individuals, and the protection of the environment. The concept of morality was founded on the totality of accepted norms deeply rooted in a culture which, for the EPC, was the culture inherent in European society and civilisation. Inventions whose exploitation was not in conformity with conventionally accepted standards of conduct pertaining to this culture were to be excluded from patentability as being contrary to morality. The assessment of both *ordre public* and morality was not dependent on national laws or regulations as stated in EPC Article 53 (a) second half sentence.

## (ii) The concept of patentability in the EPC

For the EPC, the concept of patentability was to be as wide as possible, and in the previous case law (including cases relating to plant varieties) the exceptions to patentability had been construed narrowly. In one such case (the oncomouse) a previous Board had held that “*no general exclusion of inventions in the sphere of animate nature can be inferred from the EPC*”. That Board had indicated a moral test based “*on a careful weighing up of the suffering of animals and possible risks to the environment on the one hand and the invention’s usefulness to mankind on the other.*”

## (iii) The issue of living matter

The Board held that seeds and plants cannot be excluded from patentability merely because they are living matter or because plant genetic resources are the heritage of mankind. The patenting of wild type plant resources was not in issue in the present case.

## (iv) Public opinion

The Board considered that surveys and opinion polls did not necessarily reflect *ordre public* concerns or moral norms deeply rooted in European culture. They could fluctuate or be easily influenced and controlled. To be relevant in proceedings of the present kind, such surveys would have to be directed to the specific invention in dispute. A survey or opinion poll showing that a particular group of people or even a majority of the people in some or all EPC contracting States disapproved of the invention could not serve as a sufficient criterion for these purposes.

## (v) The morality issue

Concerning the question of man’s dominion over the natural world, technology which allows a better understanding and control of natural phenomena linked to plants is not intrinsically wrong. Plant biotechnology per se cannot be regarded as more contrary to morality than traditional selective breeding because both are guided by the same motivation, which is to change the properties of a plant by introducing into it novel genetic material in order to obtain a new and possibly improved plant.

The more powerful and accurate control which plant biotechnology offers is at the origin of public concern and apprehension, but this tool, like any other, can be used for constructive or destructive purposes. Only in the latter case should a patent be refused under Article 53 (a).

## (vi) Judgment of the Board

The PGS patent was directed to the introduction of herbicide resistance into plants. This could not be considered wrong as such. None of the claims of the patent related to a misuse or destructive use of plant biotechnological techniques.

Conceding the opponent’s submission that patent offices “*are placed at the cross-roads of science and public policy*” the Board observed that such offices “*stand side by side with other authorities and bodies*”. In particular, regulatory authorities and bodies exist whose function it is, inter alia, to ensure that the exploitation of a given technology, regardless of whether it is protected by patent or not, takes place within the regulatory framework by laws, international treaties, administrative provisions etc..

On the question of risk assessment the Board referred to the difficulties of making such assessments in relation to pharmaceuticals, herbicides, insecticides etc and pointed out that these matters are the province of other specialised bodies, and are concluded usually long after a patent has been granted. Moreover it would be difficult to assess risk to the environment solely on the basis of the patent specification. To revoke a patent on this ground presupposed that the risk had been “*substantiated at the time the decision to revoke the patent is taken by the EPO*”.

The documents relied on by Greenpeace amounted to no more than suggesting a “*possibility*” or “*potential effects*” in this context. No conclusive evidence had been produced by Greenpeace that exploitation of the patent would “*seriously prejudice the environment*”. It would be unjustified to deny a patent merely on the basis of “*possible, not yet conclusively-documented hazards*”.

In conclusion, Article 53(a) did not constitute a bar to patentability in this case because none of the claims of the patent comprised subject matter the exploitation of which would be contrary to *ordre public* or morality.

### 1.3.7 Other relevant issues in the patent Directive

Articles 4, 5, and 6 of the Directive identify other areas of unpatentability. Most of these are concerned with human gene sequences and other aspects of human biotechnology and medicine. Article 6.2 (d) has been mentioned above (animal suffering). There is no proscription concerning plant biotechnology inventions under the heading of morality. The prohibition of patents for plant varieties and essentially biological processes is declaratory of EPC Article 53(b) and therefore largely superfluous.

In Article 11.1 the well-known derogation for farmers in respect of farm-saved seed (under plant variety right law) is extended to patent law. However, this freedom is no longer ensured under the UPOV Convention as revised in 1991 and now operative in some UPOV Member States. It has also been modified under Article 14 of Regulation (EC) No 2100/94 on European Community plant breeders' rights. Royalty is now payable on farm-saved seed under both legal systems but at a "sensibly lower" rate compared to the notional rate on purchased seed.

Article 11.2 applies a similar derogation to animal farmers except that no system of animal variety rights exists as a

comparable model and so this is left to national laws and regulations. Farmers can use purchased material for their own agricultural use but not for purposes of further reproduction as a commercial activity.

### 1.3.8 Conclusions

The decisions summarised above are important for the purposes of the present study insofar as they show the positions held by one pan-European Institution on the moral aspects of new technology. The European patent system, now operative all Member States of the European Union (and some non-Member States also) is firmly established as the most important patent-granting facility in Europe, which profoundly influences the positions of national patent systems on the issues under study. Of the specific cases outlined above, only the PGS case has been finally decided. When final decisions are reached in the oncomouse and Relaxin cases these, together with the PGS case, will provide representative samples of inventions which have been challenged across the field of plants, animals, and materials derived from human tissues. The European Parliament and Council Directive on the Legal Protection of Biotechnological Inventions will also contribute to the final settlement of these issues for the European public.

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## Chapter 2

### Food

#### 2.1 Overview

##### 2.1.1 Public acceptance of biotechnology and cultural aspects of food

Agriculture has always over the last 10,000 years depended heavily on plant and animal breeding. For millennia this was done by trial and error but since the beginning of this century on a progressively more scientific basis. In the past 20 years biotechnology, using the tools of molecular biology, has opened up new possibilities, particularly in crop development. Biotechnology, however, stimulates ethical concerns both in professional ethicists and in the general public. Several opinion surveys (among others, the Eurobarometers 35.1, 39.1, and 46.1 on Biotechnology) have shown that the public perception of food biotechnology is significantly different from that of other (*eg* medical) applications of biotechnology and genetic engineering. Why? One possible answer is the peculiar characteristic of biotechnology (especially of genetic engineering) of touching upon deeply rooted cultural archetypes (*ie* fundamental images inherited by everybody) related to birth and death, reproduction and family relationships and an individual's body and identity (Wynne *et al.*, 1997). The genetic modification of plants, animals and microorganisms for therapeutic purposes is generally better accepted than for agro-food applications (Hamstra, 1993). The critical character of public attitudes towards food biotechnology is probably the result of a synergy between the cultural and symbolic functions of food, the capacity of genetic technologies to destabilise cultural archetypes, and most people's relative ignorance about biology and how agriculture uses plant and animal breeding to improve crops and farm animals.

Food has always had a symbolic significance in all human cultures. It is one of the most important elements by which a social group characterises itself as different from others. Food also functions in characterising certain religions by proscribing specific foods as taboo.

##### 2.1.2 Biotechnology from a consumer point of view

In Europe, it has been suggested that public attitudes towards food are increasingly characterised by anxieties, as consumers are becoming less and less familiar with their food and its origin and composition. Public concerns have led to the increasing importance of consumer movements calling for more complete information, stricter safety controls, attention to the "ethical content" of food products and wider choice.

Consumer attitudes towards food biotechnology seem to be rather ambivalent in nature, as actual purchasing behaviours may appear to contrast with stated opinions. This apparent inconsistency has often been observed in consumer research, leading to the conclusion that there is no necessary correspondence between social acceptance of biotechnology and consumer willingness to buy its products (Hamstra 1993). This should not induce us to assume that the opinions expressed

by consumers are illogical but rather to acknowledge the simultaneous existence in the same person of different cognitive perspectives (Wynne, 1997).

The application of modern biotechnology to food production is sometimes subjected to careful scrutiny in order to assess whether other technological options might be preferable. A need for justification has clearly emerged in recent empirical research (Wynne, 1997) and this need for genetically engineered food seems not to be required by large numbers of consumers because of perceived high risk to their health. The motivations underlying such demands to show that genetic technology in food production is really needed seem to be of a complex nature. One is clearly lack of factual knowledge, as exemplified in Eurobarometer 46.1. How can the ethical implications of genetical techniques be considered, if only one-third of the population know that plants have genes? Informed debate depends on adequate knowledge. Surveys (*eg* Institute of Grocery Distribution, 1997) have suggested that most consumers in their actual shopping behaviour do not reject or accept genetically modified foods on absolute criteria, rather they weigh the perceived benefits against the potential risks. Such perceived cost-benefit balance may have more to do with individual tastes than with values and norms. The underlying motivations seem also to be of a complex ethical nature. However, few efforts to analyse them in an ethical perspective have been made so far.

A more general argument for the need for applying biotechnology in food production concerns the urgency to increase the global food supply in the face of world population growth. However, as food shortage problems mostly affect developing countries, ethical discussion of this issue is contained in the chapter on Developing Countries.

The most important areas where the use of biotechnology can provide benefits from the European consumers' point of view can be:

- (a) Price: in principle, all productivity-enhancing innovations (for example, transgenic salmon with increased growth rate) should lead to cost reductions. However, cost reductions are not always automatically transferred to consumers. Surveys (*eg* Hamstra, 1993, FhG-ISI, 1998) suggest that no direct price decrease is expected by consumers for products made by means of biotechnology, but rather an improvement of the price-performance ratio.
- (b) Quality: biotechnology and genetic engineering can help to improve various quality aspects of foods such as taste, flavour, colour, etc.. In addition, new analytical tools based on biotechnology can carry out quality control and monitoring more effectively.
- (c) Health: biotechnology can help to design healthier food products with improved nutritional value (Food and Drink Federation, 1995), *eg*:

modified fat foods: for example, genetically modified crops (corn, soya, oilseed rape, canola) with reduced saturated fat content of cooking oils);

higher protein foods: for example, crops with higher protein content to address problems of poor nutrition due to lack of proteins;

higher vitamin foods: fruit and vegetables modified to contain higher levels of nutrients, for example vitamins C and E;

longer lasting fruit and vegetables: genetic modification can slow down softening providing fruits that last longer.

In the case of the so-called functional foods (*ie* food products designed to meet the nutritional needs of specific population groups such as the elderly, pregnant women, people affected by specific disorders, athletes), biotechnology may help to prevent health problems.

### 2.1.3 Institutional actions

The regulatory activities of international bodies and national governments have been mostly directed to addressing safety concerns. In the EU safety issues have recently assumed even greater importance following the BSE crisis and have led to change in Community policy towards consumers and the creation of a new Directorate-General (DG XXIV). This is responsible for controlling enforcement of relevant regulations and promoting consumer information with eight scientific committees to assess the safety of different categories of products for human and animal health. Safety considerations are central in the most important regulation concerning food derived from biotechnology, the EC Regulation on Novel Foods and Novel Food Ingredients (258/97). Ethical issues not related to safety, however, have also been addressed. Article 8 of the Regulation establishes a specific labelling requirement to inform population groups with “well established” food practices of the presence in a novel food of a material which is not present in conventional equivalent foodstuffs and which “gives rise to ethical concerns”. Of course, distinguishing between “established” and “not established” practices may give rise to controversies over interpretation. Determination of the ethical concerns which should be considered appears still open in a social environment characterised by rapid cultural change and the spread of new religious practices in recent years.

Labelling is still a controversial regulatory issue at the international level. In the United States, where no specific regulation of the labelling of biotechnology products has been enacted, the Food and Drug Administration considers that, in the absence of any evidence that plant foods obtained by genetic engineering present greater safety concerns, no special labelling is required. The process by which a new plant food is produced is irrelevant to its safety assessment (FDA, 1992). Subsequently the FDA announced its protocol for evaluating foods derived from new plant varieties on chemical, biological and molecular considerations.

In the UK the Food Advisory Committee (FAC) which advises the Ministry of Agriculture and the Department of Health on matters relating to food safety proposed to determine labelling requirements on a case-by-case basis. In January 1997, advising the Government on a genetically modified cottonseed, the FAC

excluded the need for any special labelling but encouraged the provision of information on a voluntary basis “in response to public interest”. A similar case-by-case approach can be found in a report of the Australian House of Representatives Standing Committee (House of Representatives Standing Committee on Industry, Science and Technology, 1992) concluding that “*there should be labelling of some products which contain GMOs or which are produced by GMOs*”. However, this should be decided on a case-by-case basis.

In the field of bioethics the applications of biotechnology and genetic engineering in food production have generally received less attention than in their medical uses. Debate on the ethical implications of food biotechnology has been focused mostly on animal welfare, particularly in Northern European countries. Increasing concern for animal welfare in European societies has generated several initiatives. The most important one at the European level has been the decision of the Council of Europe in 1991 to amend the European Convention for the protection of animals kept for farming purposes of 10 March 1976, extending the scope of the Convention to genetically modified animals. The Protocol of Amendment included the requirement that biotechnological breeding programmes were “*designed to avoid foreseeable suffering or injury of the animals, such as difficult deliveries and lasting deformations*”. This general principle included the prohibition of breeding from genetically modified animals “*unless, in the light of available scientific knowledge and/or established experience... it could be reasonably expected that the animals, or the animals produced by these animals, would not suffer as a consequence of this breeding*”.

With Recommendation 1213 (1993), the Parliamentary Assembly of the Council of Europe extended the scope of its ethical reflection to the broader field of biotechnology applied to agriculture, by the following recommendations:

- \* avoid any unnecessary suffering of animals;
- \* ensure careful monitoring of risks;
- \* pay special attention to the need for better and more information to the public through the organisation of information activities and exhibitions and through appropriate labelling;
- \* protect biodiversity and ecosystems;
- \* implement technology assessments for biotechnology inventions;
- \* encourage the inclusion of bioethics in the training of specialists in the field of biotechnology.

Within the EU, the most intensive institutional activity in this field has probably been in the UK where the Report of the Committee on the Ethics of Genetic Modification and Food Use (The Polkinghorne Committee, 1993) has addressed the ethical aspects of food produced by genetic modification. The Committee found no justification for any general ethical condemnation of the use of GMOs in food production, but recommended recognising the food sensitivities of different religious groups by specific labelling provisions. For example, members of the Jewish faith have had separate production and distribution channels for kosher food for a long time. Other groups may wish to do likewise for other food preferences.

### 2.1.4 Does biotechnology raise new ethical questions in food production?

Another set of issues concerns the fundamental question whether biotechnology applied to food production raises ethical issues not raised by previous technologies.

From a scientific perspective, according to many, biotechnology is basically a further development of traditional techniques such as fermentation, baking, brewing, plant breeding, etc.. Traditional and new techniques would be “basically equivalent”, and the products of food biotechnology would not pose specific problems compared with traditional products. Breeding techniques inducing genetic variation in plant and animal species have been known for thousands of years and have profoundly modified plants and animals. Natural mutation and selection are powerful agents in evolution. During the last 30 years techniques such as cell fusion have allowed the crossing of plant or animal species across species boundaries which would not interbreed naturally. The changes brought about by biotechnology differ insofar as one or few specific DNA sequences of known function are transferred. The novelty is that the transferred genetic information may come from any organism and is better controlled. The products of modern biotechnology need to be analysed in a careful step-by-step and case-by-case procedure. Many scientists may question why a new variety was produced by traditional breeding, by biotechnology or by importing from anywhere else in the world into a new ecosystem (Am. Soc. of Ecology, 1988, Ammann, 1998). It is the rule, stated primitively, that “*the prophecy of doom is to be given greater heed than the prophecy of bliss*”. (Jonas, 1984).

Such considerations are indirectly relevant also to the ethical aspects of food consumption as some consumers are aware that their consumption choices are capable of influencing decisions made by producers, including their technological choices. There has been debate for years around the concept of “responsible consumption” mostly in Central and Northern European countries. The purchase of organic foods has been increasing, but these foods are still a product bought by a small minority usually at premium prices. Most consumers are guided primarily by the price and the perceived quality of the products, and not by how the products are produced.

In the following sections analysis of the ethical implications of biotechnology will be devoted to pre-farm gate and post-farm gate stages of production and consumption.

## 2.2 Pre-farm gate: ethical implications of biotechnology in food production

Analysis at the pre-farm gate level addresses a wide range of issues concerning the relationships between humans and other species, between present and future generations and between different social categories. The most important areas of bioethical reflection concerning biotechnology in food production are discussed below in brief in order to stress their indirect relevance to the ethical dimension of consumption.

### 2.2.1 Environmental ethics

Within philosophical reflection on the relationship between humans and non-humans, two approaches can be identified. The

first one, characterised as “shallow ecology”, does not question anthropocentrism and reduces the ecological crisis to a set of concrete problems. The second, “deep ecology” is based on the belief that the human species cannot be separated from the rest of Nature (the ecocentric perspective). While the former proposes “a careful management of resources”, the latter upholds the “principle of non-interference” with Nature. Taken at face value and in its extremist interpretation, non-interference would mean that humans would have to return to hunter-gatherer subsistence. Both views may support the ethical principle of respect for Nature and the environment.

The ontological difference between human and non-human beings leads to a different evaluation of biotechnological applications depending on whether they concern microorganisms, plants and animals or human beings. For instance, the primacy of the human over the non-human has been mitigated within the Catholic culture (see pontifical appeals to greater respect for the environment such as John Paul II, *The Ecological Crisis a Common Responsibility*, Message of His Holiness for the celebration of the World Day of Peace, 1990) and replaced with the concept of human responsibility towards the environment (humans as the keepers of the Creation). The rethinking of the relationship between human beings and Nature suggested by environmental ethics suggests the/a need to adopt a stronger precautionary attitude towards changes which are largely unknown in Nature. From a perspective of responsible consumption, consumers have a right to be informed and to choose more environmentally friendly food products (including those food products derived from genetically modified plants or animals with reduced environmental impact from that of conventional products).

### 2.2.2 Biodiversity

As a possible consequence of diffusion of agro-biotechnologies, many see risk of reduction of genetic diversity in agricultural ecosystems. “*Careless application of biotechnologies may have an impact on biodiversity if a gene of economic interest were to be associated with a very small number of varieties*” (OECD 1998). On the other hand, biotechnology could contribute to biological diversity both by creating new organisms and by providing new effective conservation techniques. There are two levels of biodiversity to be considered: organisms in their natural habitats, and plant and animal varieties developed by farmers over millennia. Modern farming practices have reduced the range of plants used for food production, whilst on the other hand the number of plant varieties has increased immensely.

Some authors forecast drastic reduction of crop genetic diversity in agriculturally influenced ecosystems as a consequence of agro-biotechnology. Cultivation of genetically modified crops is likely to expand if they are more economically competitive (by virtue of costs, incentives, industry pressures, pest resistance and yields) and they increase sustainability of farming. However, competition between the many agricultural biotechnology companies and seed producers may lead to a wide variety of transgenic crops. It will often be desirable to introduce new traits by gene transfer into landraces which are well adapted to local soil, climate, diseases, parasites etc. and which have grown out of the local culture. From a biological point of view, it is inconceivable that only very few varieties of a certain plant species can be grown successfully

throughout the world, given the multitude of varying climatic, soil type, local conditions, etc..

Intensive farming has also reduced the genetic diversity of farm animals by inducing uniformity within species. Genetic engineering is likely to have less impact on farm animals than on plant crops not only for scientific and technical reasons but also due to public perceptions which are critical of increasing the productivity of farm animals by any means possible. However, other techniques of modern biology impact on animal breeding, such as *in vitro* fertilisation, embryo transfer and cloning.

One specific ethical aspect concerns the strong link between the diversity of local crops and animal breeds and the cultural diversity (traditions, food habits, values and beliefs) which is rooted in, and contributes to preserve, biological diversity. Any loss of traditional biodiversity entails a loss of cultural heritage. This is the reason why traditional landraces and breeds are qualitatively different from industrial cultivars and breeds intended to be replaced periodically by new, improved ones. In this sense, it cannot be assumed that loss of traditional varieties will be compensated by creation of new varieties. However, it must be realised that urban societies could only develop after farmers could produce more food than they needed for themselves and that world population growth can only be sustained by continued increase in food production.

### 2.2.3 Sustainability

The concept of sustainability has primarily to do with the relationship between present and future generations. Biotechnology could effectively contribute to the food supply of future generations. However, like any new technology it involves a certain degree of uncertainty and the precautionary principle requires that other existing technological options are carefully preserved. Our concern for survival of future generations should suggest promoting diversification of food production technologies. In addition, agricultural technologies using conventional organisms (such as organic agriculture) may even be seen as cost-effective and self-supporting *in-situ* (in the field) conservation activities compared with costly *ex-situ* conservation facilities (gene banks). The two important issues are farming techniques that allow the soil to be used year after year and conservation of germplasm. Modern methods of plant breeding can lead to crops that require less tilling and thereby lead to less soil erosion. Experimental transgenic plants have also been developed that resist drought, tolerate high concentrations of aluminium or that can take up toxic materials such as cadmium from the soil. Transgenic crops already in the field use fewer insecticides and fewer herbicides, thereby reducing need for agrochemicals. One of the most important threats to plants in their natural habitats is the spread of weedy plants which were imported from overseas by horticulturists and which have become serious competitors to indigenous plants. While potential weediness of transgenic plants needs to be considered, it may not be a significant problem because weediness depends on the selective advantage of many genes functioning in combination which are unrelated to genes introduced for agronomic reasons. The second point to be considered in the context of sustainability is the preservation of germplasm for future breeding purposes, both *in situ* and in seed and tissue banks.

