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Food, Plant Biotechnology and Ethics

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I. Introduction

I.1 *Food Production*

Every living organism relies on consumption of energy and metabolites in order to live. Food is defined as material that contains essential body nutrients, such as carbohydrates, fats, proteins, vitamins or minerals, and is ingested and assimilated by an organism to produce energy, stimulate growth and maintain life. The main sources of food for animals are animals, fungi and plants. The subject of this report is focused on food for human beings, with passing reference to animal feeds.

Food is such an important topic that a United Nations Agency, the Food and Agricultural Organization (FAO) was established. The role of UNESCO in the debate on food stems firstly from the increasing reliance on scientific technology such as biotechnology to improve the quantity and quality of food, goals that are becoming more urgent in the population crisis. Culture is intertwined with food, a connection recognized by anthropologists (Levi-Strauss, 1964). Additionally, education about healthy food consumption has recently been promoted as part of preventive medicine, and thus all aspects of UNESCO are related to food.

We are told that ‘we are what we eat’, an old saying that is a half-truth linking food safety to human bioethics. Chemically our body is made from the food and water we consume, and these chemicals flow through the body throughout our life. The consumption of food is therefore of great importance for human health. Technical aspects are reviewed in Section II.

In many countries of the world, food production is delicately balanced with losses due to plant disease and every year increments in production are necessary to avoid food shortages. Delivery of food and economic policies are also issues affected by biotechnology. There are many countries where food supply is not guaranteed, and biotechnology is necessary to stimulate production and reduce losses due to disease. We could vision the losses caused to production by disease, pests and climatic extremes to mean that about one quarter of the land in cultivation is non-productive or wasted.

Once the food supply is guaranteed, the consumer tends to concentrate more on the particular individual tastes and preferences, and food quality and food choice are goals that developed economies seek, and are also important for food-exporting nations.

I.2 *What is Biotechnology?*

The word ‘biotechnology’ simply means using living organisms, or parts of them, to provide goods or services. The word can apply to agriculture in the past thousands of years, but is often used to apply to new techniques (Macer, 1994a). We should not forget that all civilizations were formed needing food, clothes and medicines, and in that sense biotechnology is not new. What is new is that we can now make new varieties much more quickly and with greater variation. The Working Group member country reports - including Argentina, Colombia, Russian Federation and Spain - and reports from Japan (Harada, 1996), provide background on the situations in each country.

Foodstuffs made from plants bred using genetic engineering are already being sold in parts of the world. They will generally be no different to the foods we already eat, but there are various advantages which are outlined in Section II.4. The range of concerns are assessed in Section III, and the roles of regulation described in Section IV.

For the purpose of this report a genetically modified organism (GMO) is defined as an organism that has had its DNA modified by genetic engineering. A legal definition is not intended, and the word transgenic is also commonly used. Some consider that an organism with DNA deleted is not a GMO for the purpose of regulations; however, we maintain a broad definition for discussion of the bioethical implications.

An important part of bioethics is risk assessment, the analysis and prediction of risks. Risk assessment is the use of scientific data to estimate the effects of exposure to hazardous materials or conditions. Risk management is a different activity: it is the process of weighing alternatives to select the most appropriate regulatory strategy or action. It integrates the results of risk assessment of different alternatives. When examining proposals for release of GMOs on an experimental level, risk assessment is needed. The first part of risk assessment is risk identification, after which comes risk estimation (OTA [Office of Technology Assessment], 1988). Only after the results are known can the wider release of the GMO be considered against other alternatives, the process of risk management. Benefits are part of risk management, whereas they are not part of risk assessment.

Bioethics combines risk assessment, the concept of avoiding harm, with an assessment of benefits, the concept of doing good or beneficence. It is important to ask whether there are any new risks compared to traditional plant breeding. There are various risks in genetic engineering, for example the risk of unintentionally changing the genes of an organism, the risk of harming that organism, the risk of changing the ecosystem in which it was involved, and the risk of harming the ecosystem, and the risk of change, or harm, to any other organism of that species or others, including human beings (who may even be the target of change). The concept of risk in biotechnology involves both the potential to change something and the potential to harm. The extent to which a change is judged to be a subjective harm depends on human values, whether nature should be 'intransient' or modified. This relates to the fears that technology is unnatural. These issues will be addressed by this report.

II. Roles of Plant Biotechnology in Food Production

II.1 *Techniques Involved in Plant Biotechnology*

This report focuses on plant biotechnology, but the general principles are also applicable to animal biotechnology. There are additional ethical concerns of using animals because of their varying capacity to feel pain, sentience and self awareness, which are discussed in Macer (1994). There may also be some additional food safety concerns to humans of using animal genes and hormones, since we are also an animal. These are discussed by Horsch (1992), Basu et al. (1993), Berkowitz (1993), Mephram (1994).

A number of plants have been modified by genetic engineering and some of these have been commercialized (Demarly, 1992; Horsch, 1993; Smith, 1994). There are a number of concerns about patenting of plant varieties and techniques to produce them (OTA, 1989), which are discussed later.