In some cases the spread of pollen from transgenic crops may be seen as a threat to biodiversity and thereby raise ethical concerns. Ever since plant breeding has been practised, there has been a spread of genes from cultivated crops to related wild species, a phenomenon called "introgression". In the centres of origin, *ie* the geographic areas where wild relatives of crop plants are found, introgression leads to hybrid formation and slow change of the original, natural species. Introgression has had much less spectacular effects on ecosystems than the introduction of foreign, horticulturally attractive plants. Introgression has been difficult to observe because changes are subtle but some have been demonstrated *eg* between sugarbeet and *Beta maritima*. One real concern using transgenic crops is the spread of a new trait, for instance herbicide resistance, which might give a related weed selective advantage. If resistance to a herbicide is introduced into oats, for example, there might be a spread of this resistance to wild oats, which are difficult to eradicate. The worst consequence would be that the particular herbicide no longer acts against the weed. Where there is possibility of introgression, releases therefore need to be evaluated on a case-by-case basis. In principle these arguments also hold for non-transgenic crop varieties.

Many common crops do not have close wild relatives in Europe, *eg* maize, potato and soya, and therefore introgression is of no relevance. However, another argument comes into play here: organic farmers may worry that their non-transgenic crops may, to a small extent, be pollinated from a transgenic crop on a neighbouring field, thus threatening the organic status of their crops. With adequate distances between fields the likelihood of an unwanted transfer can be reduced very considerably. The frequency of transfer would then be very low and below an established threshold value.

For some years to come the suppliers of food from crops that have not been genetically modified will be organic farmers. Their organisations have on a world-wide basis decided not to plant genetically modified crops. In the future some organic farmers may not consider this position ethically tenable, since genetically modified crops may make considerable contributions to a more sustainable agriculture and may prove to make a substantial difference to world food security. Once the new technology is seen to make important contributions to help solve these problems, its ethical appreciation may become very different.

### 2.2.4 Animal rights

In industrialised countries animals are increasingly considered as individual subjects of rights at both ethical and legal levels. Contemporary ethics has developed a variety of theoretical perspectives concerning animal welfare. Such ethical concerns for farm animals involve biotechnology in two ways. Ethical analysis addresses firstly new animal drugs and feed additives produced using biotechnological techniques which have the potential to improve or harm animal health and nutrition precisely like drugs or feeds produced through conventional means and therefore seem not to have novel ethical implications. Secondly, creation of transgenic animals which, on the contrary, has both direct (animal health and welfare) and indirect ethical implications, *eg* helping to find new therapies for previously incurable human diseases or paving the way to genetic interventions on human beings. Ethical concerns have

also been expressed about the potential for animal suffering, lack of respect for animals as sentient creatures and excessively instrumental modifications of their natures. Key ethical questions include: *Do particular applications of gene technology cause animal suffering or harm animals? Are animal interests given due consideration when comparing costs and benefits? Is the essential nature or telos of some animals being changed or disregarded?* All these questions need to be analysed on a case-by-case basis.

In one important way, the same arguments hold for animals as for plants. Whether a new property of an animal arises through genetic engineering or through traditional breeding, seems irrelevant. In both cases genetic information has been rearranged, either in the laboratory or through sexual exchange, but only the rearrangements that Nature accepts will survive. What is important are the properties of the new variety that has been bred, not the mode by which genetic information was exchanged. This can be seen by discussing three real experimental situations.

- (a) Many young farm animals suffer in the first few days of their lives from infections by Rota-viruses. These viruses damage the intestinal mucosa and lead to heavy diarrhoea, which in the extreme can be fatal. Farmers lose considerable numbers of animals due to this infection. The animals succumb, because there are receptors on the intestinal wall, which allow the virus to enter into the tissue and to multiply there. If these receptors could be eliminated by genetic engineering without any secondary effect, this would be beneficial for the animal's health and it would be economically advantageous to farmers. There appears to be no obvious ethical reason for not including genetic engineering in animal breeding, if this procedure improves the animal's health. However, some would argue that many of the health problems suffered by farm animals are themselves the result of ethically dubious farming practices and should not be resolved by genetic engineering.
- (b) Several proteins used in human medicine may soon be produced in farm animals after genes for these human proteins have been transferred into the genome of the animals. In this way there are herds of sheep that secrete human alpha-antitrypsin (AAT) in their milk. The milk of these animals is collected and the substance isolated from milk and purified. Several proteins produced in this manner are now in clinical evaluation. It is difficult or impossible to produce these proteins in any other way and they are used as life-saving pharmaceuticals. The sheep, goats or cows that are used are perfectly normal in their physiology and behaviour. From an ethical point of view this use of animals is arguably little different from the use made of farm animals to produce normal milk, a procedure which is acceptable to most people. Of course there are other people who refuse to consume milk products and for them the production of medicines in milk may also be ethically unacceptable. One may wonder what an emphysema patient would do if he or she were a strict vegetarian and knew that his or her life depended on having injections of ATA.

- (c) In a famous experiment in the USA some ten years ago scientists introduced additional gene copies for growth hormone into pigs. The offspring of these animals did grow faster, but they also suffered from several malformations which lead amongst other things to severe arthritis. Because of the undesirable side effects these experiments were discontinued. It is clear from an ethical point of view that the productivity of farm animals must not be increased by animals suffering and such breeding products are ethically unacceptable. It should be noted that individuals in several breeds of dogs, for example, have serious health defects and their breeding should, from an ethical point of view, be discontinued.

These examples show that genetic engineering of animals is neither good nor bad, but products of breeding need to be assessed from an ethical point of view on a case-by-case basis. The consensus is that animal breeders have to take into account sentient animal experiences and avoid unnecessary suffering.

### 2.2.5 Socio-economic impacts

Ethical assessment of agro-biotechnology must also take into consideration possible impacts at the socio-economic level and identify the social groups which are likely to be differently affected. Positive impacts include increased productivity and farmers' income, while negative impacts include market concentration and increased unemployment in the agro-food and related service sectors. The need to take into consideration possible socio-economic impacts of biotechnological innovation has been acknowledged by some for the first time with the introduction of bovine somatotropin (rBST). Following years of intense debate, the European Commission stated that in exceptional cases the three traditional assessment criteria of safety, quality and efficacy may not be sufficient (Communication SEC (91) 629). A different approach has prevailed in the USA where the US Executive Branch concluded a review of literature on the social impacts of rBST, with the statement. *"At no time in the past has the US Federal Government prevented a technology from being adopted on the basis of socio-economic consequences"* (US Executive Office of the President 1994). It is still open whether the WTO will tolerate such differences in the regulatory approach in different countries, since they might be seen as indirect trade barriers.

The social impacts of biotechnology in agriculture and food production have been classified into three major categories (Thompson, 1997):

Impacts on small farms: the most debated ethical issue in this context concerns the possibility that biotechnological productivity-enhancing products might induce market concentration and threaten the survival of small farms;

Impacts on the economies of developing countries: many authors have forecast serious impacts on rural economies of the developing world with a redistribution of benefits from small to large and relatively better-off farmers according to the same pattern predicted for the industrialised world. According to others, poor farmers too might benefit from the development of biotechnology. The overall impact is controversial, difficult to foresee, even if the majority of authors agree on focusing on

issues with relevant ethical implications. These include technology transfer from industrialised to developing countries and to increased economic and technological dependency of developing countries;

Impacts on the scientific community: many authors have predicted that increasing commercialisation of science would shift the focus of research from publicly-supported programmes aimed at publicly beneficial objectives to more profitable corporate activities. These predictions have raised ethical concerns about scientific purity, the social function of science and public trust in scientists (Thompson, 1997). However, these concerns are not restricted to food biotechnology.

## 2.3 Post-farm gate: ethics of the consumption of biotechnology food products

### 2.3.1 Relevant principles concerning the responsibility of the producer

In agriculture and food production, the producer is not only directly responsible to consumers for the safety of products, but also indirectly for the possible consequences of genetic engineering on the environment, animals, and future generations.

Concerns about risk and safety are often given prominence in discussions about the ethics of food biotechnology. However, risk and safety are not ethical issues in themselves. What risks attach to a particular food is an empirical question, not an ethical one. That it is, for example, more risky to eat shellfish than potatoes is a matter of statistical fact, not an ethical problem. Risk and safety can have an ethical dimension and become matters of moral concern when they raise further questions about responsibility, accountability and justifiability. Moral concern is appropriate when unjustifiable risks are taken which may result in harm to innocent parties.

A food producer has the moral and legal obligation to guarantee the safety of products. If insufficient care results in an unsafe product which causes harm, the producer could be held to be morally culpable and legally accountable. This approach to the principle of responsibility is complicated by the fact that no product or process can ever be guaranteed to be 100% safe; one can only talk in terms of likelihoods. With new and unpredictable technologies, uncertainty about possible outcomes is inevitable. In the case of food biotechnology, therefore, the moral responsibility of the producer can only be to ensure that all reasonable care is taken in the light of current knowledge. This in turn implies that the principles of transparency and openness are closely linked to that of responsibility.

Accountability is a more concrete requirement involving the possibility of being held answerable for the consequences of one's own actions. Liability is a more specific legal concept involving the possibility for producers to be forced to answer and compensate for negative consequences of their activities on consumers' health.

In this context the priority condition to ensure respect of consumers' rights is the willingness of producers to provide consumers with correct and complete information about the

characteristics of the product and of the process by which it is derived (openness). Such information, rather than being focused on possible risks for human health (which are still to a large extent unknown given the current level of scientific knowledge), should describe the aims, the methods and the details of the genetic modification in question. Only with access to full information can the consumer be said to freely consent to buy and consume any genetically modified product. This information may be provided in different forms, such as information brochures, leaflets, customer phone service etc. Informed consent, then, is the relevant ethical principle here.

### 2.3.2 Consumer's rights

Basic consumer claims concerning consumption of biotechnological food products are about safety and information. Actually the two issues appear intertwined as the consumer may claim a right to be informed in order to decide whether or not to accept the risk involved in consuming novel food products. The most relevant question to be addressed here is what information should be provided to consumers so that they can make informed choices, considering that different groups have different concerns for ethical, religious and medical reasons.

#### 2.3.2.1 Right to health

A first set of problems concerns food safety and the right of consumers to have their health protected from possible hazards deriving from consumption of food products obtained from biotechnology. According to the OECD definition, the concept of food safety is based on "*a reasonable certainty that no harm will result from intended use under the anticipated condition of consumption*". Three main areas of concern have been identified in this context: toxicity, allergenicity and nutritional value.

In general, risk analysts distinguish two different conditions of scientific ignorance leading to different approaches to the problems of risk and uncertainty: Risk analysis takes place when possible harmful consequences can be identified beforehand and the probability of their occurrence can be quantified. Risk assessment is a process that requires the capacity to imagine scenarios and mechanisms that can end in harm. By definition, the scenario that no one thinks of will not be included in the risk assessed in this manner. Entirely unanticipated scenarios are unlikely once scientists have worked diligently to anticipate all possible risks. However, it is not reasonable to conclude that they do not exist. Individuals accept risks to which they have given informed consent. The consumer should therefore be made capable of understanding foreseeable risks and realise that no human action is without risk. In the presence of uncertainty, the capacity to quantify risk is reduced. The level of scientific uncertainty affecting issues such as food allergies represents a challenge to safety assessment of foods produced traditionally or by biotechnology. For example, will people who are allergic to shellfish or peanut butter become allergic to any food in which a fish or peanut gene has been inserted? Not necessarily, because it depends on the nature of the transferred gene and because only very specific proteins cause allergies and these proteins can be identified and analysed by standard laboratory procedures. In addition, genetic engineering offers the possibility of removing allergens from

foods in a very directed manner, which has not been possible before. Although uncertainty with respect to food safety is controlled in part because product liability laws make food companies careful about introducing a novel product in the absence of strong scientific evidence documenting its safety for human consumption, economic interests may induce potential abuses of food technology. On the other hand, too stringent a set of regulations may prevent useful innovation, in the absence of any real risks. Reinforced public surveillance can help to reduce uncertainty and consequent public anxieties, particularly in relation to long term effects.

Most, if not all, of the institutional reports and proposals on food safety evaluation produced since 1990 by, among others, FAO/WHO, OECD, the EU, the UK, the USA, the Netherlands, Australia and Japan agree that genetically engineered food products are not inherently less safe for human consumption than traditional foods, and do not require a different standard of safety. Established systems of risk assessment can therefore be employed. A case-by-case approach based on the scientific concept of substantial equivalence is usually recommended. The FlavrSavr tomato developed by Calgene was the first genetically modified food to be approved and underwent extensive evaluation by the FDA before its release in 1994. Subsequently, case-by-case registrations of several crops and their products have gone through the regulatory process in many countries and no specific problems related to the genetic engineering of the seeds have shown up.

Concerning the concept of substantial equivalence, the 1990 joint FAO/WHO consultation has established that the comparison of the final product with an existing one having an acceptable standard of safety provides an important element for safety assessment. OECD has elaborated this concept concluding that the concept of substantial equivalence is the most practical approach to address the safety evaluation of foods or food components derived by biotechnology. However the establishment of substantial equivalence is held to mean that *“further safety or nutritional concerns are expected to be insignificant”* (OECD, 1993), though the novel or modified product has been obtained using totally different and novel processes. In other words, the concept focuses on the product, rather than the process.

### 2.3.2.2 Right to be informed

Another relevant issue in food biotechnology is the right of consumers to be informed of the natural or genetically modified character of food products. Supporters of the principle of “substantial equivalence” do not deem it necessary to provide information on the nature of food products. This is, for example, the position of the FDA in the USA. Others consider it of vital importance that the consumer is enabled to identify genetically modified materials through appropriate labels. However, not even the labelling of genetically engineered foods is considered sufficient by some who require more detailed information which may also be supplied by separate leaflets, brochures, consumer hotlines, etc.

The ethical principles of individual freedom and autonomy are involved in food choices. Consumers, therefore, need information about the foods offered to them in order to make informed choice. A major source of that information is labels.

However even labelling may be insufficient (Wynne, 1997) in the presence of widespread lack of awareness and basic scientific knowledge. Educational initiatives are crucial in raising public awareness of the issues surrounding genetically modified foods. On the other hand, education should be provided also to the scientific community and the industry about the nature and relevance of public concerns. It is crucial to ensure the balanced and unbiased nature of the information provided to the public. Communication strategies should bring together the scientific and general community in order to promote openness, dialogue and collaboration.

Now that the European Union has decided in the Regulation on Novel Foods and Novel Food Ingredients (258/97) that, in principle, labelling of food from genetically modified crops will be mandatory, two particular problems with ethical implications need to be considered. One issue is the “negative list”, which indicates which products from genetically modified organisms do not need to be labelled because no trace of recombinant-DNA or protein can be detected. The other question concerns the need to label second generation products such as meat from animals fed with transgenic maize and soya, or soft drinks containing fructose produced with the help of enzymes made from genetically modified microorganisms. Labelling second generation products might in a very few years lead to the labelling of a vast number of food items. The second point concerns threshold values for compulsory labelling. Since detection methods for genetically modified crops are highly sensitive, trace amounts of contaminants could make it necessary to label a food item, even if it contained only a small amount of a product derived from a GMO. Contamination may come from a small amount of genetically modified material which had previously been transported in the same container or on the same conveyer belt. Therefore threshold values of a few percent are necessary, otherwise even products from organic farmers might require labelling. Most of the other general regulations on food safety use the concept of threshold values for many undesirable compounds.

### 2.3.2.3 Right to choose

Another right concerns the individual’s right to choose to consume or to avoid genetically engineered products. Though apparently it coincides with the right to information, this concept is autonomous in some ways. The choice to consume or not a genetically modified product may depend upon non-scientific reasons. This freedom, which must also be safeguarded, may be a matter of religion, morality, taste or, more generally, of opinion.

The history of food-related cultural beliefs has produced a rich array of religious and ethnically based beliefs about what is and is not food, rooted in motives which have little to do with current food safety issues. However, no one challenges the right of religious and ethnic minorities to establish food rules that might also be more restrictive than those stipulated in legal codes. Kosher and halal practices, respectively Jewish and Islamic dietary rules, require specific dietary restrictions. While Jewish representatives have found the use of genetically engineered food acceptable, Muslim representatives have found it objectionable. However such positions are not definitive as Judaic and Islamic religious authority is widely distributed across many rabbis and mullahs, each of whom might interpret

the rules differently. Other religious confessions have released statements about the lawfulness of genetically modified foods. Explicit rejections have been expressed by representatives of Sikh, Hindu and Buddhist religions. Rejection may be based on the presence of forbidden substances in genetically engineered foods or on their non-natural origin. Some Christian churches have expressed relatively minor concern over genetic modification. A particular problem would be raised if genes of human origin started to be inserted in foods. Some people feel that this would be tantamount to cannibalism, which is forbidden by the world's major religions and considered abhorrent by many without a religious faith. On the other hand, it can be argued that most 'human' genes are similar or identical to homologous genes in other species so that a charge of cannibalism is inappropriate. There is some evidence that some people with a strong religious faith would find it perfectly acceptable, for such reasons, to eat food with 'human' genes.

There is also no reason to deny a right to reject genetically modified foods when it is supported by non-religious, ideological or life-style reasons such as the positions of vegetarian and naturalist groups. Considerable diversity of dietary practice is found within vegetarianism. Those vegetarians who avoid the consumption of all animal products

are likely to find the presence of even a single copy gene of animal origin in a plant species to be unacceptable. However if the animal genes involved are "synthetic" this might be acceptable to some individuals who avoid eating meat solely because of concern about animal suffering.

Finally, the concept that any consumer, even if not supporting specific beliefs, must be granted the freedom to choose, appears rationally tenable both as an application of the principles of fair treatment and of respect for the autonomy of others (including members of minorities), and as an acknowledgement of the fact that the mere safety of the product is not the only relevant component of consumers' choice.

Possible limitations of freedom of choice are also likely to be influenced by the dynamics of competition. Choice is assumed to be provided only if competition effectively exists and monopolistic positions are excluded. This indicates an ethical need to preserve existing alternatives in food production to prevent the emergence of conflicts of rights between different categories of consumers with specific wants (for example, consumers who want tomatoes with prolonged shelf life and consumers who want naturally ripening tomatoes).

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## Chapter 3

# Environment

### 3.1 Introduction

The environment is everything around us. For a bacterium it can be a crumb of soil, while for a large bird of prey it can be many square kilometres or moorland and forest. For almost all creatures, other than humans, disturbance to a specific environment can lead to loss of food supplies, breeding territory and eventually the species itself. Humans are very adaptable and have changed their environment to an enormous extent, so that in most of Europe there are few undisturbed environments for humans, plants and most animals. Indeed, most of the European landscapes we so admire are the products of agriculture and other forms of human intervention that have taken place over the last few thousand years. For example, forests have been destroyed and land taken into plant production since before the Greek and Roman civilisations. Even areas that have had no direct impact from human intervention are undergoing subtle changes arising from climate change, atmospheric pollution, and the deposition of large amounts of fixed nitrogen in rainwater. Thus when discussing the environment in Europe and our interest in it we must remember that the wellbeing of almost every environment and species we might want to preserve is in some way dependent on human activity. This is particularly true for the great variety of plants and animals whose presence in Europe since the last ice age has been very dependent upon the opening-up of the countryside through the introduction of agriculture. This does not make their preservation less desirable, but does to a large extent demand that measures to preserve them will require agricultural practices, or similar forms of interference, that will enable their habitats to be preserved and enhanced. In fact, one of the most important reasons why there has been such a large decline in wild plants and animals in Western Europe compared to Eastern Europe and less developed regions in the EU is that agricultural practices have enhanced the efficiency of food production to the detriment of wildlife.

The pressing need in European countries to halt the decline in biodiversity and reductions in populations of wild animals, plants and other organisms that result from the highly intensive and efficient agricultural practices we use today is well known. It will require changes to existing agricultural practice. But will the introduction of genetically modified (GM) crops in agriculture make the situation worse? The intention of this report is to look at agricultural biotechnology from the point of view of its possible impact in the environment. It presents a concise review of the issues involved illustrated by two case studies which follow: of biodiversity in the Mediterranean region and the development of frost-tolerant potatoes. We do not intend to promote or condemn the use of biotechnology, but to offer a range of opinions on ways in which it may be beneficial or detrimental.

### 3.2 Ethical considerations

In considering the ethical aspects of agricultural biotechnology in relation to the environment, the intrinsic “rightness” or “wrongness” of biotechnology will not be addressed. Like any

other technology, it will be regarded to be neutral. It is acknowledged that modern biotechnology may raise moral concerns, but moral arguments also exist in its favour. Biotechnology can be a tool for the improvement of human health, to increase the food supply and in the achievement of sustainable development. It can be argued that biotechnology may breach natural species boundaries and infringe the genetic integrity of species. If it is solely used to promote monocultures it can enhance the existing problem of the erosion both of biodiversity and of the ecological environment; it can equally be used to enhance mixed cultivation and to allow sustainable agriculture with lower inputs.

The ethical dimension exists primarily in the tensions that occur between rich and poor (on an individual and on an international level); between present and future generations; between Humankind and Nature; between the need to facilitate production and the need to allow democratic participation in decision making. Decisions about the application of biotechnology should take account of public concerns, which may be allayed by improved communication and public education, though studies have shown that greater knowledge does not necessarily lead to greater acceptance.

### 3.3 The Precautionary Principle

Principle 15 of the Rio Declaration states: *“in order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.”* In doing so it evokes the precautionary principle, one of the central principles of sustainability. This principle is expressed in a number of international treaties such as The North Sea Declaration and the Maastricht Treaty of the EU.

The precautionary principle, by implication, puts a high value on nature and on future generations and, therefore, on sustainability. However, it is essentially a political axiom and may be open to interpretation. It implies that public risk must be minimised. It demands a new way of managing uncertainty and ignorance by all parties involved in environmental policy, but allows for a variability of approach according to the case in hand. The precautionary principle may supersede or conflict with other principles, such as environmental capacity or cost benefit. It is useful to identify a set of preconditions where the precautionary principle might be applied. The following are suggested:

- \* there is a reasonable assumption that a significant threat to the environment or biodiversity may exist;
- \* there exist major uncertainties;
- \* great value is attached to the preservation of the existing species mix in an environment.

In applying these it will be necessary to consider how the impact will differ from effects already introduced by traditional methods and, if it does not, whether such an impact still remains acceptable.

### 3.4 Sustainable development

Sustainable development aims to combine an economic and an environmental objective: stable, non-inflationary international economic growth and long-term conservation of natural resources and biodiversity. The importance of the environment was declared at international level by the UNED Rio Declaration (1992) accompanied by an agreement on the application of the precautionary principle; demanding full scientific certainty when threats of serious or irreversible damage to the environment may occur. The importance of biodiversity as a component of the environmental objective for sustainable development was also declared and a framework for co-operation and actions was agreed (UNED CBD, 1992). Not using productivity-enhancing technologies would have adverse consequences for biodiversity, environment and sustainability given growing world population and finite area for cultivation.

Problems of modern agriculture derive from the cultivation of few high-yielding, genetically uniform and input-responsive varieties (monocultures), as opposed to the diversified cultivation of a large number of traditional cultivars. This leads to loss of valuable genetic material, the gene pool on which, crop improvement is based. It also leads to international debate on the rights of farmers and breeders to genetic resources, and is a continued source of friction between the gene-rich South and the technology-rich North. The FAO Commission on Plant Genetic Resources established in 1983 achieved an agreement for placing the genetic material collections of the twelve Centres of the Consultative Group on International Agricultural Research under the auspices of FAO in 1994 to secure unobstructed research utilisation. The World Information and Early Warning System on Plant Genetic Resources has also been established to facilitate exchange of information on plant genetic resources collections and related technologies and to report on the state of the world's plant genetic resources. The continuous loss of traditional cultivars and the impoverishment of the available genetic pool however, still needs urgent action. On the other hand the ethical concept of Farmers' Rights was defined by the 1989 FAO Conference, but the matter is still far from resolved especially concerning the Agreement on Trade-Related Aspects of Intellectual Property Rights which has been signed by over 100 countries.

In agriculture, the environmental objective for sustainable development focuses primarily on the conservation of biological diversity and natural resources in agricultural ecosystems. The unique feature of biological diversity as applied to agriculture is the emphasis on its utility to human beings (UNED CBD, 1996). This utility includes food security and human health security through the food production chain. The conservation of natural resources as applied to agriculture demands low energy inputs, increased biotic and structural diversity at the landscape level (UNED CBD, 1996) and meeting the challenge of increasing production without expanding agriculture to marginally suitable land (Agenda 21, Chapter 14).

Food and ecosystem security is perceived as food and ecosystem safety by the public in developed countries. It could perhaps be better guaranteed by exploiting and improving classical agricultural production methodologies, focusing on integrated pest management, lower fertiliser inputs and disease resistant - stress tolerant and perhaps lower productivity plant varieties. High income and low population pressure allows consumers to pay a higher price for indigenous or imported products complying with the above production characteristics. For developing countries however food and ecosystem safety is an urgent matter of quantity security (food and land) rather than risk assessment and safety.

The theoretical potential of biotechnological applications related to genetic engineering appears to be enormous and experimental results are encouraging. However, it is too early to know if in practice there will be greater long-term increases in food supplies compared to conventional agricultural practice and technology improvements. Neither has the latter been fully exploited. Finally, protection of markets and subsidised food surpluses in the North undermines food production in developing countries in a way unrelated to technological improvement.

Developing countries demand full exploitation of technological innovation, such as the application of GMOs, in their effort to achieve both short- and long-term food security and are in general more willing to accept environmental risk. On the other hand, acceptance of GMOs may help developed countries to bypass the need to use traditional gene tools to produce improved biological material and to avoid pressures from developing countries for financial rewards for providing germplasm.

Sustainable development demands that we should not exceed the limits of ecosystem function, while securing economic growth. Genetic engineering solutions should therefore be applied in agriculture according to the precautionary principle and following strict application of orientated and diversified risk assessment methodologies. It is advisable that: (1) genetic engineering applications are assessed in independent case by case studies and funds are supplied for long term experimentation and (2) alternative technologies, agronomic practices and economic policies are encouraged. For example, the linkage between sustainable utilisation of crop genetic resources and conservation of biodiversity could be strengthened by supporting local/regional plant breeding programmes, either funded publicly or by industry.

### 3.5 Biodiversity

Biodiversity has value both for theological, i.e. ethical, reasons and for biological, i.e. selfish, ones. Humans exploit it for food, necessary for their own survival, and for a fast increasing series of non-food products for industry. Biodiversity, as well as providing attractive landscapes, plays a very important role in the avoidance of desertification, hydrogeologic structure and moderating dynamics, soil erosion, water and soil pollution, fire management and global environmental changes.

It is worth considering therefore, how biotechnology in agriculture might affect biodiversity. Changes in crop plant genomes may allow the extension of agriculture and the corresponding destruction of "natural" ecosystems. Improved

crop plants, animals and microorganisms may successfully compete with natural populations. Gene flow from cultivated crops or modified microbes to "natural" species may change equilibria of existing populations eventually opening new ways to evolution.

A further cause of concern in the fact that biotechnological innovation may, if it is very profitable, have dangerous effects on already very weak agricultural economies leading to further intensification thereby inducing significant losses in in-situ conservation capability.

**3.6 Societies' interests in the environment**

It is helpful to look at the environment in terms of how people in Western Europe perceive it, and thus to examine what we need to do to ensure that changes we make in the future do not lead to changes that are unacceptable. To help in this it is useful to have an indication of what are perceived to be important indicators of a desirable environment, remembering that most Europeans live in cities and are not biologists. Table 1 lists some indicators we have chosen on the basis that they are those that most people will see from the windows of their cars. Clearly they are not those often used by regulatory authorities to monitor environmental health, which would include amphibians, lichens and other species whose populations are highly sensitive monitors of change, but they are those that one would expect non-biologists to recognise and in so doing be aware of change. As almost all the indicators have been subject to major change in most environments throughout Europe, it is not surprising that public concerns about the health of the environment have been so clearly and forcibly articulated in recent years.

Birds	Present in sufficient numbers Well-known species Songbirds
Trees	Present in sufficient numbers Well-known species Diversity Distribution Mature
Flowers	Present in sufficient numbers Well-known species Sufficient colour in the environment
Unspoilt areas	Land not growing crops and unmanaged grassland Managed nature reserves

When thinking about the role of biotechnology in environmental change it is useful to look at a "public view" as listed in Table 1 and then to consider more complex components of a "healthy environment" that are equally important, if less visible. Most of the indicators in Table 1 are affected very dramatically by changes in traditional agriculture and will continue to change independently of the introduction of GM crops and animals as long as farming in Europe is driven by commercial and political needs. For example, the types of crop grown are more determined by policy decisions in Brussels than

they are by the preference of individual farmers, and there are strong incentives to be as efficient as possible. It is for this reason that there is so much concern about the impact of the Common Agricultural Policy on biodiversity, particularly in Eastern Europe and the less intensively cultivated areas within the existing EU. (See paragraph 3.9.)

Most of the indicators in Table 1 can be met by very significantly reducing the intensity of agriculture, allowing weeds to produce seeds and leaving larger areas of land for mixed woodland and rough pasture. While this is entirely feasible, it is unrealistic to believe that if all farmland was converted to low intensity agriculture sufficient food could be produced for present eating habits, and equally unrealistic to assume that eating habits will change rapidly, if at all. Furthermore, there is little likelihood that farmers would adopt such methods without major financial support. It is important, therefore, to see how existing farming practices can be modified so that food production is maintained in an environment that is "friendly" for wildlife, while at the same time allowing sufficient productivity from agricultural land to maintain farm incomes. As damage to populations of plants and animals has already occurred, and is considered to be serious, the changes that will be needed will initially be independent of the introduction of biotechnology because GM crops have not yet been grown commercially in Europe. However, it is important that as GM crops enter commerce their environmental impact is taken into consideration.

**3.7 Some examples of GM crops and possible environmental impacts**

If, as promised, GM crops are bred for stable resistance to pests and diseases the input of pesticides will decline rapidly everywhere which might be reflected in an increase in species that are considered to be harmed by their use. If this were the case there would be good reasons for encouraging GM crops. However, we need to consider that if crops are completely resistant to attack by all types of insect, fewer insects will be found in the countryside. Fewer insects mean fewer butterflies and other "desirable" insect species, as well as pests. As insects are a very important component of the diet of birds there would also be a decline in the population of birds. Thus, in respect of the impact of insect-resistant GM crops on the environment, there are both possible advantages and disadvantages. The challenge will be to learn how to obtain the benefits of reducing the use of pesticides without introducing another procedure that will lead to environmental harm.

Perhaps one of the most harmful agricultural treatments for wildlife is the efficient use of herbicides on crops. They are used to reduce competition between crops and weeds so that the crop has the maximum access to water, sunlight and nutrients. As a result yields are higher than untreated crops. From the point of view of seed-eating birds and other wild animals such crops become essentially deserts because the weedy species that would otherwise flower and set seeds throughout the year are absent. It is unlikely that agriculture can do without herbicides and thus the availability of seed-bearing weed species in crops will remain low to the detriment of a range of bird and small mammal species, and to those who wish to see colourful wildflowers in farmers' fields. It is for this reason that environmentalists' concerns about herbicide-tolerant crops are

difficult to dismiss as alarmist. However, the concerns raised are far from being specific to GM crops because all crops are naturally tolerant to some herbicides and new herbicide-tolerant varieties derived from traditional breeding are becoming available, and it is hard to see how weed control in existing non-transgenic wheat crops could be more efficient. On a more positive note we should be aware that the herbicides to which tolerant crops are being produced are those that have lower levels of adverse effects in water, and stability in the environment, than some of the herbicides that would no longer be needed.

Another possible impact of herbicide-tolerant crops is that they might breed with wild weedy species causing environmental problems. It is indeed true that some crops have related weedy species with which they can cross-pollinate. Cross-pollination of neighbouring compatible crops will always occur if they are within pollination range. The possible harm that such events could cause to the environment is almost totally associated with problems that will be caused to the farmers concerned. It is extremely unlikely that plants receiving herbicide-tolerance genes would become invasive of undisturbed habitats. Much the most important impact will be that seed shed by the crops will produce herbicide-tolerant plants that will grow in the following crop. Any sensible farmer will be prepared for this eventuality and will use other herbicides to control the problem. In time, with the use of different herbicide-tolerant crops, the seedbank in the soil will produce plants with a range of different tolerances, further compromising weed control. The possible response will be to increase again the range of herbicides used, but in practice with sensible management the problem is unlikely to become serious. From the point of view of wildlife a worst case position in relation to herbicide-tolerant weeds would be one in which weed control was so compromised that fields became more weedy, which would be of great environmental benefit to wildlife. It is also feasible that if weeds and volunteer plants tolerant to a variety of herbicides become a problem there will be an increase in the amount and range of herbicides used.

As well as influencing the diversity and populations of plants and animals, developments in agricultural biotechnology have the possibility to affect microorganisms and other "unseen" organisms in soil. These changes can result from the changing nature of the crops that are grown and also from specific treatments to soil to influence organisms within it. Obviously, relative proportions and numbers of the different species of bacteria and fungi change when fields are ploughed, or are subjected to any form of agricultural treatment. Likewise, changes in the crops grown will have an impact by altering the amount of different chemicals exuded into soil and more intimate relationships that occur among specific groups of plants and microbes. An example of such relationships is that involved in the formation of mycorrhizas, which are associations of roots and fungi. Cereal crops are mycorrhizal (unless too much phosphate fertiliser is added), but oilseed rape is not. Thus for these fungi their ability to grow is very constrained by the presence of host plants. Similar effects might arise from the use of GM crops that contain genes making them resistant to fungi, but would this matter? It could matter for the plants concerned because their ability to extract phosphate from soil is greatly enhanced by forming mycorrhizal associations, but can be redressed by the use of phosphate fertilisers.

However, anything that might reduce the populations of these fungi should be viewed with some concern, even if the impact is the same as growing a non-mycorrhizal crop.

Another possible impact of altering the balance of microbes in soil is that some species of bacteria and fungi that are associated with roots help to protect the host plant from colonisation by pathogens. Clearly an unexpected side effect of genetic modification (or traditional breeding) could be to affect such balances. We must assume that risks of harm for food production are very small because almost anything we can imagine will shift the balance of populations of soil microorganisms, but we have no history of major adverse effects arising from plant breeding, changing rotations or soil treatments that can be attributed to shifting the balance.

### 3.8 Conclusions

Most of the environmental problems we have in the EU today are the result of the impact of enormous populations of humans through increased efficiency in agriculture, urbanisation, pollution and the exploitation of natural resources. (This is shown very clearly in the case study of biodiversity in the Mediterranean region which follows.) However, the environment is largely dependent on agricultural practices that offer the opportunity for halting and redressing the harm that is being done. As yet, biotechnological agriculture has had no impact on the problem because GM crops are only now becoming available.

It is clear that GM crops offer opportunities to enhance the efficiency of agriculture and thus indirectly put further pressure on wild plants and animals. Some GM crops might have direct impacts by killing, or preventing the growth of, insects and other animals and depending how they are used and developed could cause harm, or reduce the harm resulting from the use of pesticides. Another possibility is that the use of GM crops that enhance yields could enable larger areas to be set aside to encourage biodiversity. In this respect, the case study on potatoes (following) shows clearly that there are few simple answers to questions about the risks or benefits of new technologies, and it would be foolish of us to pretend otherwise.

We have concentrated very little of our efforts in identifying the ethical problems of the impact of agriculture on the environment. In part this is because the ethical problems are mostly at the level of the "rights or wrongs" of the use of biotechnology in agriculture and are addressed in chapter 4. Also it is because the use of biotechnology is not in itself an ethical issue if one takes the viewpoint that humans may use selective breeding to enhance the production of crops and animals. The really big ethical issues are about the "right" we have to displace and even eliminate other species. In part this "right" is assumed every time we uproot a weed or kill a mosquito, but it is clear it only extends so far. In practice to date it has been extended to the right to farm as desired and to make massive changes to natural landscapes. What may or may not be ethical in future is further confused by the situation within Europe where deforestation centuries ago has produced areas of very high biodiversity that could only be harmed by the re-introduction of tree species. Whether we like it or not, there is no resolution to ethical or environmental concerns that can be resolved by "allowing nature to take its own course". Somehow we must find ways of changing agricultural practices in ways

that ensure adequate safe food production, the livelihood of people working on the land, and the enhancement of biodiversity over large areas of the EU. Biotechnology will be a tool that can be used well, badly, or inefficiently, and in this will be little different from many other things we do that impact on agriculture and the environment.

**3.9 Biodiversity in the Mediterranean region, with special reference to Greece**

**3.9.1 Introduction**

Concerns about the impact of agricultural biotechnology on biodiversity need to be related to the extent of the existing biodiversity in Europe, the degree of our knowledge about its extent, and how it is already threatened. This brief review indicates some of the information that we have for the region within Europe that has the greatest biodiversity. We have concentrated much of the report on Greece because this is a country for which we have detailed information.

The Mediterranean area has a surface area of approx. 2,300,000 km<sup>2</sup>. It is very heterogeneous with rugged massifs often fragmented by deep narrow valleys, highlands and enormous sedimentary basins, jagged and winding coastlines with numerous islands. The very wide ranges of climatic and ecological conditions have produced the highest level of biodiversity in Europe.

**3.9.2 Fungi**

About 300 species of macrofungi are considered to be endangered throughout Europe, on the basis of published national and regional lists. They are arranged in four categories depending on the degree and geographical extent of endangerment. The evidence of losses is biased towards central, western and northern Europe, because for the southern and eastern regions of the continent data are scarce and fragmentary. For the Mediterranean countries in particular, no red data list for fungi is available for Albania, Cyprus, France, Greece, Italy, Portugal, Spain, Turkey and the former Yugoslav regions. This striking absence of information means that any conclusions drawn about overall declines are at best tentative. Any list should be expected to change rapidly during a period of rapid climatic change to which the fungi are among the first organisms to respond. Large gaps exist in our knowledge on microfungi too, except of some groups of economic importance. Conservational aspects of microfungi are more difficult to study due to methodological problems.

Air pollution threatens ectomycorrhizal fungi and presents a

severe problem. Previous EU agricultural policies have led to a fast and irreversible loss of old poorly managed pastures and their associated fungi. Increased exploitation of forests has put at risk the few remaining ancient forests with their characteristic wood-inhabiting fungi. Draining peat bogs has affected their few but strongly specialised fungi, and the strong pressures of recreation and expansion of towns have jeopardised the existence of coastal sand dunes with their striking gasteromycetes.

**3.9.3 Myxomycetes**

Despite the abundance and worldwide occurrence of Myxomycetes (plasmodial slime moulds), floristic studies in the Mediterranean region are lacking and there are still some totally unexplored countries. Knowledge is fragmentary, as indicated by the variation in number of species recorded in each area. Relatively well studied are France, Italy, Morocco, Portugal and Spain; little studied are Algeria, Greece, Israel, Tunisia and Turkey; while practically no information exists from Albania, Cyprus, Egypt, Lebanon, Libya, Malta, Syria and the former Yugoslavia. The region provides a wide range of climatic and ecological conditions, which support one of the richest Myxomycete flora in the world. According to a recently established database, 413 species representing approx. 70% of the known world species are reported from this area.

**3.9.4 Flora of Greece**

Greece participates in most international conventions on environmental protection issues and has undertaken specific international commitments towards the protection and conservation of its natural heritage. Special reference must be made to the Ramsar Convention, in which 11 Greek areas were included among the internationally most important areas. The first National Park, created in 1938, was Mt. Olympus. In 1971 ten National Parks, 19 Aesthetic Forests and 51 protected National Monuments were designated to protect the flora, fauna, forest and natural formations. Specific protection measures were also taken through the application of the "Natura 2000" project, whose aim is to ensure biodiversity by means of the establishment of a network of protected sites, and by the protection of specific habitats deemed of high conservation priority or of interest to the EU.

The Red Data Book of Plants contains 263 species and subspecies of vascular plants from the Greek flora, classified under Extinct (6 species), Endangered (36), Vulnerable (146) and Rare (75). IUCN (1982) estimates the total number of endemic species and subspecies in Greece to be 739, out of which 5 are Extinct, 21 Endangered, 37 Vulnerable and 355

**Table 2 Number of Greek Taxa (Species-subspecies) per category as included in different description classes**

	Total	Endemic	Red Data Book	Rare	Vulnerable	Endangered	Extinct
Plants	6308	1275	263	75	146	36	6
Mammals	102	28	60				
Reptiles 176	74	8			7		
Amphibians	18	3		1			
Freshwater fish	107	39	21				
Invertebrates	25000	2000					
Birds	425	100					

Rare (Table 2). The work that is currently conducted for compiling the *Flora Hellenica* shows that the known numbers of species and subspecies in Greek flora, as well as the numbers of endemic and rare plants, are constantly changing. In the *Flora Hellenica* the number was calculated to be 6,308 (cf. Denmark with about 1,300 and Great Britain with about 1,800). The most recent figure for the number of endemic taxa is 1,275, or 20.2% of the total Greek flora, and is the highest figure for any territory of a comparable size in Europe, or the Mediterranean area (cf. mainland Spain has 501 endemic species and Morocco 536).

### 3.9.5 Fauna of Greece

The fauna of Greece is very rich compared to that of the other European States. However, the presence of humans and their activities have created pressures on many populations and has driven several species and subspecies to extinction. The Habitat Directive, although not as complete as would have been expected, is a good opportunity to conserve what still exists today. The animal species listed in the Annexes to Directives 92/43/EEC and 79/409/EEC are in Table 3.