For millennium plants and animals have been selectively bred to develop varieties that are more productive, or suitable for human use. Our modern varieties originated from gene transfers within crop species by selective breeding. There are, however, some major exceptions. For example, about 5,000 years ago wheat was created, when the three genomes of Triticum monococcum, Triticum tauschii and a species of Aegilops came to be combined. The definition of a species rests on the concept of genetic isolation but sexual exchange of genes between species can and does occur in nature without human intervention.

Often, the crop species does not contain sufficient genetic diversity to allow the desired improvements, hence the search for diversity has led plant breeders to use new genetic technology. The aim is to arrive at a breeding population consistently expressing the desired trait(s). One of the main weaknesses of conventional plant breeding is its dependency upon sexual crosses and thus to genes that exist only in one species. Recombinant DNA technology allows the transcendence of inter-species barriers and makes very novel genetic combinations possible. The first transgenic plants were created in 1983.

One of the most popular methods of gene transfer is the use of the soil bacterium Agrobacterium tumefaciens, which can transfer genes to many plants at wound sites. However, it works mainly on the dicotyledonous plants which excludes many crop plants, such as cereals. Direct DNA transfer can be used to transfer genes to protoplasts (cells which lack a cell wall) from which plants can be regenerated. About 150 species of plants have already been regenerated from protoplasts, so the potential application of the technique is already very large.

Among the techniques for gene transfer another common one is 'biolistics', the use of particle guns to shoot DNA into cells. Some techniques use tungsten particles or gold beads. There may also be advantages of up to a 40% reduction in time for crop production via some biolistic based approaches over using Agrobacterium. Micro-injection also has potential.

The method of gene transfer alters the risks, for example homologous recombination inserts DNA at the corresponding site of the replaced DNA sequence in the genome, whereas non-homologous recombination does not. In the latter case there is less certainty about where the gene is inserted and whether it may have disrupted a regulatory or gene sequence in the genome (Day, 1996). Whereas the former case would generally be considered more stable and improbable to have unknown consequences. It is increasingly becoming possible to use homologous recombination, which is the preferred option (Paillotin, see Volume II of the Proceedings).

Gene transfer technology has advanced at a far faster pace than our understanding of plant biotechnology and the factors which are important within the plant in determining other useful agronomic traits. Because of this, attention has been focused largely on characters which might be determined by single genes. In order to provide more basic knowledge, some plants are included as model genome project. The Arabidopsis genome project is expected to be the first to be completed. Complete yeast artificial chromosome (YAC) libraries have been made, and a physical map. The complete sequence is expected at a similar time to that of the human genome. Arabidopsis is a small sized rapidly reproducing plant which is suited to laboratory studies. It is closely related to Brassica family of vegetables, so for example, Arabidopsis genes can be used directly in rapeseed without a need for recloning the Arabidopsis gene (Murphy, 1996).

II.2 Food, Food Additives and Medicinal Products

There are a range of non biotechnological techniques which are being used to alter food products, including engineered foods, aseptic processing, extrusion, hydroponics, intermediate moisture foods, micro-encapsulation, supercritical fluids extraction and ingredient technology (Smith, 1993). Ingredient technology includes fat substitutes, which could include fat products that are made from genetically engineered plants. However, the novel foods which have drawn the most debate are those made using biotechnology.

Sweeteners are one group of food additives. The thaumatin is a class of intensely sweet proteins isolated from the fruit of the tropical plant *Thaumatococcus danielli*. Thaumatin is approved for use in many countries and has application as both a flavor enhancer and a high-intensity sweetener. The gene encoding thaumatin has been introduced into plants (potatoes) and micro-organisms under transcriptional control of heterologous gene promoters (Zemanek and Wasserman, 1995). Yields to date have been low, but commercially viable levels are expected. The thaumatin gene can also be engineered directly into selected fruit and vegetable crops to improve their flavor and sweetness.

Another group of products that are made from genetically modified organisms are food additives, such as amino acid supplements. In 1990, a case of impure batches of an amino acid, L-tryptophan, was associated with many cases of a disease, eosinophilia-myalgia syndrome, which led to 38 deaths and 1,511 total reports of the disease in the United States of America. The L-tryptophan preparation was produced by Showa Denko and the cause was insufficient filtering of the preparation, so that one substance was left in the preparation that later was converted to a toxic substance. The Food and Drug Administration (FDA) said the disease was caused by a toxic compound EBT formed when acetaldehyde reacted with L-tryptophan, and it could have been removed by a simple charcoal filter. There were also other possible contaminants (Belongia, 1990). The reason for its inclusion in those batches may be because of the reduced purification procedures used in those batches, but it may also be connected to the different bacterial strain (which was genetically modified) used in production. Following that, the FDA regulated the sales of L-tryptophan as a drug, requiring more testing. Not all food additives may need to pass the extra safety tests, but this case must be considered when regulating food additive safety.

Vitamins and food supplements and traditional medicinal foods are often unregulated. Health foods include high fiber, reduced fat, reduced energy, reduced caffeine, sodium and alcohol, low cholesterol and calcium fortified foods. These components can also be sold as food supplements. In the United States of America alone the health food market is worth US\$ 100 billion annually.