**Table 3 Number of Greek species per category as included in Directives 791409/EEC(Annex I) and 92143/EEC (Annexes II, IV and V).**

	Annex I	Annex II	Annex IV	Annex V
Mammals		22	52	4
Reptiles/Amphibians			51	2
Freshwater Fish		49	2	13
Invertebrates			21	8
Birds	129			
Totals	129	71	126	27

World-wide, mammals are a very diverse group comprising ca. 4,000 species that have adapted to diverse environments. The wild mammal fauna in Greece consists of 100 of the 190 species in Europe. Among these, two species (the insectivore *Crocidura zimmermanni* and the rodent *Acomys minous*) and 26 subspecies are endemic. In addition three priority species are included in the "Natura 2000" project: *Ursus arctos*, *Canis lupus*, and *Monachus monachus*. The taxa have been recorded in all the zoogeographical regions of Greece.

Greece offers habitats to a number of mammal species that are threatened with extinction, or are already extinct in other European countries (eg otter, wolf, brown bear, and jackal). However, mammal populations and their habitats also face serious threats in Greece. During the last 100 years species such as the beaver, brown bear, wolf, lynx, or the deer have disappeared from most, or all, of areas in Greece. The reasons for their reduction are attributed to various human activities, such as illegal hunting and fishing, deforestation, intensification of agriculture, pollution, excessive use of pesticides and fertilisers, road construction, destructive interference in wetlands and urbanisation.

Greece is one of the richest countries in Europe as far as its avifauna is concerned. According to recent unpublished data, 425 bird species (100 of which are included in the Red Data Book) have been recorded in Greece. Most of these species (ca.

60%) breed in Greece, while the rest are migratory; winter in Greece, or are present during migration periods. The high diversity in Greece is due to overwintering birds, its geographical position at the crossroads of several migratory corridors, the wide diversity of habitats, and the quality of the habitats.

The Greek reptile fauna is very diverse, comprising 59 species and 117 subspecies of chelonians and squamates (as compared to over 95 species of reptiles in Europe). There are eight species of chelonians, 28 of lizards, and 22 of snakes. There are nine endemic reptile species in Greece; six of them are lizards and three are snakes. Perhaps the most serious threat to the reptiles of Greece is the alteration or destruction of their habitats, summer fires, pollution, and collection for trade. However, very few of them are threatened with extinction, and in the Red Data Book only seven reptile species are mentioned.

In Greece, there are 18 amphibian species, as compared to about 50 species in Europe. The anurans are represented by 12 species of toads and frogs, while all five of the six tailed amphibians belong to two genera of the family Salamandridae. At least 2-3 subspecies are considered to be endemic to Greece. During the last 30 years an obvious decline in all European species of amphibians has been noted, which is due to natural (eg ageing of lakes and ponds) or anthropogenic degradation (habitats destruction, pollution, disturbance, over-collection, etc.). The status of the amphibians in Greece is not well known. At the species level, only one, the Luschan's salamander (*Mertensiella luschani*), is mentioned as "rare" in the Red Data Book of Threatened Vertebrates of Greece.

According to recent investigations on the freshwater fish fauna of Greece, 112 fish species have been found in the rivers and lakes of the country. Of these, 21 are euryhaline, while the remaining live exclusively in freshwater. Among them, 81 species are autochthonous primary freshwater, of which 39 are endemic to Greece and some to the southern parts of neighbouring countries; there are also 40 endemic subspecies.

The group of invertebrates is the least represented in the EU Directives. It is estimated that approximately 25,000 species of invertebrates are found in Greece, of these at least 2,000 are endemic (some have been recorded in only one site). About 10% of the species have very small populations, or are threatened with extinction. However, only 33 species found in Greece have been included in the various Annexes to the EU Directive.

### 3.9.6 Agricultural biodiversity

Many areas of non-intensive agriculture in Greece are characterised by significant species richness, both in fauna and flora, which is often comparable to that of adjacent "natural" ecosystems. Many agricultural areas are of particular aesthetic and ecological value, mainly in mountainous regions and in islands. The co-existence of agro-ecosystems with "natural" ecosystems reinforces the land variability and contributes to the conservation of biodiversity. They often produce a dense network of ecological pathways that facilitate species mobility.

In Greece, a large number of plant species and varieties are cultivated which have been selected locally by farmers. Most of these varieties represent mixed populations and this prevents

them from being included in the European and National Conservation Lists (they can not be declared as “unique”, “uniform”, and “stable”). Hence today, there are only about 150 plant varieties registered in the National List out of about 500 known varieties (non-qualifying populations), and an estimated existing total of about 1,000. All of them are conserved on farms in scattered and confined geographical regions, where they thrive under very heterogeneous conditions and are undergoing constant change. In contrast, there are ca. 7,500 varieties of cultivated plants that are conserved in gene banks, but unfortunately the maintenance conditions are not ideal. Sixty-three species and 281 varieties of cultivated plants and about 100 species, subspecies and varieties of important autochthonous plants in 35,000 hectares of agricultural land are about to be included in a conservation programme.

Pertinent to the issue of the protection of the Greek flora is also a group of species of special interest, namely that of traditional plantation trees. Beyond any sentimental value they might evoke, these species are of scientific interest as gene reservoirs. Typical examples are the olive (*Olea europaea*), the fig (*Ficus carica*), the apple (*Malus sylvestris*), and the carob tree (*Ceratonia siliqua*) which have formed a significant element of agricultural production for centuries.

Rare and endangered species and tribes of farm animals are also a concern. EU Directive 2078/92/EEC and the STAR Commission of the EU have provided a framework for their protection and conservation. In Greece today, there are 6 tribes of cattle (Extinct: 4, Endangered: 1, and Vulnerable: 1), 18 tribes of sheep (Extinct: 7, Endangered: 3, and Vulnerable: 8), 1 tribe of goats (Vulnerable), and 6 tribes of horses (Extinct: 3, Endangered: 3). It is expected that poultry and pigs will be added in the first update of 2078/.

It is clear from this brief survey that the Mediterranean region is one in which there is great biodiversity and some of the last areas in Europe in which “traditional” agricultural practices allow the persistence of a high degree of natural diversity, and also diversity in the genotypes of many crops. Thus, this is an area within the EU in which economic pressure and “advances” in the efficiency of agriculture could have a disproportional impact on biodiversity. The introduction of very popular GM crops could further add pressure to reduce the number of local mixed genotypes of a variety of field crops. It is not our business to discuss how socio-economic policy should be planned within the EU, nor to suggest how to protect small “traditional” farmers. However, unless action is taken the drift from the land of such people will inevitable result in the erosion of extremely important and visually attractive centres of biodiversity.

### 3.10 Frost tolerant potatoes

#### 3.10.1 Background

The potato is one of the major world crops, particularly in temperate regions. For example, in 1994 twelve EU countries produced about 45 million tonnes of potatoes, of which two thirds were used for human food. Potato production is affected by disease, insects and frost. While the first two can be controlled chemically, frost damage can only be avoided by planting tubers when spring frosts have finished, with the not

infrequent risk that late frosts will devastate crop production. Cloning genes encoding antifreeze proteins could produce frost-tolerant potatoes, but no fully frost resistant crops have been obtained using antifreeze proteins (AFP) from fish. This is because fish AFPs can only reduce the freezing temperature by 1.0 to 1.5°C. They can also inhibit ice crystal formation and reduce the harm caused by late spring frosts.

Far more active antifreeze proteins are found in insect larvae. The genes for two such proteins, usually called THP (for thermal hysteresis proteins) have recently been isolated from the spruce budworm and from the common mealworm beetle. These insect THPs are 10 to 100 times more effective than fish AFPs. Until THP plants are available there is a role for AFP potatoes in regions where spring frosts are a problem. In Russia, for instance, morning frost in the spring can severely damage early potato seedlings, and the only solution is to replant the fields with new plant material. Therefore, even the limited protection conferred by fish AFPs could be beneficial. In the near future, frost resistant transgenic plants will express insect THP genes encoding superior antifreeze proteins. Such problems as safety for humans and animals as well as allergenicity will have to be elucidated. As the flounder is a common part of the human diet, it is likely that AFPs will be fairly rapidly accepted as safe, but for the insect proteins it is likely that there will be a need for very extensive studies of their potential toxicity and allergenicity.

#### 3.10.2 Environmental risks

The most obvious risk to the environment is that a greatly reduced sensitivity to frost damage could make potatoes into weeds that will cause problems for farmers, and if they became invasive could cause harm to undisturbed environments. We do not know the extent to which these two sources of harm could happen. However, we do know that potatoes are not a pest in Egyptian agriculture, and that weedy native potatoes exist in the Andes that are very frost tolerant and, as wild plants, obviously have genes that enable their existence outside of arable agriculture. It is logical to assume that the GM cultivars are very unlikely to pose as much of a risk as these wild plants.

Perhaps of more concern in the long term is the possibility that GM potatoes will transfer the genes for frost resistance to very weedy wild relatives whose weedy properties are kept in check in cold areas by frost. While no such relatives exist in Europe, this could give rise to problems in the Andes. However, if selection for frost tolerance is so strong, why is it that over the last few thousand years cross pollination under natural conditions has not produced such weedy hybrids? The fact that the frost tolerant phenotype of the GM potatoes is determined by a single dominant gene enhances the frequency with which the phenotype can be inherited compared to the native resistance, which is likely to be polygenic. It can only enhance an existing probability. The obvious way to avoid any possible problem is to prohibit the cultivation of GM frost resistant crops close to wild populations of potatoes; something that is almost impossible to demand, let alone enforce, if hungry people are able to gain access to frost tolerant tubers. It is important to remember that farmers are not stupid and that they will wish to take advantage of valuable sources of new germplasm and will do so without regard to laws that they may know nothing about. For example, there is evidence that Mexican small farmers who

take casual work in the USA are bringing home seed from GM insect-resistant maize.

Ever since it was first grown on a large scale the potato has been recognised as perhaps the most productive food crop for temperate regions in terms of the number of people that can be fed per hectare of cultivated land. From the point of view of the environment such high productivity potentially has great advantages because it reduces the area needed to feed a given population. In a perfect world with no population increase, this would be reflected in an ability of farmers to release land for other uses, and would decrease the pressure for utilising previously uncultivated areas for agriculture. In reality it is likely that potato cultivation would expand into areas in which they have not previously been cultivated. While this would most likely be at the expense of other crops there might still be adverse impacts on the environment. This is because the cultivation of potatoes is very effective for reducing weed problems. However, from the point of view of birds and other animals the loss of weeds leads to starvation and significant population declines. In balance it would appear that the introduction of frost tolerant potatoes will offer major advantages to farmers whose production is highly susceptible to spring frosts, but may be of less benefit to farmers whose problems with potatoes acting as weeds in following crops is of more concern than frost damage.

### 3.10.3 Socio-economic issues

A major concern arising from the cultivation of any staple crop is overdependence, so that serious diseases, such as potato blight, can cause major famines as occurred within Europe in the 1840s. The other likely cause of crop failures, frost damage, should be obviated by the use of frost tolerant potatoes unless the areas cultivated expand to regions in which temperatures are marginal for the tolerance mechanism. It is very hard to see how this would not happen as people living in marginal areas, such as the high Andes, will want to maximise the production of potatoes and will inevitably wish to plant in cooler situations. The likely long-term outcome will be the ability to support increased populations in environments that could not sustain them without frost tolerant potato varieties. Greater dependence could produce a situation in which a serious outbreak of disease could lead to malnutrition. How likely it is that disease epidemics would develop will to a great extent depend on the genetic diversity of the frost tolerant varieties being introduced into agriculture.

Just how much diversity will be available will be determined by the amount of breeding done for farmers in marginal areas. Present experience suggests that this will be very limited, which will have two major adverse effects. The first will be the cultivation of a very restricted range of genotypes, greatly enhancing the risks from disease. The other will be a decline in the number of local landraces grown because they will not have the same desirable frost tolerant characteristics. The loss of landraces has occurred everywhere and is not a particular problem arising from the use of GM crops. However, if GM varieties do have significantly greater advantages over existing landraces than conventional varieties, they will be expected to speed-up the rate of loss of species diversity. From the point of view of the farmers and people who eat potatoes there will be a

corresponding loss of the ranges of flavour and other culinary characteristics that they have become accustomed to. Who is to judge whether it is better to retain diversity and be hungry, than to be well fed and lose the benefits of choice and variety?

An important secondary benefit arising from the cultivation of frost tolerant potatoes that will influence the likely spread of diseases is that colder regions are less conducive to the development of large aphid populations greatly reducing the potential for the transmission of virus diseases. Just how important this might be in reducing the risks inherent in the replacement of diverse genotypes, as discussed above, is unclear. We have experience from northern Europe in that seed potatoes for the UK are produced in Scotland because aphid populations, and thus virus infection, are much lower than in the relatively warmer England. However, potato blight, which does not need an insect vector, spread very effectively throughout Scotland in the 1840s.

Another important impact is likely to be a significant shift of the cultivation of potatoes for the high value "early potato" market. Thus, exporting countries such as Egypt might lose important European markets because early potatoes can be cultivated within Europe, benefiting some of the poorer areas on the far west of Europe that presently produce a limited amount of relatively early potatoes with production being very dependent on the absence of late spring frosts. The benefit to these farmers would be in direct conflict with the need for a relatively poor neighbour to generate foreign earnings. It is very unlikely that genetically modified potatoes would be the only crops whose culture would become possible in Europe causing a series of conflicts of interest. It is hard to imagine that artificial barriers, such as those used to control the production of corn starch syrup and provide access to cane sugar, will have a place in world trade agreements in the 21st century.

Whether or not we should be concerned about socioeconomic impacts will depend as much upon our political views as so-called level headed scientific judgement. There is a clear problem of malnutrition in parts of the Andes that can be addressed now by the cultivation of frost-tolerant potatoes, but as with all such problems associated with poverty, increasing peoples' opportunities to generate wealth is probably the only long-term solution.

A much more interesting problem is: who has the responsibility to decide whether or not genetically modified potatoes should be cultivated in regions, such as the high Andes? Two concerns are important in examining this problem, The first is related to the environmental damage that such potatoes could cause when a major constraint to their ability to overwinter and spread is removed. How important is frost damage in killing tubers left in the soil and in harming growth in the early spring? If people are hungry does it matter that potatoes may spread and become weeds in farmers' fields, or even become invasive in uncultivated land? It seems unlikely that they would become invasive, but even if they did would it be unreasonable to allow their cultivation? Risk assessment procedures as practised in Europe are ill equipped to make this type of decision and should not be assumed to be copied by countries that have serious food shortages. We should recognise that the development of much of the technology that could be useful to alleviate hunger in

areas of the world with poor soils or adverse climatic conditions will be in Europe and other regions of the world with strong research environments. But, will scientists be encouraged to isolate appropriate genes and develop suitable crops for hungry regions in an environment in which food is essentially unlimited

and thus novel crops with probable risks are unlikely ever to be approved for cultivation? Will it be seen to be unethical to produce crops for the developing world that could not be grown "at home", or unethical not to help to solve other countries' immediate problems?

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## Chapter 4

### Medicine

#### 4.1 Introduction

The Group has confined its remit to a number of key areas within the general field of medicinal products produced using biotechnology and intended for use in human and/or veterinary medicine. Within this field it has considered products, in the widest sense, which originate from an agricultural source. Review papers which include the present state-of-the-art have been commissioned from a number of experts in the relevant fields (xenotransplantation, vaccines, plant biotechnology, prospects for producing human/animal medicines by genetic engineering and cloning) and these are available separately. In this report we consider the following aspects for each key area:

- \* The science
- \* The technologies
- \* Safety, including risk/benefit
- \* Socio-economic aspects
- \* Regulatory framework
- \* Social acceptability and education.

Crucial to the study are the ethical issues raised by the various topics studied. Rather than having an ethical view on each individual area, we have chosen to provide an overview so as to avoid needless repetition and also to make clear the key ethical issues. This overview follows the sector reviews.

#### 4.2 Products from transgenic animals

##### 4.2.1 The techniques used in animal biotechnology

A few basic and increasingly straightforward techniques are required to isolate genes, sequence DNA, cleave DNA into fragments and reassociate them in different ways to generate new genes, which can be micro-injected into fertilised eggs, thereby producing transgenic animals. The specific amplification of a given gene region can easily be achieved by using the polymerase chain reaction (PCR). Reproduction is an essential technique to generate animals and also to multiply the best genomes. Biotechnology can contribute in a number of ways. Artificial insemination has been in use for many decades and superovulation, embryo collection, freezing and transfer largely contribute to accelerate genetic selection. For instance, a cow can provide up to 300 embryos whereas she can generate no more than 10 calves during her lifetime. *In vitro*, mechanical splitting of early embryos can give rise to multiple offspring. Nuclear transfer into the cytoplasm of enucleated oocytes can generate genetically identical animals from the same individual. Such transfers can be efficient as there is the possibility of selecting only those cells which express the transplanted gene. Whilst over the last ten years cloning of embryos has only been achieved using fresh embryonic cells as the nuclear source,

recent progress has shown it is possible also with cultured embryonic, fetal and possibly adult cells. So the reproduction of large numbers of genetically identical animals is now virtually possible. Such techniques as gene transfer in most cultured cells can now be done with little difficulty, although if the aim is to generate animals with additional genetic material this is much more difficult. The cloning of embryos from cultured cells should greatly simplify gene transfer.

##### 4.2.2 Production of pharmaceutical products

Looking to the future, milk products from transgenic animals might become an important source of recombinant proteins in the next century. Such proteins may potentially be pharmaceuticals for humans and animals, antigens for vaccination or tools for diagnosis. Improvement of animal production is theoretically possible by gene transfer. The optimisation of milk composition could also contribute to reduce the presence of allergens, to express the best alleles of milk protein genes and to add factors capable of reducing infection in animal or human consumers. A number of products are at or near the marketing stage: *eg* human  $\alpha$ -glucosidase for treating Pompe's disease, Factor VIII & Factor IX for haemophilia types A & B,  $\alpha$ 1-antitrypsin for cystic fibrosis, fibrinogen for surgery, insulin for diabetes, human growth hormone.

##### 4.2.3 Safety including risk/benefit

In general recombinant DNA technology has aroused considerable fears over safety. The most likely risk is environmental with the possibility of the release or escape of a bio-engineered animal which might disrupt a local ecosystem by competing with or destroying other species. However, it should be stressed that the alterations made to animals using recombinant techniques are relatively minor and for the production of human proteins by transgenic cattle for instance the risk of the cattle escaping is low especially when stringent fencing precautions are used. A crucial issue is the safety of such bio-engineered medicines for humans: there are stringent testing procedures for such drugs and they can only be marketed in the European Union when licensed by the European Medicines Evaluation Agency following the demonstration of proven safety and efficacy. It is noteworthy that the majority of proteins likely to be produced by transgenic animals are human proteins and so not foreign to the human body. This fact is of course highly beneficial when human proteins are being produced especially when the likelihood is that such products should be safer - no danger of virus or prion infection in the product - and can be produced in large quantities.

##### 4.2.4 Social acceptability

Provided the transgenic animals used to generate products appear healthy and well looked after, social acceptability is likely to be widespread. However, there is bound to be a

significant minority for whom the production of transgenic animals is unacceptable.

### 4.3 Expression of pharmaceuticals in plants

#### 4.3.1 The science

Many products used in human health care have traditionally been isolated from blood, placenta or other tissues. Often the products can only be produced in small quantities and it may not be possible to guarantee their freedom from unwanted contaminants such as viruses or prions, thus potentially leading to pathogen transmission. Genetic engineering has particular advantages here. After isolation, the gene of interest can be introduced into a heterologous system where the protein is subsequently expressed. Genetic engineering in plants is creating an attractive and cost-effective alternative for the production of biomolecules. There are examples of successful plant expression in a number of fields. Albumin for instance can be produced successfully in tobacco and potato - although the amount of recombinant protein is small. Commercial efforts to use cereals for this purpose have been successful -  $\alpha$ -antitrypsin being expressed in genetically engineered rice plants. It may become possible to produce vaccine candidate antigens in transgenic plants. A most promising development here is the demonstration that a recombinant tobacco plant monoclonal secretory antibody can be used successfully to provide specific protection in humans against oral streptococcal colonisation. Considerable progress has also been made in engineering immunogenic proteins into transgenic plants. This raises the possibility that human or animal consumed fruit (eg bananas) or other plant parts could have suitable vaccines engineered into them for the immunotherapeutic prevention of mucosal infections in humans and animals although much work remains to be done in this area. It has been shown that potato and tobacco plants can synthesise and assemble Norwalk virus capsid protein, hepatitis B surface antigen and certain bacterial antitoxins. Eating uncooked potato tubers synthesising one of these enterotoxins has been shown to induce both systemic and mucosal responses in human volunteers. Recombinant DNA technology has also been demonstrated to allow the production of industrial enzymes, carbohydrates and lipids tailored for particular purposes.

#### 4.3.2 Safety, including risk/benefit

The essential feature is to determine how the transgenes might alter the environment compared to the non-transgenic stock. A major concern is that the inserted information may be transferred to wild populations and hence give rise to the transmission of undesirable traits. However, it would appear that such hybridisation, if it does occur, typically leads to sterile hybrids so that the resulting gene flow is likely to be highly restricted. Studies of gene flow from transgenic rape to wild show that while the possibility cannot be excluded significant instances should be infrequent. A further concern is the possibility of horizontal gene transfer from genetic material as has been proven between different bacteria. Whilst horizontal gene transfer from plants to micro-organisms may be quite frequent, the likelihood of stable inheritance is very low.

#### 4.3.3 Socio-economic aspects

Transgenic plants extend the advances achieved by conventional plant breeding and apart from the possibility of producing pharmaceutical products can lead to the improvement of crop products. The world's fourth largest crop is bananas. It is an ideal plant species for vaccine production especially in tropical/semiotropical areas where enteric infectious disease is endemic.

#### 4.3.4 Social acceptability

Surveys throughout Europe suggest that the use of plants for the production of pharmaceuticals is likely to be acceptable to the great majority of citizens. Only those who object to any form of genetic engineering find this aspect of the technology ethically problematic.

### 4.4 Vaccines

#### 4.4.1 The science

Recombinant DNA technology offers opportunities to create attenuated organisms by deliberate molecular manipulation and to clone and express genes encoding immunogenic proteins for use in vaccination. It enables the development of genetically altered live vector vaccines. (In the future it seems possible that subunit or peptide vaccines may be introduced. These could have considerable advantages over conventional vaccines in controlling or eradicating animal disease.) These vaccines can now be developed due to increased knowledge of the immune system, in particular increased knowledge of the immune effector mechanisms, antigen recognition, the presentation of antigens to the immune system and the different cells which are active in the immune system. In addition, knowledge of the basis of microbial pathogenicity (*ie* the interaction between host and pathogen) has increased as has the identification of the antigenic components of pathogens which induce immune protection. This permits the production of designer vaccines by pathogen modification. The newly developed vaccines usually allow the possibility of discriminating between vaccinated and infected animals, as these vaccines include a marker protein which provokes a detectable antibody response. Such marker vaccines provide a potentially powerful tool for future disease control strategies as their use does not prevent the serological identification of infected animals and thus allows combined vaccination and eradication programmes.

#### 4.4.2 The technologies

Several approaches to vaccine design by modification of the pathogen can be envisaged using modern molecular technologies:

- \* The production of attenuated mutant organisms by deliberate molecular manipulation. For instance, a strain of pseudorabies virus is marketed in which the genes encoding the GI glycoprotein and thymidine kinase have been disrupted. This has been shown to be avirulent and to stimulate immunity against challenge with native virus. Targeted mutation(s) in a pathogenic organism can result in altered virulence, which negates the possibility of reversion to virulence.

- \* Creation of subunit vaccines, using antigenic components of pathogens that can be used to induce protective immune responses. Purified recombinant proteins can be used for vaccination if the specific antigenic capacity of the protein has been identified. (The human hepatitis B vaccine recombinant viral core protein is the most notable success in this area.) However, these proteins usually need to be administered in a potent adjuvant.
- \* Use of non-infectious viral capsids by expressing all of the capsid proteins in a single construct which leads to an immune reaction. The four main structural proteins of bluetongue virus have been incorporated in this way and have been shown to be immunogenic in sheep.
- \* Use of modified viruses or bacteria as “live vectors” for vaccination. The modified organisms may express antigens of more than one pathogen.
- \* Using DNA injection in animals. Vaccination of mice with plasmids containing the influenza haemagglutination gene has been shown to result in protection against virus challenge.
- \* Stimulation of protective responses at mucosal surfaces using attenuated organisms as vectors
- \* The time may come when it will be feasible to manipulate host genomes so that hosts become more resistant to diseases. As this would entail gene therapy of animals or humans, such procedures are likely to prove ethically contentious.

#### 4.4.3 Safety

For human or veterinary use an ideal vaccine would encompass some or all of the following:

- \* effective against all variants of the pathogen and species
- \* safe with low incidence of side effects
- \* highly immunogenic conferring long lasting protection
- \* efficient with as few doses as possible
- \* rapidly protective
- \* stable at ambient temperatures
- \* economically acceptable
- \* biologically stable
- \* not interfering with diagnostic tests for the natural disease
- \* easy to administer.

#### 4.4.4 Benefits

Vaccines have been of major importance in controlling or preventing several diseases (*eg* clostridial diseases, bovine lungworm infection and many viral diseases). However, this has not always been the case: in some diseases vaccines have turned out either to have been relatively ineffective (*eg* respiratory syncytial virus) or unavailable (*eg* African swine fever virus). A disadvantage of classic vaccines is the impossibility of distinguishing between a vaccinated and an infected animal. It is difficult to provide accurate cost benefit analyses of disease control and these will vary for different diseases. However, the costs of a disease outbreak can be huge (one has only to consider the enormous outlay for the control of mad cow disease to see the potential savings) and the animal health and welfare problems are considerable. Prevention of the outbreak of a disease by vaccination is recognised as one of the most efficient and cost effective tools for the control of certain transmissible diseases.

#### 4.4.5 Risks

Vaccines can cause adverse reactions which can vary from a mild local reaction at the injection site to anaphylactic shock. The incidence of such side effects is low. Vaccines may show residual virulence (due to improper inactivation or inadequate attenuation), reversion to virulence (due to recombination in animals co-infected with virus complementing other gene deletions; multiple gene deletions should eliminate this possibility), contamination - which is preventable; shedding or persistence of the organisms which is usually transitory and of little consequence. (It should be noted that in some circumstances, for instance in polio immunisation, spread of the inoculated virus is of value for the development of population immunity.) The risk of environmental contamination and the damaging effect of long term infection is present.

#### 4.4.6 Social acceptability

Vaccines are widely accepted and there is every chance that the use of new technologies to produce them will be socially acceptable provided their development is not seen as being a technological “fix” to problems that could be tackled by more conventional means.

Vaccines are socially accepted for use in animal populations and are usually seen as a more acceptable alternative to disease control than the use of antibiotics and chemotherapeutic agents. But if vaccines are used to prevent or cover up problems caused by the housing or husbandry system, the acceptability of such use is questionable. In some situations the origin of the vaccine (the way it has been produced) may lead to adverse public reaction. For example, the production of rubella vaccine for human use from a cell line originally derived from an aborted fetus caused considerable controversy.

#### 4.4.7 Regulatory framework

- \* Veterinary medicines have to be effective and safe for both animals and humans.
- \* Veterinary medications: Directive 81/852 as later modified and extended.

- \* Veterinary medications produced by “high technology” such as biotechnology: Directive 93/41.
- \* Procedures: Regulations: 2309/93 and 542/95.
- \* Others: Specific biotechnology directives: Directives 90/219 and 90/220.

#### 4.5 Xenotransplantation

This review has been restricted to the possibility of using agricultural animals as a source of organs for transplantation into humans. To set this review in context we noted that the demand for organs for transplantation, *eg* kidney, liver, lung, heart, from human donors far outstrips the possible supply. It seems most unlikely that however widely or enthusiastically organ donation from humans is pursued supply from this source alone will ever match demand. This means that the possibility of breeding agricultural animals to provide a larger supply of organs demands most careful consideration. Other possible applications include pancreatic islet cells from pigs being transplanted into humans for type 1 diabetes, porcine fetal brain cells being used to produce dopamine in patients with Parkinson’s Disease, baboon bone marrow being transplanted to help restore a failing immune system and the application of porcine skin as a temporary dressing.

##### 4.5.1 The science

It seems likely that organs from genetically modified animals *eg* pigs or monkeys (the latter being outside the scope of this paper) can provide adequate substitutes for human hearts and lungs. Livers and kidneys are more complex. The most promising animal source is the pig though porcine pancreatic cells may have only a short life span in humans. However, the very real problems associated with immune responses of the host have not as yet been wholly solved. Nonetheless there has been some success and future progress can be anticipated. The problems of possible rejection are much less where isolated cells are transplanted rather than whole organs. The most worrying aspect is whether the safety of the transplant from the point of view of transmitting infection - whether from zoonotic fungi, bacteria or, especially, viruses including retroviruses - can be guaranteed.

##### 4.5.2 The technologies

A diverse range of technologies underlies the sciences described. Setting aside well established techniques such as methods of organ storage, surgical procedures and anaesthetic techniques, there are a number of key novel technologies. These may be described under two general headings:

- i. Molecular technology. Transgenic manipulation of source animals has generated animal tissues which, by expressing human regulators of complement activity, apparently do not stimulate hyperacute rejection. More recently, nuclear transfer offers further possibilities for targeted alteration of genes in species such as pigs. It is this technology which has stimulated public concern in relation to “cloning” of animals or humans.
- ii. Animal production technologies. Producing source pigs of appropriate health status involves a range of

procedures: *eg* surgical methods of embryo transfer, early weaning of offspring, removal of biopsy samples for genetic testing, birth induction by hysterectomy, and isolation of offspring from their mother at birth. Such procedures involve an element of harm to the animals. It is clearly desirable that there are suitable stringent regulatory frameworks to control such activities.

##### 4.5.3 Safety, including risk/benefit

The key issue here relates to the risk of infection arising in humans from xenotransplantation. Whilst the risk may well be greater if primates were used as the source, it is still a significant problem for other species such as pigs. Infection may be confined to the recipient. But, perhaps of even greater concern is the spread of infection to a wider population. This may be associated with new variants of the infecting organism especially in relation to viruses. In addition an organism or variant may reinfect the animal population with increased pathogenicity. A particular problem is with respect to the risks of viruses. They may cause more serious illness if transmitted to a new species; screening techniques especially for unknown viruses may be inadequate and treatment problematic. Of especial concern here is whether retroviruses may present an insurmountable problem. Strategies designed to minimise these problems can be designed. Nevertheless some risk will remain and this will have to be balanced against the prospective benefit of this form of treatment to human beings.

##### 4.5.4 Socio-economic aspects

- i There will be animal wastage: not all harvested organs will be suitable for a particular recipient and a back up organ will be required.
- ii The use of xenotransplants may lead to a reduction in the rate of human donation - and may also lead to reduced funding of research into other alternatives.
- iii The costs to a health care system will be massive.
- iv The likelihood of researchers somewhere going ahead suggests that some form of control of possible research implants is desirable.

##### 4.5.5 Intellectual property rights including patenting

Enactment of the amended Directive on the Legal Protection of Biotechnological Inventions would appear to confirm the patentability of many gene sequences involved in the genetic manipulation of pigs for xenotransplantation.

##### 4.5.6 Regulatory framework

In the EC: Directive 86/609/EEC. However, this only covers the use of animals for experimental and scientific purposes. If xenotransplantation became an accepted clinical procedure, the Directive would not apply. Neither does it follow that animals bred for xenotransplantation purposes would be covered by legislation covering agricultural animals, whilst laws designed to prevent animal cruelty would not necessarily be adequately drawn. It seems likely that no existing legislation would contain

the necessary provisions both to protect human health and to ensure the stringent health monitoring of the source animals. Some guidelines already exist for the conduct of clinical trials in various countries - but these may not apply to xenotransplantation.

#### 4.5.7 Social acceptability and education

The social acceptability of any new technology is extremely difficult to predict. Heart transplants are a case in point. Initially, these operations gave rise to considerable public concern. Within a relatively short space of time, though, they became widely accepted in many countries. However, heart transplants are still almost unknown in some countries, notably Japan, for reasons that are entirely due to social acceptability rather than anything else. Public debate and consultations about xenotransplantation suggest a considerable diversity of views as to the acceptability of the practice. The debate is likely to intensify should trials become widespread. One presumes that patient groups and those with relatives and friends whose lives are saved through xenotransplantation will be positive about the technology while those against the increasing use of animals for human ends will remain opposed to the practice. The situation is further complicated by the fact that the animal most likely to be used is the pig, an animal considered unclean by two of the world's great religions, by the uncertainties surrounding the safety of the practice given our continuing lack of certainty about the seriousness of the risk of viral infections and by the difficulty of predicting how people will feel about the consumption or non-consumption of animals containing genes of human origin. It seems inconceivable that the cadavers of pigs from whom organs have been removed would end up in the human food chain. However, it is feasible that surplus animals - which may or may not have been genetically modified - might become available for human consumption. Public education about xenotransplantation is likely to take place through a number of media. Already, school examination questions on the subject can be found in some European countries while debates on the television and radio and in newspapers and magazines are considerable, if spasmodic.

#### 4.6 Ethical overview

The case studies considered here raise a large number of ethical arguments both for and against the use of biotechnology and as yet it may be premature to expect to see widespread consensus on many of the issues raised. Nevertheless, many of the ethical issues raised are not new. Those that are most contentious relate mainly to our use of animals but even here, while disagreements exist, some agreement is possible.

##### 4.6.1 Medical products from genetically modified animals or plants

As yet the production of medical products from genetically modified animals and plants is at the research stage though clinical trials are in progress. It is worth noting the lessons that can be learnt from the use of "human insulin" made from genetically engineered bacteria and yeasts. For over a decade such genetically engineered human insulins have been widely taken. On the whole, their introduction has been a considerable success. Such insulins are identical to human insulins whereas animal-derived insulin (bovine and porcine) differ slightly from

human insulin in their structures. However, there have been some reported problems with genetically engineered human insulins. Some diabetics have reported that the symptoms they experience when their blood sugar levels become too low ("having a hypo") now differ. The significance of these changed symptoms is controversial but the important point to note is that, as is so often the case, a new technology, while being beneficial overall, may have some unforeseen and unwanted consequences.

Few people object to the use of genetically modified plants for the production of medicines. Provided the new products are found to work and to be safe, they are likely to be widely accepted and few ethical objections to them can be raised. There are potential risks from the use of transgenic plants in open field situations. However, precautions can be taken to prevent spreading of introduced genes. One possibility is if breeding is done so as to make the plants male sterile to prevent unwanted gene flow. In addition the areas likely to be planted are relatively small and the value of the crops very considerable which should make monitoring and containment more feasible.

The situation with regard to the use of genetically modified animals for the manufacture of medicines is more complicated. The surgical and other procedures needed to produce transgenic animals (superovulation, collecting of eggs, microinjection) are invasive and must cause a certain, limited amount of pain and discomfort. On the plus side, though, such animals are extremely well looked after, though some would argue that the natural, social behaviour of many animals is affected by the clinical environment in which they may be kept. Nevertheless, to someone who objects on principle to the use of animals for human ends, such practices are unacceptable whatever the human benefits that may flow. Indeed, there will be those who accept certain uses of animals but reject any genetic engineering of animals, for example on the grounds that this would be a violation of their integrity. At the same time, medicines produced from genetically modified animals may prevent much human suffering and save many lives and these are, obviously, powerful arguments against forbidding their use.

##### 4.6.2 Vaccines

The use of farm animals and plants for the manufacture of vaccines raises few ethical issues beyond those already considered in the use of genetically modified animals and plants to make medicines. The use of vaccines, both for humans and livestock, is very widely accepted. The main issue to have given rise to ethical debate is the extent to which pressure should be put on individuals to be vaccinated, or to have their children vaccinated, when the benefits to them may be small whereas the benefits to society as a whole may be significant. Some vaccines carry a very small but non-zero health risk to the individual being vaccinated with the result that, when a disease is scarce, people may choose not to be vaccinated. However, this autonomous behaviour can permit the disease to maintain itself in the population leading, eventually, to more overall human misery than if vaccination had been compulsory. In countries where certain diseases have been all but eliminated through vaccination, people can be unaware of how damaging some of these diseases may be. A further ethical issue raised by the use of vaccines for farm animals is that such usage can be a means of "covering up" problems of poor husbandry or

excessively intensive production methods rather than addressing the underlying cause of disease transmission. However, even the best managed farm animal systems cannot entirely eradicate all infectious diseases.

#### 4.6.3 Xenotransplantation

Xenotransplantation raises a considerable number of ethical issues. On the one hand, those in favour of the technology may see the prospect of tens of thousands of human lives being saved each year through a procedure which causes less suffering to animals than they endure on many farms. On the other hand, those opposed to the technology may object to the increasingly instrumental view with which we regard animals, to the blurring of the distinction between what it is to be human and what it is to be non-human, to our failure to increase the use of organ donor cards, to the dangers that may follow the transmission of certain viruses from farm animals to humans and to the fact that we are trying to reduce, for example, morbidity from heart disease in this complicated and very expensive way rather than encouraging people to take more exercise and eat healthier diets.

#### 4.7 Conclusions

Biotechnology offers many new opportunities for the production of medicines, vaccines and other medical products

using agricultural sources. New products can be developed using this technology, or the production of already existing products made more cost-effective.

It is a very promising technology for further improvement of human and animal health in the future.

Application of plant molecular biology to preventive medicine may enhance the health of humans and agricultural animals.

The disadvantages of the use of biotechnology must not be overlooked: although safety regulations do exist unforeseen and unwanted consequences may still occur.

The continued development of biotechnology in relation to the use of agriculture for medicine will undoubtedly raise new ethical questions and controversies. However, there is good reason to expect that the very considerable body of expertise that exists in relation to medical and other areas of ethics will help to give rise to some degree of consensus in many of these novel areas, though it must be recognised that ethical debate is characterised by conflicting arguments and viewpoints

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## Chapter 5

### Developing Countries

#### 5.1 Introduction

The term “Developing countries” is used to refer to much of Africa, Asia and South America and contrasts these with “industrialised countries” where industry and agriculture are more industrially advanced (Bulawayo, 1997). Agriculture in the “developing” countries may be industrialised in a manner similar to that in the “West”, or not. Where the agricultural practices are industrialised, the issues raised in this chapter may not be appropriate. There remain agricultural practices in “industrialised” countries which many associate with subsistence agriculture.

This chapter will attempt to identify those issues which are of prime importance to developing countries and those which impact on the “developed” world’s relationships with other countries while not addressing issues which are in the domain of other chapters.

This distinction between “developed” and “developing” countries is largely artificial, especially with regard to the transfer of a technology such as biotechnology, which has relatively low entry barriers. Within the “developing world”, it is possible to distinguish at least the following groups of countries that each have a quite different situation *vis-à-vis* the transfer of biotechnology:

- \* Large countries such as China and India, which have developed fully integrated research and development chains from basic molecular biology to the applications in the field and in medical practice.
- \* The newly industrialised countries in Asia and Latin America, most of which have formed a strong biotechnology base as part of their efforts in building manpower skill bases for all modern technologies.
- \* The intermediate countries that would find it difficult to develop a fully integrated biotechnology sector, but have the agricultural research and extension systems into which products of biotechnology can be integrated.
- \* The least developed countries, most of which are so resource poor that they often lack the basic agricultural research and extension facilities which are essential to bring the products of biotechnology to the farmer.

An increasing fraction of the population of less developed countries is living in cities, sometimes in “mega-cities”, that need large quantities of agricultural produce. These cannot be provided by subsistence farmers alone. The less developed countries also need cash crops for export in order to pay for necessary imports. Such cash crops are often produced in an industrialised agricultural structure.

It is agreed that those living in the “developed world” have more than enough to eat, yet the majority of the world’s population do not. World population, currently 5.8 billion, is projected to reach 8 billion by 2020 and stabilise around 10

billion by 2050 (Kendall *et al*, 1997; Vasil, 1998). These projections indicate that the quantity of food produced will increasingly lag behind that required to provide sufficient for survival of a very large proportion of those alive. It is argued that biotechnology may provide one means, in addition to redistribution, of increasing the availability of nutritious food (Potrykis, 1997). The analysis provided the following figures for current consumption (*ibid*):

“800 million people are hungry eating 1800 kcal/day  
3400 million survive on 2230 kcal/day  
730 million have sufficient at 2910 kcal/day  
800 million enjoy 3400 kcal/day”

Such data is approximate since desirable population intakes may be estimated in different ways, may vary from actual utilisation and may not be readily applicable world-wide (see for example Department of Health, 1991, Table 1.1 Estimated Average Requirements for Energy). The Potrykis study concluded that agriculture has to produce much more food, where it is needed and under sustained conditions.

It may be that the concerns and fears regarding safety of foods produced by modern biotechnology will stifle or slow the development of the technology within the Developing Countries, which would result in condemning many to starvation (*ibid*).

There is need to increase food production markedly for the expected increase in the world’s population. The increase would have to be at a greater rate than the rate of increase in population. (Engelman & LeRoy, 1995; Plunkett, 1995)

“The task of meeting world food needs to 2010 by the use of existing technology may prove difficult, not only because of the historically unprecedented increments to world population that seem inevitable during this period, but also because problems of resource degradation and mismanagement are emerging. Such problems call into question the sustainability of the key technological paradigms on which much of the expansion of food production since 1960 has depended” (Oram & Hojjatti, 1995)

There are many who argue that an insistence on “biosafety” and the precautionary principle is an expensive luxury which cannot be sustained where such a large increase in food is needed in order to feed millions who would die of starvation unless attempts are made to ensure that sufficient food is available in the right place at the right time.

There are also concerns that the new technology will lead to

- \* exploitation of those living in the “developing” countries
- \* monopoly control of chemicals used in agriculture and of seeds which allow plants to resist these chemicals might be exploitative and place a strain on the economy of developing countries

- \* major changes in social structures which might sequentially affect the types of agriculture and needs for distribution of foods and food products.

Although modern biotechnology (while not specific to it) is often seen as providing a means for integrating the process of agriculture, many in the non-industrialised countries view the technology as providing (Cohen *et al.*, 1998):

- \* Disease-free planting material. Tissue culture techniques are used in laboratories to allow the micropropagation of plant material which is free of disease and can be provided to farmers. This technology is not only important for crops traditionally cultivated using vegetative propagation (banana, potato) but also coffee, cocoa, oil palm and sugar-cane.
- \* Biocontrol agents which are not integrated into the plants, but may be used directly.
- \* Diagnostics and vaccines for livestock diseases. Diagnostic tests and rDNA vaccines for rinderpest, cowdriosis (heartwater), theileriosis (East Coast fever) and foot-and-mouth disease have been developed.
- \* Plant varieties which offer disease resistance, either through traditional breeding and selection techniques or through the introduction of genes from other organisms.