The boundaries between foods and medicines may be made more cloudy with the introduction of edible vaccines. Vaccines can be genetically expressed in plants, such as banana or potato, and these may allow low cost distribution of these 'medicinal foods' (Prakash, 1996).

II.3 *Current Status of Food Products made from Genetic Engineering*

Calgene released its 'Flavr Savr' (Flavour Savour) tomato into United States supermarkets in 1994, labeled as a MacGregor tomato. By 1996, the sales were reported to be mildly successful as far as public acceptance, however the tomato was not so disease resistant as hoped and there were picking, packaging and transport problems (Rothenburg and Macer, 1995). Further improvement is being sought before it may be a financial success. Other companies, like Zeneca in the United Kingdom, also market tomatoes, and many are used in tomato-based foods for processing and tomato paste.

Biotechnology can provide alternative ways to solve the same problem. For example, the insect resistance of tomatoes can be altered by insertion of insecticidal genes in tomato, the spraying of insecticidal bacteria or viruses on the plants, or altering the type of leaf hairs on the tomato. All are being investigated (Wood, 1994). Tomato leaves have many miniature hairs (trichomes) which have glands that emit aromatic chemicals that repel or poison insects.

The Cooperative and Wholesale Society in the United Kingdom produces a vegetarian cheese based on a recombinant chymosin, which has been labeled. Fermentation is a major use of genes and enzymes, and includes alcoholic beverages and dairy products in daily consumption, for example.

Genetic engineering can be used to increase, decrease or add specific compounds to the edible parts of transgenic crop plants. Companies like Calgene have engineered the chemical composition of canola vegetable oils (Knauf and Facciotti, 1995). The transgenic canola produce seed with oils: a) that are modified in average fatty acid carbon chain length; b) that are modified in content of saturated fatty acids (both lower and higher); or, c) that contain structured lipids. This can also be applied to peanuts or soybeans for example. A healthier oil content could have more medium chain triglycerides or fatty acids from fish. There is research by different groups on changing the amino acid composition of proteins in basic grains.

II.4 *Foreseen Benefits and Uses of Products of Plant Genetic Engineering*

The greatest need for food production in the world is that the food is made in sufficient quantity, quality and sustainably given that the permanent need for food for a world population that may be double the current one in size, and of considerably higher average living standards. The issue of food production has been discussed in a number of conferences (Wahlqvist et al., 1994). The targets of genetic engineering not only involve insects or deletion of single genes, but manipulation of metabolism (Herbers and Sonnewald, 1996).

The benefits that are hoped for from genetic engineering include:

II.4.1 Increased productivity of crops, growth rates and ratio of utilisable plant product

The first goal of any farmer is to increase productivity of crops, which can be accomplished by improvement of the growth rate. An alternative way is to alter the ratio of the product of the plant which can be used, something seen in the green revolution with the increased proportion of the seed that was made in rice plants (Sasson, 1988). Many of the following examples also indirectly increase productivity.

Increasing the productivity of plants makes better use of the land that they are grown in. Currently at least one quarter of arable land used each year is made effectively non-productive because of losses caused by disease, pests and environmental extremes. We could see enhanced resistance to these factors as a way to decrease the lost farm land in the world, which is another way to increase productivity.

II.4.2 Increased quality of crops, including nutritional quality and storage properties

Future work on altering the nutritional content could include altering specific vitamin contents such as Vitamin A or the type and content of fiber may eventually be manipulated (Knauf and Facciotti, 1995). Sulfur-containing amino acids have been added to maize to increase the protein quality. Caffeine or phytic acid might be eliminated in the source plant, eliminating current processing steps that add cost and that lessen flavor and nutrition. Fat components are being modified for healthier diets.

There are also efforts to remove current food contaminants and toxins. Aflatoxins are mycotoxins produced by species of *Aspergillus flavus* group. They show a high toxicity against humans and animals. Different methods to control the aflatoxin contamination include inhibiting the biosynthetic and secretory process responsible for aflatoxin contamination, using biocompetitive agents that replace aflatoxigenic strains with non aflatoxigenic strains in the field, and using genetic engineering techniques to incorporate antifungal genes into specific plant species (Sanchis, 1993).

The composition of many cereals and crops is not actually optimum for some of the purposes they are used. Research on improving the composition for specific uses and types of cooking is underway. Genetic engineering allows levels of each component to be adjusted, which should improve the diversity of varieties available for food processing, for example wheat optimized for either bread or pasta making.

The so-called tasty tomato, Flavr Savr, was approved for sale in the United States of America in 1994. The FDA doesn't need to examine food products, but Calgene sought their advice for public acceptance. Calgene says the tomato will stay fresh about a week longer, and used the name 'MacGregor'. Other countries will no doubt want to use the tomato, especially those with difficulties in transport of fresh vegetables, and has public approval as seen in many countries (Macer, 1994).

II.4.3 Adaptation of plants to specific environmental conditions

This includes the better adaptation of crop plants to the changing environmental conditions, including climate change, increased UV radiation, changed rainfall patterns. Plants may be able to be more resistant to drought, flooding, salinity or sensitivity to heavy metals, so that they can be grown in areas of the earth currently beyond the tolerance range of species, or even those areas unable to be used for agriculture at all. About 30% of the world's land area has major plant stress conditions, including insufficient soil nutrients or water, or toxic excesses of minerals and salts.

To exploit other environments, tolerance to low temperature is also important. The antifreeze gene from an arctic fish has been transferred to soybean, with the goal of creating plants tolerant to low temperature. There is research by a number of groups on the development of aluminum resistance in plants. Aluminum toxicity is a problem in low pH soils, where it may reduce plant growth. By making plants tolerant, they will grow better in such soils.

Pine trees are being made more drought resistant and suited to warmer weather, because of the expected climatic changes due to global warming expected in North America in 30 or 40 years when the trees mature. Due to the long reproductive cycle, and the need to wait 20-30 years before mature traits can be evaluated, we are now using only the second and third generations of genetically improved trees. The long juvenile periods, large size and high natural heterozygosity limit the application of conventional breeding techniques, so genetic engineering is more applicable to tree improvement than to herbaceous agronomic crops. The traits that will be targeted include climatic adaptation, fusiform rust resistance and herbicide resistance to allow better plantation establishment. There are other long term targets such as nitrogen fixation, lignin biosynthesis, cellulose biosynthesis, photosynthetic efficiency, cytoplasmic male sterility and apical dominance.

II.4.4 Broaden plants tolerance to stress

Not only may the ability to survive in specific environmental conditions be improved, but also the range of stress conditions that can be tolerated could be improved. This includes for example, tolerance to heavy metals, pollution, fluctuations between wet and dry, and cold and hot climate, especially for longer lived plants.

II.4.5 Increase disease and pest resistance

The main focus of most biotechnology programs is to produce new cultivars with improved pest and disease resistance to promote more environmentally acceptable alternatives for food production. Natural disease resistance is complicated. Plant breeders have long sought to increase the disease resistance of crops through selection of resistant varieties and by hybridizing crops with wild relatives. About one third of total crop losses are directly attributable to plant disease. Molecular techniques, such as insertion of antiviral or antibacterial genes from other species into plants, and cellular methods to allow rapid screening for the desired phenotype, have led to more rapid progress.

Viruses cause serious diseases in many crops. The genetic basis of viral resistance in plants is narrow, so resistance breaking strains of virus frequently appear. Isolating the plant's own resistance genes to combat disease is not practical until they have been isolated. The function of such genes depends on complex factors, such as the right genomic background. However, they could be used as good starting materials for protein engineering. Good viral disease control has been obtained using three different approaches:

- **cross protection** occurs when plants are deliberately inoculated with a mild strain of virus. Coat protein genes of several viruses have been inserted into transgenic plants to provide protection;
- **insertion of Satellite viruses** (which are unable to replicate themselves) into the plant's genome to provide protection;
- **antisense RNA**: the translation of a specific mRNA can be inhibited if the plant contains a complementary antisense RNA, which will form a double-stranded RNA molecule with part of the messenger mRNA, preventing translation of the protein, and thus protecting the plant.

Plants expressing the insecticidal protein of a bacterium, Bacillus thuringiensis (Bt) are pest resistant. Insect pests will die if they eat the plants. The Bt insecticidal protein gene, or delta-endotoxin gene, has been expressed in many plants as an effective insecticide (on the safety of it: Goldberg and Tjaden, 1990). Larvae of moths and butterflies can be selectively killed by different insecticidal proteins. The control of caterpillar pests with plants expressing this insecticidal gene offers several advantages. Control is independent of the weather, and in conditions which would be unsuitable for spraying chemicals or bacteria, the crop is still protected. All parts of the plant are protected, such as the roots or new growth previously susceptible between sprayings. The pests are affected as soon as they begin to feed. Broad spectrum insecticides kill all insects, which include spiders and beetles which are useful predators. The B. thuringiensis endotoxin kills only leaf-eating species. Different insecticidal proteins have been expressed to kill larvae of Lepidoptera (moths) and Coleoptera (beetles). There are different proteins produced by different strains with varying specificity. Being proteins, they are biodegradable, and can be much cheaper to develop, and to obtain environmental release approval for use.

An alternative way to control herbivorous insect pests is by introducing the gene for digestive protease inhibitors into the plants, so the animals cannot digest food. The expression of these plant genes, which are thought to be a defensive response to insect attack, can be enhanced. Wounded plants produce a factor which induces the synthesis of protease inhibitors specific against insect and microbial proteases. They have an effect on a wide range of insects and are known not to be harmful to humans.

There has also been work on the development of insecticidal micro-organisms to be sprayed onto plants. The current application costs of spraying micro-organisms containing a toxin gene are similar to the costs of applying chemicals, but with the significant

environmental advantages. These need continual application, but may not require additional regulatory approval for human consumption, as they will need to be if they contain novel genes. Losses to crops also occur during storage after harvest. It is possible that increased levels of antifeedant could be added to plants to reduce such losses.