## 5.2 Is Biotechnology an economic or regulatory issue for Developing Countries?

The ability to ensure that the products of biotechnology which are intended for food or feed use are as safe as the corresponding traditional products is critical to the development of the technology and to consumer acceptance of products, whether in the developing or developed countries. This is not to assume that biotechnology products are more risky than traditional products, simply that procedures need to be in place to ensure the safety of both.

The UNEP Guidelines on Biosafety (UNEP, 1996a) provide a baseline on which guidelines or regulatory frameworks may be built within countries willing to provide a framework for the safe use of biotechnology. These Guidelines provide for the provision of internal structures within countries. If a protocol is produced by the Conference of the Parties to the Biodiversity Convention, it will apply to the transport of modified organisms across international boundaries.

The Guidelines indicate the points that need to be considered in a risk assessment to identify the risk management procedures that may be needed to ensure the safe use of the product derived from the use of biotechnology. In general, risk management procedures may be required during field trials, depending on the knowledge available about a specific crop. If a new variety has been extensively tested and/or successfully grown commercially, then a risk management procedure may be superfluous. There is a recognition that the management of risk at the testing stage is different from that which may be required when the product is marketed. The UNEP Guidelines identify general precautions as:

- \* appropriate information and training for those handling the organisms

- \* monitoring procedures to allow appropriate action in the event of unexpected events
- \* control of the dissemination of the released organism
- \* controlled access to the release site and then specify precautions specific for plants, animals and micro-organisms.

Where a risk assessment has been done under similar conditions in another country and the new variety has been recognised to be risk-free, a further detailed risk assessment procedure is likely to be unnecessary, unless the geographic or climatic conditions and the presence of weedy relatives indicate that the risk assessment is not adequate. Risk assessments are costly in that they require considerable skilled personnel.

There is evidence that major international companies are wary of marketing the products of genetic modification in countries in which there are no guidelines or regulatory structures.

This issue is more important because of the impact of the GATT (General Agreement on Tariffs and Trade) Treaty. The transport of goods between countries may only be resisted on the basis of good scientific evidence. The assessment of risk associated with a product produced in a country, however, takes account only the environmental issues which might be of significance in that country. Absence of close relatives of a particular species, for example, may lead to a finding of minimal risk for release of that organism within the borders of the country but the risk assessment may not be applicable in other countries to which the product is exported.

If the product is a major commodity crop, the problems of identifying the product as "genetically modified" become intense. Importing countries may have regulatory requirements different from the country of export, but the nature of world trade makes it virtually impossible to control its movement across national boundaries. The regulatory structures could be used in particular to stop imports from countries which have not instituted regulatory systems, as the scientific basis of the decision to stop imports is not easily challenged.

## 5.3 Are there any other International Conventions which deal with biotechnology as it relates to the Developing World?

The Convention on Biological Diversity (Rio de Janeiro, 1992) includes a number of Articles which deal directly with issues relating to "developing" countries. Access to Genetic Resources is covered in Article 15 of the Convention. It requires Contracting parties to provide conditions which facilitate access to genetic resources for environmentally sound uses by other Parties to the Convention. Access must be on mutually agreed terms and where possible, any research conducted on material from other States must be with the full participation (and where possible in) those States. Article 16 identifies conditions for Access to and Transfer of Technology (including Biotechnology). Article 19 relates to the handling of Biotechnology and distribution of benefits "Each Contracting Party shall take legislative, administrative or policy measures, as appropriate, to provide for the effective participation in biotechnological research activities by those Contracting Parties, especially developing countries, which provide the

*genetic resources for such research, and where feasible in such Contracting Parties.”*

Chapter 16 of Agenda 21 (adopted at the United Nations Conference on Environment and Development in Rio de Janeiro in 1992) required Governments to consider international cooperation on the “Environmentally Sound Management of Biotechnology”. It also required Governments to take appropriate measures to ensure that developing countries have effective participation in biotechnological research activities and have priority access to the results and benefits of biotechnology on a fair and equitable basis. The conference of the Parties to the Convention on Biodiversity decided to develop a protocol for biosafety, specifically focusing on transboundary movements. This protocol is still being considered. The UNEP Guidelines on Biosafety attempt to provide a uniform baseline for the regulation of biotechnology throughout the world. The Guidelines “*seek to ensure safety in biotechnology development, application, exchange and transfer through international agreement on principles to be applied on risk assessment and management*”.

The European Convention for the Protection of Human Rights and dignity of the Human being with regard to the application of Biology and Medicine (Convention on Human Rights and Biomedicine, 1996) makes no reference to any difference between those living in the “developed” and “less-developed” world. There is also a European Convention on the humane treatment of farm animals. The European Convention on Civil Liability for Damage resulting from Activities Dangerous to the Environment (1993) specifically defines “Genetically modified organisms” as “*any organism in which the genetic material has been altered in a way which does not occur naturally by mating and/or natural recombination*”, but excludes:

- \* organisms obtained by mutagenesis on condition that the genetic modification does not involve the use of genetically modified organisms as recipient organisms
- \* plants obtained by cell fusion (including protoplast fusion) if the resulting plant can also be produced by traditional breeding methods and on condition that the genetic modification does not involve the use of genetically modified organisms as parental organisms.

The WTO Agreement on Sanitary and Phytosanitary Measures (SPS) is a measure resulting from the Uruguay Round of Multilateral Trade Negotiations. This agreement is intended to ensure that Governments are able to provide health protection within their boundaries but not if they inhibit international trade. The agreement attempts to ensure that sanitary and phytosanitary measures only apply to ensure the safety of food or animal and plant health. The agreement allows an individual Government to protect its “inhabitants” (including humans, animals and plants) from pests and diseases resulting from the import or inclusion in imports. The scope includes the protection of the inhabitants from additives, contaminants, toxins or disease-causing organisms in foods or feeds, and allows Governments to limit or prevent damage arising from the entry, establishment or spread of pests within their territories.

The WTO Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) (GATT TRIPS Agreement, 1994) is a further measure resulting from the Uruguay Round of

Multilateral Trade Negotiations which may have an impact on the use and protection of products derived from modern biotechnology within the “developing” world. The agreement harmonises patent law within Member States so that both process and product may be patented and tightly regulates compulsory licensing of product for members of the WTO. The TRIPS agreement does allow Member States to exclude from patentability: (1) diagnostic, therapeutic and surgical methods for the treatment of humans or animals, and (2) plants and animals other than microorganisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, there is the obligation to offer at least *sui generis* protection under the UPOV convention. The second of these categories is to be reviewed four years after the entry into force of the WTO Agreement.

The International Plant Protection Convention (IPPC) is in place in order to improve international cooperation to control pests and plant disease. IPPC may cover genetically modified organisms if they are pests, but the agreement does not provide a mechanism for the assessment of risk associated with plant pests, assuming that the “country of origin” is aware of the potential to cause disease.

The FAO Code of Conduct on Plant Germplasm Collecting and Transfer (1994) “*aims to promote the rational collection and sustainable use of genetic resources, to prevent genetic erosion, and to protect the interests of both donors and collectors of germplasm*”. The objectives of the code which relate specifically to the topics of this chapter include Article 1.2 which stresses the need to foster direct participation of farmers, scientists and organisations in countries where germplasm is collected in programmes to conserve and use plant genetic resources; and Article 1.2 which aims to promote the sharing of benefits derived from plant genetic resources between the donors and users. The code stresses in Article 6 that States have a right and responsibility to establish and implement policies for the use of their genetic resources which includes the provision of permits to collectors.

The FAO International Undertaking on Plant Genetic Resources is currently being renegotiated to take account of the Convention on Biological Diversity (FAO, 1997a). The original appears in Resolution 8/83 of the 22nd Session of the FAO Conference. Rome, 5-23 November 1983.

#### 5.4 Is Biosafety an ethical issue?

Biosafety evaluation is an investigation of the impact of a product or process. In the context of biotechnology it is often referred to as risk assessment, which is incomplete. The environmental impacts of any technological development include positive as well as negative elements.

It is necessary to distinguish between biodiversity of natural populations and that of crops. The former will only be maintained if tropical rain forests (and a few other natural ecosystems) are not destroyed, for example by the expanding farming. Man-made biodiversity of crops may be increased by biotechnology because new breeding options are available. This does not mean that certain traditional breeds of crops should not be maintained. However, storage facilities for crop varieties *in situ* and seeds *etc* in germplasm banks are always limited.

A risk assessment which identifies the management procedures needed for ensuring minimal risk for any use or release of the products of biotechnology is usually required in most countries which have regulatory structures or guidelines in place. These risk assessments invariably only consider the likely risk within their borders. Risk assessments, therefore, are not necessarily applicable in other countries.

Is the stress on biosafety and ensuring that as little harm as possible is caused to the environment likely to affect the availability of food in areas of the world where people are starving? If so, is it ethically justifiable to deny the fruits of the possibly untested technology to the hungry?

The major difference between developed and developing countries may be the capacity to assess impact, manage the minimisation of any risk, and ensure that the infrastructure is in place to assure countries to which the products are exported that a proper consideration of the risk has been conducted.

### 5.5 What are the issues for the Developing World?

The importance attached to issues associated with the use of modern biotechnology may be very different in “developed” countries where there is already a surfeit of food. There are many positive benefits which will accrue if biotechnology is able to provide the means for food and feed to be available where needed. However, the technology is often seen as controlled by powerful financial interests and its use inevitable (Grove-White *et al.*, 1997). The same researchers report that “perhaps progress was going too far and that technical innovation should develop more cautiously”.

There are significant concerns being expressed regarding the use of this technology, and many of these relate to their application within the “developing world”. There are significant benefits that may result from this technology as well as risks but the intention here is to identify both positive and negative issues.

#### 5.5.1 Empowerment

Modern biotechnology promises much. The slogan associated with some of the expectations from the technology has indicated a potential to “feed the world”. This is an obvious oversimplification since no single measure, technical, political or otherwise - will on its own resolve the problem. Although there is a perception within Europe that more than sufficient food is produced there is obvious malnutrition in much of the world, and the population is growing rapidly. There is a belief amongst many of those who form opinion in Europe that “organic” agriculture is a “good thing”, yet there is little appreciation that a sustainable reversion to organic farming within Europe would require a substantial reduction in population. If enough food is to be available to feed the world’s population, then:

- \* crops which are important within local economies must be made more readily available;
- \* yields of current crops must be increased;
- \* foods need to be able to withstand the rigours of distribution from the point of production to the towns and villages where they are consumed;

- \* crops must be modified (by modern biotechnology or by traditional means) so as to provide food when and where needed.

The causes of malnutrition are seen either as a social problem (distribution of income) or as an agricultural problem (production). This is a false dichotomy as both causes operate and are inextricably linked economically. Any increase in access to food through better distribution of income or of physical distribution has to be met with an increase of production. If it is not, it will be met with an increase in price.

The most important means of providing aid to those living in countries which rely on subsistence agriculture is to ensure adequate food and clean water. There are very important benefits that may accrue from the provision of technological expertise.

Modern biotechnology is easy to “transport” - the “entry fees” which enable use of the technology are low when compared to the costs of implementing many other new technologies. Transfer of knowledge should not only include scientific expertise, but all the skills necessary to implement the technology, to assess and manage the impact, and to identify the ethical issues which arise within a country from the exploitation and use of biotechnology. In order to be successful, the application of biotechnology requires “a broad research and knowledge base in biology, breeding, agronomy, physiology, biochemistry and genetics”. The developing countries must develop the infrastructure and need financial support and expertise to allow development of biotechnology (Moffat, 1994).

A majority of the world’s resource-poor farmers are women. World-wide, women produce more than 50% of all the food that is grown. In many developing countries, this percentage can be much higher. For instance, it is estimated that women produce 80% of the food grown in sub-Saharan Africa, 50-60% in Asia, 46% in the Caribbean, 31% in North Africa and the Middle East and about 30% in Latin America. The advent of modern crops may release those working in the fields from much of the tedium of subsistence agriculture.

#### 5.5.2 Exploitation?

In terms of control over genetic resources or food resources, two quite different types of exploitation of a position of power may be distinguished:

- \* “blocking access” to products or to technology. Some fear that this will happen on a significant scale by the abuse of the IPR systems in place. Although this is theoretically conceivable, it does go against the primary interest that owners of IPR have, which is to make money out of their ownership by selling the product.
- \* “dumping unwanted products” that have not been properly tested, or that are not approved in the industrialised countries.

The crops which have so far been modified and tested in field trials or marketed are those which are of importance in the “developed” world. The vast majority of releases in Europe have been maize, oil seed rape, potatoes, and sugar beet. Most

of the modifications made so far have been designed to increase yield, either directly or indirectly through pest resistance and herbicide tolerance. Many are at the same time designed to use fewer insecticides, fungicides or herbicides. Examples which have been quoted as directly affecting the rural population in Africa involve the use of herbicide-resistant crops. There are arguments as to whether this would be beneficial or harmful to the economies within developing countries. To some, relief for those currently spending much of their time weeding to do other, useful or less arduous work is important; to others, the increased poverty that might result where labour is no longer needed to weed, and therefore, the increased depopulation of rural areas and over-population of urban areas is the major issue. Irrespective of this hypothetical negative impact of biotechnology, there is and has for a long time been a rapid increase in population and a massive migration to the cities, whose inhabitants need feeding.

“It is often stated that only 30 crops “feed the world”. These are the crops which provide 95% of dietary energy (calories) or protein. Wheat, rice and maize alone provide more than half of the global plant-derived energy intake. These are the crops which have received the most investment in terms of conservation and improvement. A further six crops, or commodities, sorghum, millet, potatoes, sweet potatoes, soybean, and sugar (cane/beet), bring the total to 75% of the energy intake. This information is based on data for national food energy supplies aggregated at the global level (FAO, 1996).

When food energy supplies are analysed at the sub-regional level, however, a greater number of crops emerge as significant. For example, cassava supplies over half of plant-derived energy in Central Africa, although at a global level, the figure is only 1.6%. Beans and plantain also emerge as very important staples in particular sub-regions. These major food crops, as well as others such as groundnut, pigeon pea, lentils, cowpea and yams are the dietary staples of millions of the world’s poorer people, though they receive relatively little research and development attention (*Ibid*).

Resource-poor farmers constitute over half the world’s farmers and produce 15 - 20% of the world’s food. These farmers have not benefited as much as others from modern high-yielding varieties. It is estimated that some 1,400 million people, approximately 100 million in Latin America, 300 million in Africa and 1,000 million in Asia, are now dependent on resource-poor farming systems in marginal environments.

### 5.5.3 Socio-economic Issues

Many regional crops have importance on a world scale because of the availability of particular chemicals. The possibility of modifying common industrial, commodity crops grown in temperate climates to produce higher value chemical products may have devastating impacts on the original products and producers.

#### Case Studies:

Many “case studies” on the effects of biotechnology on socio-economic structures are oversimplifications. An example to illustrate the point:

- \* It has become common wisdom that High Fructose Corn Syrup (HFCS) produced from starch with enzymes has destroyed much of the export industry for cane sugar from developing countries during the seventies by undermining world sugar prices. The production of HFCS is a much less important reason than the massive production price subsidies given in the EU and the USA for sugar beet production which left these countries with large surpluses of sugar that were then dumped on the world market.  
There are a range of problems associated with coconut (Nichterlein, 1997):
- \* Coconut provides about 5% of the world supply of vegetable oil. Copra, the dried kernel of coconut, contains 65-72% oil which is used for a wide range of edible and industrial purposes. The main advantage of this oil is its high lauric acid content. Lauric acid is a short chain (C<sub>12</sub>) saturated acid which constitutes 45-50% of the fatty acids found in the oil from coconut
- \* The Philippines are the largest exporter of coconut oil, producing about 40% of copra and 70% of the oil for sale on world markets. 29% of the cultivated land in the Philippines is used for coconut production. The oil is also important in the economies of Malaysia, Indonesia and India.
- \* The industry has not modernised, palms tend to be low in productivity and replanting is not taking place in an organised fashion. There are also viral diseases (“Cadang-Cadang”) which kill many of the trees each year. Little research has been done in South-East Asia on the genetic variety of the coconut, nor has there been much work on diversification of the products which are available from this “tree of life”. The competitive downfall of Philippines coconut as the major world supplier of high lauric acid oils is due to two factors:
- \* The age of the coconut plantations in the Philippines. The average age of the trees is well over 50 years. They are of old genetic stock and in the declining years of their growth cycle. From the sixties until recently, the Philippines have not had an agricultural policy in place to renew their crop base by systematic replanting with new generations of high yielding palms.
- \* At the same time came the enormous growth of the oil palm sector in Malaysia and Indonesia. This development was underpinned by a heavy investment in breeding for new elite planting material and rapid replanting of old plantations. As a result, the average oil palm estate in Malaysia or Indonesia yields 5-8 times more oil/ha than the average coconut planting in the Philippines.
- \* There is strong competition between coconut oil and palm-kernel oil which is also high in lauric acid. The oil palm is farmed intensively and two different oils may be extracted (palm-kernel and palm mesocarp) which are raw materials for the food and detergent industries.
- \* The largest user of coconut or palm-kernel oil is the USA, with a market of approximately US\$350 million.
- \* Genetic modification has made the production of high lauric-acid oils in commodity crops possible. A transgenic variety of rapeseed producing lauric acid oils has been

produced by Calgene by the insertion of a thioesterase from the seed of the California bay tree. Initially the oil contained about 38% lauric acid, but in the research laboratory this has been raised to about 60% by the insertion of multiple copies of the gene and selection for high yielding transgenic varieties. These new products will, eventually, displace the coconut and palm-kernel oils. Costs are still high because of the need for segregation of these new, high-value oil products.

- \* There is controversy over whether the impact on the coconut industry of the introduction of high lauric acid oil in oil seed rape is likely to be significant:
- \* It is likely that the genes from the coconut (rather than the bay) will be used to further improve the new product. Although oil is not the only product available from coconut, the production of lauric acid oils from other sources could result in the loss of the industry. Investment and research are needed to improve productivity of the coconut, to develop existing and new products and to restructure the industry to meet the challenge.
- \* High lauric acid oil in oilseed rape (current projected production up to 100000 tonnes per year) is not likely to become a major competitor for coconut oil. The main competitor is and will remain palm kernel oil.
- \* High lauric acid oil is essentially a by-product of oil palm production. It is the oil produced by crushing the oil palm kernel after the main crop, palm oil, has been extracted. During production of the 20 million tonnes per year of palm oil, 3-4 million tonnes of palm kernel oil are automatically produced as well. As it is a by-product, it may win any price competition, whatever the price of the other sources.
- \* For oilseed rape and coconut the situation is different. High lauric acid oil is their main product. If prices slip, this effectively puts them out of the market.

#### 5.5.4 Research & Development for Agriculture

Most developing countries have their own national agricultural research establishments, which are often linked to an extension service. The extension services are intended to analyse what the farmers are doing, find out what their main technical and economic problems are and communicate research results to them. The performance of the research establishments and extension services varies a great deal, depending amongst other things on the financial situation of countries. In addition, many international aid organisations and NGOs are aimed at helping small farmers to improve their performance. Some developing countries are specifically targeting modern biotechnology to improve productivity and economic competitiveness and have already brought their own transgenic crops to the farmers' fields.

In addition to the national research establishments the Consultative Group on International Agricultural Research (CGIAR) does much in developing countries. CGIAR is financed by the World Bank and by separate contributions of most industrialised countries. The Rockefeller Foundation has also been a long term supporter. The CGIAR institutes, of which there are 18 in total, are spread all over the developing world and each institute has a specific mission. The

International Rice Research Institutes (IRRI) for instance is in the Philippines, wheat and maize research is carried out at CIMMYT in Mexico and research on potatoes in Peru. The quality of the research done at CGIAR is of the highest international standards. Wherever appropriate, modern biotechnology is made use of, for instance to produce improved crop varieties. Many CGIAR institutes have joint projects with molecular biology and agronomy laboratories of universities in industrialised countries. Also UNIDO, the United Nations International Development Organisation, supports agricultural research in third world countries and runs its own research programmes.

Several organisations initiated in the industrialised countries are specifically devoted to technology transfer to developing countries. Once such institution is ISAAA, the International Service for the Acquisition of Agri-Biotech Applications.

The role of the private sector in Research and Development for agriculture, and in technology transfer generally, is often ignored. Companies developed in developing countries as well as multinational corporations are key contributors to technology transfer and to capacity building in developing countries.

#### 5.5.5 Intellectual Property Rights

One of the perceived advantages of subsistence farming is that farmers save their own propagation material (seeds, tubers, cuttings *etc*) for their crops. This does not take into account two costs however:

- \* First the cost of keeping back this part of the harvest from the food supply of the family. In case of tuber crops, the propagation material that has to be saved for the next year often makes up more than 20% of the harvest.
- \* Second, planting material is usually contaminated with diseases and pests from the previous crop.