II.4.6 Lessen need for agrochemicals

Herbicide tolerant plants remain controversial although they can reduce the consumption of agrochemicals, and allow use of environmentally friendly herbicides. This is also because the same companies that are marketing seed are also producing the specific herbicide, and it raises economic monopoly concerns. There have been successful varieties of maize, soybean, sunflower and rapeseed made. Soybeans and modified oilseed rape resistant to the herbicide glyphosate were approved by the Food Advisory Committee of the United Kingdom in 1994 and 1995. They were made by inserting a bacterial gene with reduced sensitivity to the herbicide.

Current intensive agriculture has multiple applications of chemical fertilizers and pesticides. Although they may need to be used in many countries to produce food, efforts should be made to switch to crop and animal systems less dependent upon intervention. However, companies in industrialized countries are continuing much research on applications of biotechnology that require such inputs because they are more profitable. Multiple application means farmers must continually buy products from a company, and the company receives constant income. A field of a herbicide-tolerant crop can be sprayed with the herbicide and only the weeds die. In the development of herbicide-tolerant plants by genetic engineering, both seed and herbicide are controlled by the same companies (Macer, 1992). The use of these new herbicides and herbicide tolerant crops should have environmental advantages when substituted for systems using non-biodegradable herbicides, but there should also be attempts to use biological pest control. There should be genetic engineering in plant breeding to insert genes directly into openly pollinated and fertile crops, which can be used by farmers without dependence upon seed and chemical companies (which are often controlled by the same multinationals).

II.4.7 Production of substances in food crops

Plants can be made to express antibodies or for use as oral vaccines. Crop plants can also be used to produce non-edible products, such as medicinal products and proteins, fuel alcohol, transport oils, bioplastics or biopolymers, industrial raw materials, and products for later processing as foodstuffs, such as cooking oils, food packaging materials, sweeteners.

The genes for polymer production may be put into food-crops, such as potato tubers. This would also avoid using nonrenewable and energy intensive production techniques. This research area is attracting much commercial research, and it is already feasible to produce industrially one type of polymer, based on polyhydroxybutyrate, as a specialty plastic. It will take further work before bioplastics can compete financially for the commodity plastic market.

Rapeseed has been one crop which has already a variety of modified varieties made by genetic engineering that produce different oils (Murphy, 1996). In 1995 a lauric oil rapeseed was cultivated that makes 40% lauric acid (normally <0.1%). It contains a lauroyl-ACP thioesterase gene from California Bay plant, just one extra gene. It is useful for soaps, but may also be used in foods. By 2010, it is thought that oil palm will replace soybean as the major oil crop, ahead of rape and sunflower; all these crops are targets.

II.4.8 Utilization of new raw materials

Traditional foods often involve consumption of only one or several parts of a plant, for example fruits, leaves, roots or stems. Plants grown in one culture for roots may be eaten for their leaves in another, such as beet-root. Some plants may be eaten by humans in one culture, such as the plant rape in Japan, whereas it is used for rapeseed oil production in Europe. There is existing diversity in human diet, and biotechnology may allow consumption of further food products.

Microbes have a long history of use in foods, and genetically engineered enzymes are among the first products of biotechnology to be consumed. There has been research in the production of single cell protein throughout the 20th century, firstly through addition of brewer's yeast extracts. In the United Kingdom, Imperial Chemical Industries manufactures an animal food, Pruteen, by growing bacteria on methanol made from North Sea gas. Mycoprotein from fungi can also be made, and efforts to use wastes from the pulp and paper industry are also underway. Given the same amount of surface area, the energy yield from the algae *Spirulina* in lakes can be tenfold over the yield of wheat, and in countries with a food shortage these sources may become important dietary sources of protein.

III. Ethical Concerns about Plant Biotechnology

III.1 *Public Attitudes to Plant Biotechnology*

In the United States of America, there is a group of one to two thousand restaurants who maintain the position that they will not serve food from genetically modified organisms (*Nature* 359 (1992), 8). In the United Kingdom the Co-op supermarket chain has released a statement 'Your right to know' which claims they do not stock any food containing human genetic material; no vegetables or fruits which have been modified from a food product containing genetic material from animal sources; and that they will label any foods with genetic material from non-related species. There will no doubt continue to be further statements, and this is people's right to choose.

There are various strategies being used to study public opinion scientifically. The first type is the use of fixed response questions, to choose from set answers. These include surveys in the United States of America (OTA, 1987; Hoban and Kendall, 1992), Canada (Canadian Institute of Biotechnology, 1994) and the Eurobarometer in all 12 countries of the European Community (Eurobarometer 35.1 (1991), 39.1 (1993)). Recent survey strategies look at reasoning more than just statistics which may shed more light on the factors which will affect policy development, and have been conducted in Europe (Hamstra, 1991, 1992, 1993; Martin and Tait, 1992; Chadwick et al., 1996) and New Zealand (Couchman and Fink-Jensen, 1990). In Japan there have been several studies, including one among different groups in society, public, academics and high school teachers (Macer, 1992; 1994a).

There is some diversity between countries, but there is large diversity within each country. The surveys using open questions found that some arguments that are often used in biotechnology debates, such as eugenic fears or environmental risk, are not the major concerns voiced by people in open questions. The more common concerns are interference with nature or general fear of a less concrete nature. Also the survey found that many people perceive both benefit and risk simultaneously, they are attempting to balance these. Although some speculate that education will ease concern, educated people show as much concern, and in Japan biology teachers considered there was more risk from genetic engineering than the ordinary public (Macer, 1992; 1994a, b). There is however a great need for education about biotechnology.

Martin and Tait (1992) conducted surveys of selected groups of the public in the United Kingdom. They conclude that groups with an interest in biotechnology have probably already formed attitudes to it, which are unlikely to significantly change. They looked at industry and environmental groups and local communities, which are major players in the development of policy at both national and local levels. They also suggest that people with the least polarized attitudes are most open to multiple information sources. Consumer research in the Netherlands (Hamstra, 1992) conducted by SWOKA, an Institute for Consumer Research, has involved two major studies of what people in the Netherlands think about eating foods made through biotechnology. They found that plant food products were more acceptable than meat products made from biotechnology.

In Australia, Hong Kong, India, Israel, Japan, New Zealand, the Philippines, Russian Federation, Singapore and Thailand (Macer, 1994a) there is a positive view of science and technology. Less than 10% in all countries saw it as doing more harm than good. When asked about specific developments of technology, including in vitro fertilization, computers, pesticides, nuclear power, biotechnology and genetic engineering, both benefits and risks were

cited by many respondents. People do show the ability to balance benefits and risks of science and technology (Macer, 1992 ; 1994a, b). People do not have a simplistic view of science and technology, and can often perceive both benefits and risks. This balancing of good and harm is necessary for bioethics, and is an indicator of the bioethical maturity of a society.

In all surveys using the comparison (Hoban and Kendall, 1992; Macer, 1994), plant-plant gene transfers were most acceptable, with animal-animal less, and animal-plant or human-animal gene transfers were least acceptable. A variety of reasons were cited, as was the case in questions about the concerns of consuming products made from genetic engineering. The results of a question comparing dairy products, meat, vegetables and medicines (Couchman and Fink-Jensen, 1990; Macer, 1992a) found people have most concern about meat. One of the main concerns was that the products would be unnatural, but there were also a variety of other comments, such as that the health effects were unknown, could be long term and who could guarantee the safety. The generally higher fears about animal genetic engineering and meat is also seen in Europe (Eurobarometer 39.1; Hamstra, 1991, 1992, 1993).

III.2 *Intrinsic Ethical Concerns*

A common and useful separation of ethical concerns is into intrinsic concerns about the plant or gene itself and extrinsic concerns because of consequences. The latter type of concern includes health and environmental concerns that can be more readily answered by scientific research and monitoring, as well as socio-economic concerns which are more political in nature. Public acceptance of food depends upon intrinsic concerns and culture.

III.2.1 What is natural?

The argument of being natural is considered illogical by many, however it is part of human culture. There is a clear mandate for some degree of interference with nature even in human existence, as we must eat, let alone use the many medical techniques developed. However, we all have limits.

The term 'Playing God' is a term applied to situations where humans make life or death decisions without reference to God and perhaps even the opinions of other people, this being seen as pride or arrogance. It is not the use of power and creativity that is wrong, but rather attributing power to our own resources (Macer, 1990). What is wrong is not the act itself, but the attitudes that could be involved. However, useful applications of technology are advocated in all religious traditions as part of good stewardship of the earth's resources.

There have been many accusations that scientists are 'creating new life forms'. However, our present technology is capable only of transferring one or two genes into a genetic background containing the order of a hundred thousand genes. Also, nature has been changing itself constantly, and continues to do so, especially stimulated by environmental changes and pressures. In the case of chimeras or cell hybridization, rather than a new life form being created, two species may be combined that were closely related. It is possible that future techniques will allow combinations across wider differences.

The expression usefully suggests that we should be cautious in the use of technology whose potential risks and side-effects we do not fully understand, which are consequences discussed in the extrinsic ethical concerns below.

For some there is a feeling that we should not explore all the secrets of life, that the mystery of life will be gone if we discover too much. However, as many scientists will say, the more we know, the more appreciative of the workings of life we become. Discovery itself may not be wrong, but how we use it or abuse it raises ethical questions. The fact that we have practical requirements, such as to feed, house and heal people of the world, are major justifications for the pursuit of practical knowledge in any system of religion or philosophy that places a high value on human life.

III.2.2 Cross species DNA transfer

Modern biologists generally think of species as reproductive communities or populations. The species are limited by an arbitrary limit to variation. There is no universal or absolute rule that all species are discretely bound in any generally consistent manner (OTA, 1989). One species may exchange little or no genetic material with related or adjacent species,

while another may seem to be almost promiscuous, inbreeding frequently with a neighboring, related species. To challenge the integrity of a species requires more than a single gene change. Mammals like mice contain 50,000 or more genes and changing a small number of genes will not violate species integrity. Species exist in nature as reproductive communities, not as separate creatures.