One of the biggest jumps in productivity in any agricultural system is always made by the supply of seed material that has been grown in special conditions where disease infections are particularly controlled. In Europe, the high potato yields of 50 tonnes/ha or more would never be possible without the annual supply of disease free seed potatoes from special fields. The increase in yield and in crop security is so large that farmers are prepared to pay up to a third of their total production costs of potatoes for this seed material. In several developing countries, the crop security of small farmers has been revolutionised by the supply of disease free planting material (*eg* bananas in the Philippines, sweet potatoes in Zimbabwe).

There are concerns that as a result of new Intellectual Property Rights over seeds the cost to the subsistence farmer would be too great. It is important to distinguish between subsistence farmers' own varieties, which can of course be saved freely, and genetically modified seeds which may be the subject of intellectual property rights in the country concerned. To the present, very few of the plant genetic improvement inventions have in fact been patent-applied-for in developing countries. The 1991 revision of the UPOV convention will also have an impact on the rights of plant breeders to use existing varieties as the starting point for making new varieties. This may have an important impact on the economics of developing new varieties

in the “developing” world. This revision also allows the protection of inventions using both this plant protection system and patents. However, the WTO agreements do not oblige countries to introduce a patenting system for plants where a *sui generis* system (such as that in the UPOV Convention) exists. In addition, the most important agricultural institutions in less developed countries, those belonging to CGIAR, give away their seeds without restrictions and at no cost. However it should be recognised that the current scale of use of saved seed deprives the breeder of significant legitimate income.

The protection offered by Plant Variety Registration (UPOV) in some countries, both developing and industrialised, may be important as information relating to the plant variety must be disclosed. This may be of importance as discussed in the section on “genetic diversity” below.

Protection of Intellectual Property is seen as a means of providing finance for the implementation of the technology. It is believed that Patents and Plant Variety Rights provide the incentive for development of the technology. Several patents have been taken out by public institutions involved in biotechnology in the less developed countries.

The European Patent Convention differs from Patent Law in many countries in that it incorporates a requirement that patents be not granted if the invention is seen to offend on moral grounds. This particular clause has only been used for products resulting from the application of modern biotechnology. In addition certain products which have medical uses are not capable of being patented under this Convention. These clauses may be important in restricting the availability of protection for inventions outside the borders of member countries. The exclusion of plant varieties may relate to the protection available to all member countries by the UPOV Convention

Although patents are important in spreading a technology because of the necessity for disclosure, the requirement to pay royalties may inhibit the use of biotechnology in developing countries. The TRIPS agreement, and the virtual prohibition of compulsory licensing may inhibit use in countries where hard currency is not readily available.

The TRIPS Agreement may threaten plant genetic resource conservation and farmers’ rights. Intellectual Property Rights are seen by some as having been “developed by industrial societies in order to reward inventors of machinery. They are hardly appropriate for life forms, such as plants which have been developed over centuries and are constantly changing. ... also disregards the traditional rights of indigenous and local communities over their resources and knowledge” (Madely, 1996). Others argue that there is no reason not to allow the protection of intellectual property in a specific, newly developed field such as biotechnology. Indigenous, traditional knowledge should not be affected, as only inventions not in the public domain can be protected. On the other hand, many are concerned that the “temporary” exclusion of plants and animals from the TRIPS Agreement is a problem. Bruce Lehman, Commissioner of Patents and Trademarks of the US PTO has been extremely critical. At the Pasteur Centennial Colloquium in 1995 “He criticised the exclusions in the European Patent Convention and the Patent Cooperation Treaty, although acknowledging that that at the time they were made in

ignorance of their effects on the subsequent development of biotechnology”. He continued:

*“There was little excuse, however, to perpetuate this unreasonable prejudice against biotechnology in the late 80s and early 90s, other than an unwillingness to review and revise earlier-held views despite overwhelming evidence of the benefits of biotechnology. Yet, the mistakes of earlier years were not only repeated in the TRIPS Agreement, they were compounded even further. In Article 27, paragraph 3 of that Agreement, biotechnology has not merely been forced to take a back seat it has virtually been forced out of the arena altogether.*

*...This development is an international giant step backward as far as biotechnology is concerned ... Thankfully, Article 27 of the TRIPS Agreement contains a clause mandating its review in 1999. It is our fervent hope that our negotiating partners will finally be convinced by then that their previous actions regarding Biotechnology were not in their best interests and that the patent system should not be used as a tool to satisfy concerns that could easily be addressed through other means.” (Gallochat, 1995)*

The public-sector is seen as being extremely important in development of products derived using biotechnology in many developing countries. However, the public sector may be unable on its own to meet the costs of developing new products, and the expertise available from multi-national companies may be vital in the exploitation of biotechnology. Multi-national companies have provided countries with the genes and cassettes to enable their insertion into crops of local importance. Where “gene-cassettes” have been synthesised for insertion into major crop plants, the availability of the genes for insertion into locally important crops may be crucial to the development. In order to use these phenotypes some form of intellectual property protection may be essential. Many agricultural crops and innovations in developing countries are exempted from national legislation governing intellectual property (Cohen, 1994). In a number of cases, multi-national companies have provided countries with the genes and cassettes to enable their insertion into crops of local importance. In some instances genes and cassettes are being used in the less-industrialised countries without clear knowledge or information regarding the Intellectual Property Rights (Cohen *et al.*, 1998). It appears that in CGIAR centres more than “35% of the applications are being used without any written agreement. This leaves centers in an unclear position as to their legal responsibilities, both to the owner of the technology and to other research partners” (*Ibid*). There are also likely to be problems for those in the non-industrialised countries failing to protect their intellectual property resulting possibly “from lack of familiarity with IPR issues, the fact that suitable IPR options are not yet developed and approved, and the traditional reliance on goods and services developed as international public goods” (*Ibid*).

The Convention on Biological Diversity (CBD), by recognising the sovereign right of states over their genetic resources and allowing access only upon the prior informed consent of the source country, has necessitated a re-examination of the commonly-held view that intellectual property law is irrelevant to discussions on access and use of genetic resources. The CBD expressly recognises that “patents and other intellectual property rights may have an influence in [the treaty’s] implementation” (Ochave, 1997).

A number of countries, notably India, have raised concerns at what they see as conflict between the TRIPS Agreement and the Convention on Biological Diversity, although this remains to be established. India has indicated that the TRIPS Agreement should be modified to remove inconsistencies with the CBD (WTO, 1997). In particular India has suggested that the changes should require that applications for patents should clearly mention the biological source material in the country of origin and that there be prior informed consent of the country of origin. In line with the Convention, where the biological material involves traditional or indigenous knowledge, there should be an obligation on the rights holder to share benefits. A Paper was prepared for the third meeting of the Conference of the Parties to the Convention on Biological Diversity held in Buenos Aires in November 1996 which examined the relationships and synergies of the CBD and the TRIPS Agreement (UNEP, 1996b). The document reports that the treatment of Intellectual Property during the debates which led to the CBD was contentious. Many developing countries had argued that the IPR systems hinder the transfer of technology to the developing world and unfairly disregard the contributions of generations of farmers to the world's plant genetic resources. These countries objected to the expansion of IPR to new crop varieties and products based on their genetic resources (UNEP, 1996c).

### 5.5.6 Crop Genetic Diversity

Intensive agriculture may result in the use of a particular variety of plant (or animal) which may lead to the loss of other varieties. Use of a small number of varieties may cause problems when a significant part of the total area planted is uniformly susceptible to a pest or environmental hazard. "One of the main causes of genetic vulnerability is the widespread replacement of diverse varieties by homogeneous modern varieties" (FAO, 1996).

Genetic Diversity has three values - portfolio, option and exploration (*Ibid*):

- \* Portfolio: "stability for farming systems at the local, national and global levels by smoothing yield variability through the maintenance of a wide range of crops and intra-crop diversity."
- \* Option: "provides insurance (Option Value) against future adverse conditions as needs are constantly changing and because genetic resources may later prove to provide useful characteristics, such as resistance to new diseases or adaptability to changed climatic conditions."
- \* Exploration: "genetic diversity represents a 'treasure chest' of potentially valuable but as yet unknown resources."

*"In The Netherlands, for example, the three top varieties of nine major crops covered from 81 to 99% of the respective areas planted. One cultivar accounted for 94% of the spring barley planted. In 1982, the rice variety '1R36' was grown on 11 million hectares in Asia. Over 67% of the wheat fields in Bangladesh were planted to a single wheat cultivar 'Sonalika' in 1983, and 30% of Indian wheat fields to the same cultivar in 1984. Reports from the USA in 1972 and 1991 indicate that for each of eight major crops fewer than nine varieties made up between 50% and 75% of the*

*total. Ireland's Country Report cites 90% of its total wheat area sown to just six varieties. The accumulated anecdotal evidence from various sources suggests that there are large areas planted to a small number of varieties, and although in some major wheat producing areas the situation is improving, it is still worthy of concern. The case of bananas provides another example of the costs of genetic uniformity. All five major varieties used for commercial production derive from one original banana variety (Cavendish). All these varieties are highly susceptible to the fungal disease black Sigatoka which can only be controlled by regular chemical applications. The cost of controlling the disease is high, surpassing US\$350 million in fewer than eight years in Central America, Columbia and Mexico. Moreover, small landowners cannot control the disease in their fields as they lack both the equipment and the funds required for fungicide applications. Yield losses approaching 47% have been reported in Honduras and other Central American countries. The disease is also causing major losses to plantain producers in West Africa." (*Ibid*)*

*"The improvements in agricultural production brought about through the use of modern varieties have been possible because of the rich and varied genetic diversity in farmers landraces, and of wild and weedy species." (*Ibid*)*

Plant breeders have used species of plants sexually compatible with important crop plants to acquire new and desired traits.

*"The initial stages of breeding for most crops have been based on locally adapted landraces. For instance, the wheat variety 'Marquis', which was grown across 90% of the spring wheat acreage of the North American Great Plains originated from a cross between the Indian landrace 'Hard Red Calcutta' and the European landrace 'Red Fife'. Similarly, the breeding of winter wheat in Europe is historically based on a large pool of selections derived from numerous wheat landraces from many countries. It has been estimated that 11 landraces contributed to the malting barley genepool, while the prominent commercial alfalfa ecotype, AWPX3, is known to have originated from 13 ecotypes collected in nine countries. The development of improved breeding lines for many crops which are in the early stages of formal plant breeding (eg fonio, amaranth, Chenopodium spp, teff etc) also relies heavily on the use of land-races." (*Ibid*)*

Several major incidents related to the narrowing genetic base of staple crops occurred in the seventies. The Southern Corn Blight in the USA is probably the most notorious one. It destroyed a major part of the US maize crop in 1972-1973. This was due to the fact that most of the US maize production was dependent on a single cytoplasmic genotype.

From that period on, diversification of the gene pool base for crops has been a priority for all major breeding programmes, and over the past decade, we begin to see the result of this in a steady widening of the genetic base of these crops. With the advent of molecular marker assisted breeding, this effort is likely to quicken, as the technique allows selection for many more traits simultaneously than in the past.

The FAO report suggests that about half the spectacular increase in yields of rice and wheat in the last 30 years have been obtained through the use of plant genetic resources. There is seen to be a need for:-

- \* The collection and storage of the germplasm of a wide variety of landraces and plant varieties will form a bank of genetic resource invaluable in the improvement and protection of crop plants.
- \* Protection and characterisation of wild relatives of currently cultivated plants. They have evolved over a longer period of time than domesticates and have co-evolved with pests and diseases.
- \* Increased use of a small set of plant varieties, which have been modified to improve yield, modify nutritive value or resistance to depredation. This would increase the vulnerability of the crop to other predators or diseases.

The Balay Declaration of the Southeast Asian NGO Conference on Trade and Food Security in February 1996 issued a statement on genetic diversity *“Protecting community control over genetic resources is both a moral and food security issue. We must prevent the earth’s genetic pool from falling under the control of transnational corporations. We strongly oppose the patenting of life forms ... We strongly urge Southeast Asian countries to cooperate with farmers and NGOs in developing sui generis systems of control over genetic resources”* (Madely, 1996).

### 5.5.7 Genetic Erosion

*“Genetic erosion is the loss of genetic diversity, including the loss of individual genes, and the loss of particular combinations of genes (ie of gene-complexes) such as those manifested as locally-adapted landraces.”* (FAO, 1996)

The main cause of genetic erosion in crops, as reported by almost all countries, is the replacement of local varieties by improved or exotic varieties and species. This is mainly due to the replacement of a large number of varieties by a small number of new varieties.

*“In China, in 1949, nearly 10,000 wheat varieties were used in production. By the 1970s, only about 1,000 varieties remained in use. Statistics from the 1950s showed that local varieties accounted for 81% of production, locally produced improved varieties made up 15% and introduced varieties 4%. By the 1970s, these figures had changed drastically: locally produced improved varieties accounted for 91% of production, introduced varieties 4% and local varieties only 5%”* (Ibid)

The production of new modified varieties of crops will continue to result in genetic erosion. This may not be important as long as the germplasm of a vast range of varieties is maintained. The maintenance of such static libraries, however, does not satisfy the need to evolve and adapt to changing environments.

### 5.5.8 Biodiversity

It is often stated that fauna and flora of industrialised countries tends to be much poorer in diversity and better characterised than that of developing countries. Both statements are misleading.

- \* The knowledge of fauna and flora in the North relates mostly to higher animals and plants. Other groups of organisms, which make up the bulk of the biodiversity in most industrialised countries are by no means well characterised.
- \* Several industrialised countries have vast expanses of tropical rainforest (eg Australia) and/or coral reefs (eg Australia, the USA), the two types of ecosystems that are seen to harbour the highest levels of complexity and biodiversity in the world.

Much of the debate on the sustainable creation of wealth from biodiversity focuses on medicinal products. This ignores the fact that many other uses of biodiversity can be promoted that have smaller overall markets than the much coveted drugs, but that can keep a much larger part of the added value in the country or region of origin because the development risks are much smaller, for example, ornamentals, newly domesticated animals, flavours and fragrances, biological pesticides, building materials, newly domesticated tree crops.

The search for new sources of genes with characteristics transferable to varieties grown in industrialised countries or gene products which can be used in foods and medicines is termed “bioprospecting”. The Biodiversity Treaty attempts to ensure that countries from which such products are obtained are compensated. Until the Convention on Biological Diversity *“living organisms were considered a common heritage of humankind; this Convention presents them as a sovereign property of the nation state”* (Madely, 1996).

It may be possible to identify genes from plants and other organisms which have not been identified before and use these in foods and medicines. The contribution of the source country to the “costs” of identification and safety-assurance may be relatively small, and the benefit which could be derived may therefore also be small. There are, however, uses of biological material by indigenous peoples which guide “bioprospecting”. The knowledge of food or medicinal properties of plants and micro-organisms may have been gained over centuries and not be fully understood by those using them, but still form a significant “intellectual property”. An example provided by RAFI (a pressure group opposed to patenting) may be Kava (*Piper mystheticum*) which is the basis for a ceremonial drink in many Pacific countries. *“Drug Companies are racing to patent Kava’s many beneficial uses. ... patented the use of Kava to reduce hair loss”* (RAFI, 1998). They provide other examples, including turmeric (*Curcuma longa*) which has been patented by researchers at a University in the US for *“methods of promoting healing of a wound by administering turmeric to a patient afflicted with the wound”*. RAFI argue that this has been used *“For thousands of years, Indians have applied ground turmeric root to cuts and scrapes to prevent healing, ... The Indian Council of Scientific and Industrial Research has asked the US to revoke the patent.”* (Ibid)

Many non-governmental organisations (NGOs) term bioprospecting “bio-piracy”. *“Bio-piracy is cheating developing countries and their indigenous peoples out of \$4.5 billion a year”* according to a RAFI report prepared for the United Nations Development Programme (RAFI, 1994). Some countries have imposed national legislation to prevent the

unauthorised collection of germplasm (including Ethiopia, Iran, Iraq and China) (Madely, 1996). However, other developing countries have made contracts with industries from the North to allow the collection of materials in exchange for compensation which could include training of personnel, setting up of research facilities, sharing of possible future profits resulting from the exploitation of the collected materials *etc.*

*“At present there is immense interest in the bioprospecting for new drugs from plant sources. In developed countries, up to 25% of all pharmaceuticals are substances extracted from plants, very frequently on the basis of the indigenous knowledge of the peoples where they originated. The so-called “hit-rate” for useful drugs in bioprospecting can be made up to 5000 times more effective by incorporating the indigenous knowledge of traditional cultural groups into the screening process.”* (RAFI, 1994)

The use by companies of such “community-based knowledge” for profit motives leads to complex ethical questions regarding the value of, protection of, and compensation for the use of indigenous knowledge. Most such ethnobotanical prospecting occurs in the tropical and sub-tropical areas rich in biological diversity, where most developing countries are located (Esquinas-Alcázar, 1995).

It may be that a European Convention would have to identify the manner in which bio-prospecting is regulated so that all attain the maximum benefit from the genetic heritage.

A number of developing countries have introduced legislation or guidelines for “bioprospecting”. An example are the Rules and Guidelines which have been put into place in the Philippines (BINAS, 1998). The Philippines argues that countries which have “genetic resources” should obtain some of the benefits from the *“nature and content of their contractual relations with prospective bioprospectors”* rather than from attempting to use the patent system” (Ochave, 1997).

- \* The Philippines, acting pursuant to Article 19 of the Convention on Biological Diversity (Rio de Janeiro, 1992), have introduced Rules and Regulations on the Prospecting of Biological and Genetic Resources. (BINAS, 1998) They have decided that *“It shall be the policy of the State to regulate the prospecting of biological and genetic resources so that these resources are protected and conserved, are developed and put to the sustainable use and benefit of the national interest”*. They have also required that such prospecting shall be allowed only with the *“prior informed consent of indigenous cultural communities, obtained in accordance with the customary laws of the concerned community”*.
- \* The rights of the “collector” to collect samples are severely restricted, and *“a complete set of all specimens collected shall be deposited by the Commercial / Academic Collector with the National Museum or a duly designated governmental entity”*. There is a requirement that the Collector must inform the Government and the local communities if a commercial product is derived from specimens gathered within the Philippines.

Legislation relating to National Policies for access to genetic resources may contain:

- \* sections on principles, objectives and definitions

- \* the scope of application with reference to definitions on which genetic resources are covered (plants, animals or microbial, wild or domesticated lifeforms)
- \* considerations relating to organisms, either in whole or in part
- \* regulations for derivatives prepared from biological organisms (not modified or modified chemical compounds, associated materials, services derived, models, chromatographic traces *etc.*)
- \* considerations relating to the sources of genetic resources: *in situ* and *ex situ* sources, land ownership: publicly, privately or communally owned, protected or unprotected areas
- \* considerations relating to the use and free exchange of genetic resources for the economic, religious and cultural well-being of indigenous and local communities
- \* designation of institutions to oversee access to resources
- \* export restrictions and sanctions and penalties
- \* consideration of the establishment of the necessary financial support to ensure and enforce the regulatory scheme as well as the management of the financial benefits from bioprospecting” (Sittenfeld, 1997; Sittenfeld and Villers, 1993).

### 5.5.9 Centres of Origin

The introduction of modified crops in centres of origin may pose problems. In some, the farmers’ landraces provide a well of genetic resource which is worthy of protection. Farmers in these countries, however, may wish to use varieties which are better able to resist predation and which offer better yield, leading to genetic erosion. If there are to be controls over the introduction of modified varieties within centres of origin, an international system of compensation for not being allowed to use “better” varieties may have to be implemented. The draft revision of the International Undertaking on Plant Genetic Resources suggests that Governments will “organise” (or facilitate) missions of exploration to identify potentially valuable plant genetic resources that are in danger of becoming extinct in their territory. *“In particular*

- (a) *known land races or cultivars in danger of becoming extinct due to their abandonment in favour of the cultivation of new cultivars;*
- (b) *the wild relatives of cultivated plants in areas identified as centres of genetic diversity or natural distribution;*
- (c) *species which are not actually cultivated but may be used for the benefit of mankind as a source of food or raw materials such as fibres, chemical compounds, medicine or timber.”* (FAO, 1997b)

Funding is needed for *“research activities that will result in scientifically substantiated estimates of the environmental impact of transgenic crops in centers of origin.”* (Frederick *et al.*, 1995)

There is a need to quantify the environmental impact in centres of diversity, and research is needed on traits which might have neutral, low or high impacts on fitness. Issues of biodiversity and the potential impact of undesirable traits being transferred to the “ancestral” plants need consideration. (*Ibid*)

There has been little contamination of landraces of maize in Mexico from the high-yield varieties of United States corn grown in Mexico for more than 50 years. This is seen by some scientists as an argument for allowing the new varieties to be grown in the centres of origin. (Braun, 1997)

There is a need to “*protect, promote and compensate the use of knowledge, innovations and practices of farmers relevant for the conservation and sustainable use of plant genetic resources for food and agriculture...*” (FAO, 1997a)

#### 5.5.10 Liability

The European Convention on Civil Liability for Damage resulting from Activities Dangerous to the Environment (Lugano, 1993) identifies any activity involving genetically modified organisms (production, culturing, handling, storage, use, destruction, disposal, release) as a “*dangerous activity*”. The Convention requires that the operator “*shall be liable for the damage caused by the activity as a result of incidents at the time or during the period when he was exercising control of the activity.*” (Article 6, para 1). There is nothing in the Convention relating to the liability of a multi-national company based in Europe in the event of damage in a developing country. Currently this Convention has been signed by 9 countries in Europe, of which 6 are members of the European Union. There may well be implications where a product, produced in a country which requires strict liability, is then grown in a country which does not have the requirements.