Both cell fusion and recombinant DNA techniques allow species barriers to be readily overcome. Cell fusion can be used when the characteristics of interest are controlled in a complex manner by a large number of genes, so that large portions of the genome can be combined. This technique is used on a large scale in the commercial production of monoclonal antibodies.

The greatest public concern is over the mixing of human and animal genes. People object to the insertion of human growth hormone genes in pigs. Since much transgenic animal research is aimed at increased understanding of human diseases, the insertion of human genes will be very common. Other research also involves the insertion of human genes into animals. The reason for this is convenience, as a large number of human genes have been cloned. The most convenient, readily available form of a gene will be used for manipulation. It is unlikely that animal genes will be introduced into humans as therapy at this stage, and it is unlikely that any will be needed as the appropriate human genes should be available. However, reflecting this public concern, the government of the United Kingdom labels products that contain genes from humans, from an animal that is the subject of religious dietary restriction, or an animal gene when in a plant or microbe. The label says 'contains copies of X gene'. The labeling of plants containing animal DNA may be important for some vegetarians.

III.2.3 Does it work?

The adoption of new technology should rely on the improvement to the provision of products and services to a community. At the time of writing there were doubts as to the effectiveness of insect resistant cotton which included the Bt resistance gene. After large scale field trials of the cotton made by Monsanto, cotton boll-worms were still found to have infected some of the cotton (MacIlwain, 1996). Different management strategies could alter field success of transgenic crops. Ecological and scientific studies to produce better crops and farming practices should lie at the heart of biotechnology.

III.3. *Extrinsic Ethical Concerns*

III.3.1 Health effects

There are two basic types of health effect on humans. Those which are confined to the individual and those which could be infectious to either families or the wider community. The first type focuses on toxic substances, pleiotropic or allergic effects in an individual, while the latter could involve the spread of a gene transfer vector between consumers, which is improbable for plant viruses. Some food like fruits and vegetables include intact DNA when consumed, especially when fresh. Other food is consumed after cooking, and other only reaches the consumers after food processing which breaks down the DNA.

Human beings consume food infected with plant viruses almost every day and it is extremely unlikely that any plant genetic vector would transmit between persons, if it did manage to enter the bloodstream of the consumer. With virus-resistant plants, which are made to express part of the virus protein (analogous to human vaccination), the plant will be the same except that it will contain this extra protein. Already we probably consume more of this virus protein in our food, because the vegetables we eat contain plant viruses from the natural infection of crops. There is no harm at all for humans from most plant viruses, so virus-resistant vegetables made in this way should in general require little testing.

On the other hand, when we attempt to improve the nutritional qualities of vegetables, which have been achieved for potato, we will need to examine the new variety more carefully. But, if the improvement was made by the addition of a protein gene from soybean to potato, for example, because we already consume soybean we would have little fear of consuming the new potato variety. We may still want to check that the levels of substances produced in the

potato were safe however, because there are some naturally occurring toxins in vegetables that have been selected by plant breeders to remain at a low level of expression, and we should not consume a variety that contains a lot more of this toxin than is in the varieties we already consume. This test could be performed very simply by food scientists and biochemists, without the need for extensive safety testing, unless there was something strange about the observed composition. We should also note the future potential of genetic engineering to produce more nutritious and safer food than we consume now, by the breeding of new varieties of crops excluding the naturally occurring toxins and carcinogens that we consume everyday from our food.

The transfer of genetic material and DNA does occur in the digestive tract of human beings, and the rate of transfer can be quantified. The most common type of DNA transfer is among micro-organisms which inhabit the digestive system. A study of Gruzza et al. (1993) studied conjugal transfer, both *in vitro* and *in vivo* (in mice digestive tract) of DNA from Lactococcus lactis donor strains to an Enterococcus faecalis bacterial strain isolated from human faeces. They followed the transfer of: a self-transmissible plasmid pIL205; two non-self-transmissible but mobilizable plasmids, pIL252 and pIL253; and, one plasmid, pMS1.5B, integrated into the chromosome of L. lactis. *In vivo*, only transfer of pIL205 and pIL253 occurred, but the transfer of pMS1.5B was not detected *in vitro* or *in vivo*. Therefore it would appear that genetic elements incorporated onto the chromosome are more stable than those remaining as plasmids.

The pleiotropic effects include the possibility that there are toxic or carcinogenic substances. Carcinogens have evoked much concern, typified by the Delaney Clause of the United States Federal Food, Drug, and Cosmetic Act 1958 prohibited the addition to the human food supply of any chemical that had caused cancer in humans or animals. Because of progress in the understanding of the mechanism of carcinogenesis and cancer causation, and in analytical technology allowing accurate determination of trace amounts of chemicals, the Clause is being modified under a law in the US Congress in 1996 (Weisburger, 1994). Carcinogens will be allowed in foods if they create a 'negligible risk' of causing cancer. Risks will be assessed separately for children, who may be at greater risk because of lower body weight.