#### 5.5.11 Monitoring

There are many concerns related to the introduction of new genes into organisms that could not have been naturally achieved. There may be a need for some sort of international monitoring. This could, however, be seen as interference by the industrialised countries rather than as an international effort to ensure the safe use of the technology.

There is a clear need perceived within the scientific community to monitor releases of novel organisms particularly within centres of diversity (Frederick *et al.*, 1995). It is possible to identify problems which although unlikely, may occur with the introduction of organisms into new habitats, and schemes for monitoring to ensure that these do not occur (or are corrected) may be able to be put in place.

#### 5.5.12 Uniformity

Uniformity of regulations is seen as a primary concern mainly to ensure that trade barriers are not used as a means of discriminating against countries which do not have the resources to determine the impact of modified products (*Ibid*). The UNEP Guidelines (UNEP, 1996a) were an attempt to provide a baseline. A protocol is being developed relating solely to transboundary movements of the products of biotechnology which may succeed in providing a common definition of a “*living modified organism*” and a workable system of “*Prior Informed Consent*”. Products derived from but not containing a viable organism are not within the scope of the protocol. The operation of the WTO may well be the major force behind ensuring uniformity. The GATT rules will enforce a

consideration of the scientific safety of the product transferred between countries regardless of the process by which it is manufactured.

### 5.6 Conclusions

The issues that are identified in this paper need to be addressed regardless of the technology used to manufacture or market a product; these need to be within the context of (agricultural) need and/or food resources.

The view in countries where there is enough to eat, and where choice of what to eat is assumed may be significantly different from that pertaining in other countries. Choices need to be made by those who have to live with their consequences.

Many of the issues identified which are of ethical concern are not specific to developing countries, but occur within parts of countries considered to be developed. The developing world is much too diverse to be treated as a whole. The issues which result from moving from “*traditional*” agriculture to industrialised agriculture are those which need consideration.

Biotechnology *per se* does not lead to a loss of biodiversity; all modern agricultural techniques contribute both positively and negatively.

Technology has the capacity to contribute to the empowerment of rural communities.

The increase in the world population will mainly occur in the developing countries and therefore food increase needs to occur in those countries. According to the figures in the Montreal statistical yearbook the developed world is supplying food to the developing world. Furthermore, Governmental Agencies control access to the staple crops that form the major starch, oil and protein sources. It is important to provide a mechanism for sustainable food production where and when needed.

Developing countries contribute significantly to the added value made in agriculture. In this respect it could therefore be beneficial for these to set up a balanced system of IPR.

There are five major players that contribute to agricultural research: Governmental and Public Institutions, international institutions, NGOs and industry.

Developing countries should be free to use their land according to their own view. The prejudices and views on industrialised agriculture which colour the “*Northern*” approach to agricultural produce should not be imposed on those not getting enough to eat.

Developing countries should be helped to have access to biotechnology based on their genetic resources (Convention on Biological Diversity).

All parties to the Convention on Biological Diversity have an obligation “*to provide for the effective participation in biotechnological research activities by those Contracting Parties, especially developing countries which provide the genetic resources for such research, and where feasible in such Contracting Parties (Convention on Biological Biodiversity)*”. There will be costs associated with maintaining biodiversity within a centre of origin, which should be borne by the international community.

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## Chapter 6

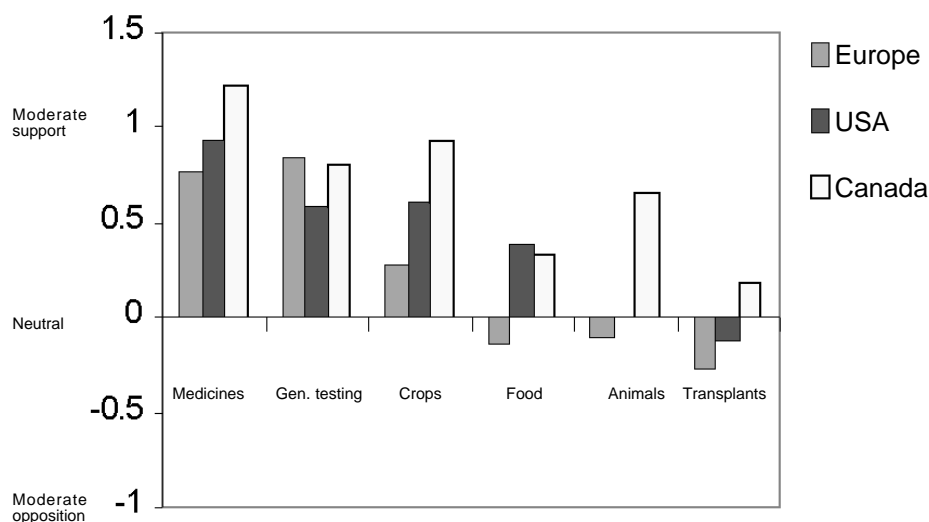
### Industry

#### 6.1 Introduction

Biotechnology is employed in three main sectors of industry: healthcare, agriculture and food production, and environmental protection. There is no single “biotechnology industry” as such. “Industrial biotechnology” consists of a number of scientific and technological techniques which are used, together with other non-biotechnological techniques, in the life science or bio-industries. These include:

- therapeutic substances for the treatment of human and animal diseases;
- diagnostics for identifying human and animal diseases;
- platform technologies with broad application in the life science industries, e.g. combinatorial chemistry, genomics;
- agricultural biotechnology genetically modifying crop plants and animals to produce desirable properties such as pest resistance, improved nutritional profiles or to make high-cost pharmaceuticals and chemicals more economically;
- environmental biotechnology using biological techniques to protect environmental resources, including bioremediation and other techniques to monitor or prevent pollution by means of microorganisms;
- food processing using techniques such as genetically modified enzymes to improve food quality.

Figure 1: Support for six applications of modern biotechnology



For 1997 it was estimated that Europe’s small and medium-sized life science companies employed some 39,000 people, compared with 27,500 in 1996, reported revenues of ECU 2.7 billion compared with ECU 1.7 billion in the previous year and increased R&D spending by 27% to ECU 1.9 billion. The US industry is much larger than Europe’s. US companies invested ECU 8.3 billion in R&D in 1997, employed 140,000 people and generated revenues of ECU 16 billion (Ernst & Young, 1998). Multinational pharmaceutical and agrochemical companies are not included since data for their biotechnology-related employment, investment and revenue is not readily available but probably exceed small and medium-sized companies both in Europe and USA.

Table 1: LEVEL OF ENCOURAGEMENT FOR SIX APPLICATIONS OF BIOTECHNOLOGY

NEGATIVE <-----											-----> POSITIVE										
-1			-0.5			0			0.5			1.0			1.5						
A	F	CT	A		MG											A					
CH	T	A	F	C		G	M									CH					
NO		T	F	CA		GM										NO					
D		A	T	FC			GM									D					
S		F	AT	C						GM						S					
DK		F	T	AC						GM						DK					
EUR			T	FA		C				MG						EUR					
LUX				FTA	C					GM						LUX					
IRL			T	A	F	C	M			G						IRL					
NL			T	A	F	C				MG						NL					
UK			TA	F		C				M	G					UK					
FR			F	T	A	C				M	G					FR					
B				AT	F		C			GM						B					
GR				FT		AC				M			G			GR					
I				TF	A		C			M	G					I					
FIN			T		A	F				CM	G					FIN					
USA					A	F	CG			M						USA					
E						AFTC				MG						E					
P					T	F	A			CM	G					P					
CAN					T	F	A			CG	M					CAN					

F - Food                      A - Lab animals    M - Medicines  
 C - Crop Plants            T - Transplants    G - Genetic Testing

Public attitudes to the different applications of biotechnology, together with the different bio-industry sectors, vary considerably between applications and countries. This has been shown by many public opinion surveys (Hamstra, 1998). Figure 1 compares the support for six applications of modern biotechnology in Europe, USA and Canada and Table 1 compares the level of encouragement for six applications of biotechnology between European countries using data from the Eurobarometer 1996 survey (Durant *et al.* 1998). These authors conclude that the implications of such studies are that:

- 1 Usefulness is a precondition of support, in no case is a “not useful” application given support.
- 2 People will accept some risk if the application is (a) useful and (b) morally acceptable.
- 3 Moral concerns act as a veto regardless of views on risk and use.
- 4 If risk is less significant than moral acceptability in shaping public perceptions, then public concerns are unlikely to be alleviated by technically based reassurances and other policy initiatives dealing solely with risks.

**6.2 Competitive performance**

The entrepreneurial bioscience sector is based on the following three types of companies: small research-intensive businesses, larger-scale enterprises and suppliers of specialist materials, services and equipment. These companies form a critical part of the innovation system for biotechnology. They are also a source of new and highly skilled jobs and additional output and investment in the economy. (EuropaBio, 1997)

European companies operate in a global market in which the US has been most successful in creating a biotechnology-based industry. The US government may be investing 5-6 times as much in research as Europe. Similarly, the Japanese government is increasing greatly its support for life sciences and technologies research, but Japan has been less successful than the European and US biotech industry (Ernst & Young, 1997 & EuropaBio, 1998).

For the period 1996 to early 1997 it can be concluded that in creating a new biotechnology industry, the US has been most successful followed by Europe and Japan being the least successful. In Table 2 the specialist biotechnology sector in

	Europe	US
Turnover	1,700	11,700
R&D expenditure (ECU in billions)	1,910	8,268
Net loss (ECU in billions)	2.0	3.8
Number of companies	1036	1274
Number of publicly quoted companies	50	300
Number of employees	39,045	140,000

Source: Ernst & Young 1998, EuropaBio 1997

**Table 3 Number of biotechnology patent applications and biotechnology granted patents over the period 1990 - 1996.**

	Patent applications	Granted patents	Percentage granted patents
1990	2850	829	29%
1991	2758	1210	44%
1992	3200	1827	57%
1993	3219	1951	61%
1994	3389	1889	56%
1995	3844	1729	45%
1996	4142	1695	41%

Source: European Patent Office, Statistics on Biotechnology

Europe and the US are compared for 1997. Nearly 80% of the biotechnology companies in Europe have been founded after 1986, while many companies in the US were founded in the 1980’s resulting in many relatively young specialist companies in Europe.

Knowledge-based industries, such as biotechnology, are the key to economic growth. The most successful economies are those that are best able to adopt new technologies and to use them effectively. The US has been able to do so, while Europe has created obstacles to structural growth and therefore has reduced competitiveness, growth and employment. (EuropaBio, 1997) The number of biotechnology patent applications is used as an indicator of commercialiseable activity and the annual total made at the European patent office increased over the period 1990 to 1996 but the number of biotechnology granted patents peaked in 1993 and decreased afterwards (Table 3).

Entrepreneurial bioscience companies are unevenly distributed in Europe, with most of Europe’s leading biotechnology companies being located in Britain, Germany, France, Sweden and the Netherlands. Until recently, southern and eastern Europe have had few start-up biotechnology companies although this has changed for Spain and Portugal over the last year where biotechnology companies are beginning to emerge. Scandinavian companies have been very successful in developing biotechnology. Finland is home to many pulp and paper and forestry industries, while Norway applies biotechnology in relation to the fishing industry.

In addition to the efforts of the European Commission many national and regional governments have been working to promote the development of domestic biotechnology activities. Britain, Germany and France are making the most efforts in launching programmes to stimulate further developments and new start-up companies and to nurture their fledgling bioindustries. In each case the transfer of biotechnology knowledge from the laboratory to the market is a key target.

More than half of the European biotech companies are based in the UK and in comparison to other European countries the UK had the most start-up companies. The UK government has

**Table 4 Number of companies and employees in the bioscience**

	1993	1994	1995	1996	1997
Number of biotech companies	386	485	584	716	1036
Employees		16,100	17,200	27,000	39,000

Source: Ernst & Young 1997

invested heavily in a number of biotechnology specific initiatives. Germany has gone through a major attitude change towards biotechnology from previously being fairly hostile. In recent years the German government has developed several programmes to achieve the goal of becoming a leading biotechnology country in Europe and this trend has continued. France has been very supportive of fundamental research, but this has not been reflected in the strength of the country's entrepreneurial bioscience sector. In short, governments throughout Europe are making the financing of biotechnology-based research a priority.

### 6.3 Employment

Depending on the definition of entrepreneurial bioscience companies, data on numbers of companies, employees and finances can vary greatly. Here bioscience companies are defined as those using modern biological, rather than conventional, techniques to develop commercial products for the human and animal healthcare, agricultural production, food processing and environmental services sectors. In 1997 1,036 entrepreneurial bioscience companies were identified in Europe employing some 39,000 people and investing more than ECU 1.9 billion in R&D (Ernst & Young, 1997). Table 4 gives an overview of these companies and the number of people employed in the biotechnology sector over the last 5 years. It should be noted that these figures do not include those employed in biotechnological activities in large, usually multinational, companies for which data is not available but their numbers probably exceed those employed in small and medium-sized enterprises.

Employment has not been considered generally as an ethical issue in itself. Biotechnology is characterised by the comparatively high skill levels of the majority of those

employed in it. It is important in this context especially for its creation of highly skilled jobs, second only to information technology, and in the maintenance of facilities for training people for them.

### 6.4 Maize case study

Europe is an important maize producer ranking second in the world. Within the EU, France is the largest maize growing country with 41.5% of both the total maize area and the total yield (in 1996/7

from an EU total of 34.8 Mt grown on 4.1 Mha, France produced 14.45 Mt on 1.7 Mha). The Association Générale des Producteurs de Maïs (AGPM) represents the interest of maize growers and coordinates the interests of French maize breeders and industries. The AGPM represents some 300,000 maize growers, predominantly medium-sized and larger farmers on areas of arable land of 500ha, of which 130,000 are principally maize growers.

In the EU, and consequently in France, it is currently not possible to grow transgenic maize, although there are three cultivars available and approved by EU authorities. Under pressure from the Austrian government there was a ban until recently on these varieties so that they could not be grown in France. Conflicting legislation between the World Trade Organisation (WTO) and European Union GMO regulations is likely to lead in the short term to disadvantageous effects in the economy of agricultural chains. Under the WTO regulations, the EU cannot prevent the importation of US maize, including genetically modified maize, into the EU. This maize is cheaper than European maize, so disrupting the European maize chain. Consequently, medium-sized and large-sized farmers suffer badly from this situation and sometimes face bankruptcy.

A further aspect of this situation is the lobby by environmentalists to prevent France, and other countries, from accepting transgenic maize products into the food chain. This results in an ambiguous policy: on the one hand promoting a good agricultural position as strongly as possible and on the other hand blocking any global position by banning competitive varieties from being grown by medium- and large-scale farmers. This ambiguous attitude by several European countries causes uncertainty which harms the public debate and perception on whether or not to accept genetically modified plants and foods and, if so, under what conditions.

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## Glossary

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Allele	One of several alternate forms of a gene occupying a given locus on chromosome, which controls expression (of product) in different ways.
Antigen	Also called an immunogen. Any large molecule or small organism whose entry into the body provokes synthesis of an antibody or immunoglobulin (i.e. an immune system response).
Bioaugmentation	Increasing the activity of bacteria that break down pollutants by adding more of their kind. A technique used in bioremediation.
Biochip	Electronic device that uses organic molecules to form a semiconductor
Biodegradable	Describes any material that can be broken down by biological action (e.g. dissimilation, digestion, denitrification, etc.). The breakdown of material (chemicals) by microorganisms (bacteria, fungus, etc.).
Biomass	The totality of biological matter in a given area. As commonly used in biotechnology, refers to the use of cellulose, a renewable resource, for the production of chemicals that can be used to generate energy or as alternative feedstocks for the chemical industry to reduce dependence on renewable fossil fuels.
Biopreservation	The control of technologies, technical processes and equipment used in the application of biotechnological procedures in the production processes to avoid or reduce environmental and health costs.
Bioremediation	The use of microorganisms in the management of hazardous waste. The waste substances are degraded by the microbes into nontoxic substances.
Biotechnology	The application of biological knowledge and techniques to develop products and services. Production may be carried out by using intact organisms, such as yeasts and bacteria, or plants or animals, cultures of their cells, or substances (e.g. enzymes) from organisms.
Chromosome	Discrete unit of a genome carrying many genes, consisting of (histone) proteins and a very long molecule of DNA. Found in the nucleus of most plant and animal cells.
DNA	(Deoxyribonucleic acid) The molecule that carries the genetic information for most living systems. The DNA molecule consists of four bases (adenine, cytosine, guanine and thymine) and a sugar-phosphate backbone, arranged in two connected strands to form a double helix.
Electroporation	The creation of reversible small holes in a cell wall or membrane through which foreign DNA can pass. This DNA can then integrate into the cell's genome.
Enzyme	A protein catalyst that facilitates specific chemical or metabolic reactions necessary for cell growth and reproduction. Many enzymes can be isolated and used for industrial purposes.
Eukaryote	A cell or organism containing a true nucleus, with a well-defined membrane surrounding the nucleus. All organisms except bacteria, viruses and blue-green algae are eukaryotes.
Expression	In genetics, manifestation of a characteristic that is specified by a gene. With some hereditary diseases, for example, a person can carry the gene for the disease but not actually have the disease. In this case, the gene is present but not expressed. In industrial biotechnology, the term is often used to mean the production of a protein by a gene that has been inserted into a new host organism.
Gene therapy	The replacement of a defective gene in an organism suffering from a genetic disease. Recombinant DNA techniques are used to isolate the functioning gene and insert it into cells. More than 300 single-gene disorders have been identified in humans. A significant percentage of these may be amenable to gene therapy.
Gene	A segment of a chromosome. Genes direct the synthesis of proteins.
Genetic code	The mechanism by which genetic information is stored in living organisms. The code uses sets of three nucleotide bases (codons) to make the amino acids that, in turn, constitute proteins.
Genetic engineering	A technology used to alter the genetic material of living cells in order to make them capable of producing new substances or performing new functions.
Genetic modification	See genetic engineering

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Genetic manipulation	See genetic engineering
Genome	The total hereditary material of a cell, containing the entire chromosomal set found in each nucleus of a given species.
Germplasm	The total genetic variability, represented by germ cells or seeds, available to a particular population of organisms.
Host	A cell or organism used for the growth of a virus, plasmid or other form of foreign DNA, or for the protection of cloned substances.
In situ remediation	Treatment of a hazardous waste site entailing no excavation or removal of soil or water.
Introgression	The incorporation of transgenes (genes from transgenic organisms) into a wild type organism's genome.
Locus	The position of a gene on a chromosome.
Monoclonal antibodies	Monoclonal antibodies are antibodies derived from a single source or clone of cells (MABs) that recognise only one kind of antigen.
Nucleic acids	Large molecules, generally found in the cell's nucleus and/or cytoplasm, that are made up of nucleotides. The two kinds of nucleic acids are DNA and RNA.
Nucleotides	The building blocks of nucleic acids. Each nucleotide is composed of sugar, phosphate and one of four nitrogen bases. The sequence of the bases within the nucleic acid determines what proteins will be made.
Nucleus	The structure within eucaryotic cells that contains chromosomal DNA.
Phenotype	Observable characteristics, resulting from the interaction between an organism's genetic makeup and environment.
Polyclonal Response	<i>(of immune system to a given pathogen)</i>  Because a given pathogen generally has several antigenic sites on its surface, the B lymphocytes (activated by helper T-cells in response to a pathogen invading the body) synthesise several antibodies against that pathogen. Since the antibodies are made by different cells the response is known as poly(many)clonal.
Protein	From the Greek proteios, meaning "the first" or "the most important". High molecular weight compounds composed of amino acids, including enzymes, antibodies, hormones etc.
Recombinant DNA	The DNA formed by combining segments of DNA from different types of organisms.
Regulatory gene	A gene that acts to control the protein-synthesising activity of other genes.
Ribonucleic acid	(Also called RNA) A molecule similar to DNA that functions primarily to decode the instructions for protein synthesis that are carried by genes and carries it to the protein synthesing machinery of the cell.
Splicing	The removal of introns (nonfunctioning part of the DNA molecule) and joining of exons (codes for a specific domain of a protein) to form a continuous coding sequence in RNA.
Structural gene	A gene coding for a protein.
Suppressor gene	A gene that can suppress the effect of another gene.
Transformation	Change in the genetic structure of an organism by the incorporation of foreign DNA.
Transgenic organism	An organism whose gamete cells (sperm/egg) contain genetic material originally derived from an organism other than the parents or in addition to the parental genetic material.
Wild type	The form of an organism that occurs most frequently in nature.
Xenobiotics	From the Greek word xenos, meaning "stranger". Man-made chemicals originally not occurring in Nature and frequently resistant to environmental degradation. A branch of biotechnology called bioremediation is seeking to develop biological methods to degrade such compounds by adapting micro-organisms to metabolising them.
Xenotransplant	Xenotransplant is the implantation of a tissue or an organ from one species to another organism in a different species. Rejection of the transplant by the recipient's immune system is a common response, which biotechnology seeks to resolve.

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