Many documented human carcinogens are DNA reactive or genotoxic, and attention should be on prohibition of the addition to human foods of proven genotoxins. Such genotoxic carcinogens are those reliably positive in a battery of three tests, the Ames test in Salmonella typhimurium, the Williams test with evidence of DNA repair in hepatocytes, and direct documentation of DNA adduct formation in the 32P-postlabeling technique of Randerath (Weisburger, 1994).

There have been extensive safety tests conducted on some transgenic foodstuffs, for example the Calgene Flavr Savr tomato which was given to rats and no serious health effects were found even in large quantities; for glyphosate-tolerant soybeans over 450 different components were studied for 20 lines of six different crops; and other studies on virus resistant squash (OECD, 1996). These products are therefore unregulated as GMOs in the United States of America.

Some transgenic crops still contain antibiotic resistance genes when they are grown. This concern led to rejection of a maize with an inserted Bt gene that is resistant to European corn borer, that was being marketed by Ciba-Geigy (Coghlan, 1996). The maize includes three extra genes, including a resistance gene to ampicillin, and only France seemed to support the introduction among the European Union countries. Technically unanimous disapproval is needed to block a product, but it raises further questions of international versus national regulation. Studies in mice and rats of the protein product of the marker gene for neomycin resistance found it is safe for consumption (Fuchs et al., 1993). A general review of the issues is Advisory Committee on Novel Foods and Processes (ACNFP, 1994).

In the European Union a program FLAIR (Food Linked Agro-Industrial Research) was conducted from 1990 to 1993 to stimulate research in food. This included hazard analysis and food safety. The toxicity of Bt gene protein in concentrations up to 4,000 times the maximum likely to be ingested (1kg of tomatoes per day) was found to have no harmful effect

on the growth of mice after exposure for 28 days. This product also has a history of previous use, being licensed in various formulations since 1962 (OTA, 1988). It is available in a number of formulations in over 400 products in the United States of America. There have been very few instances of harm being noted, even though hundreds of thousands of tons of the protein have been administered. One harmful effect observed was an association with corneal ulcers in humans (Samples and Buettner, 1983). It will be important to clarify all possible effects before approving the consumption of transgenic plants that contain this toxin.

People express a variety of allergies to food components, and studies show that allergic components can be transferred by genetic engineering. Nordlee et al. (1996) showed that 2S albumin which is the principle allergen of Brazil nuts can be transferred to soybeans. Skin-prick tests can be used to detect allergies, but it is not feasible on a population scale. Therefore if allergens are associated with the traits being transferred, people should be warned of the potential allergic reaction to the novel food. In that study, the particular variety of soybeans that was made by Pioneer Hi-Bred would have had to be labeled under FDA policy, however it decided to abandon development of this variety (Nestle, 1996).

In fact genetic engineering can alleviate allergic reactions. Shiseido is marketing rice without globulin as a health product, a new class of food, physiologically functional food, which is an alternative for about 70% of the people who have allergies.

These concerns also apply to animal food, both because of animal welfare and disease concerns, and because of downstream effects upon humans of consumption of animals. Food is not the only product, for example increasing the sulfur containing amino acids in clover for sheep food is designed to increase wool production.

A practical problem in farming will be the segregation of similar looking seeds that produce different varieties of the same plant designed for different uses. For example, some rapeseed with altered oil composition are suited for food oils and others are not. Crushing mills will have to distinguish the different types also.

III.3.2 Environmental impact

The major concerns are ecological and have been the subject of a number of studies and reports (OTA, 1988; Tiedje et al., 1989; HMG, 1991). The issue has, and continues to need to be, addressed by scientific studies.

In Europe a BRIDGE program study in five countries including industry and academic researchers developed materials to allow better monitoring of environmental safety (Rudelsheim et al., 1994). They found greenhouse tests were useful predictors of environmental behavior, but could not predict everything. They found the relative weediness or fitness was not significantly different from the corresponding non-modified plants. Of specific plants, they found potato did not transfer genes to weedy relative species, but sugarbeet could transfer genes to wild beet species. Oilseed rape did transfer genes to Brassica rapa, but special circumstances were required for transfer to three other weedy species they tested. Gene transfer was later reported by this group in Alfalfa to non-cultivated relatives. The rates of transfer decrease rapidly with distance, however the problem is that weeds often invade the crop fields so the distances may not be major.

Pollen transfer is the easiest method that one could imagine for transfer. The distances for different crops are already known from experience with plant breeding. Research in the United States of America on genetically modified cotton shows that pollen movement decreases rapidly after 12 meters (Umbeck et al., 1991). Around a central transgenic test plot of 98,800 plants with rows running north-south, they planted 23 one-meter border rows of non-transgenic cotton to the east and to the west, and 25 meters of non transgenic cotton border rows to the north and to the south, each divided into two 12.5 meter long plots. The border rows to the north and south were continuous with the transgenic rows. They took 32,187 seed samples from all border rows at bottom, middle and top plant position (representing seasonal variation) and used a kanamycin resistance marker gene to test for seeds resulting from pollen movement out of the central transgenic plot. To the east and west, gene movement at the first row was 0.057 and 0.050 and dropped rapidly to row 8, and was

not detected in subsequent rows to the east and detected occasionally at <0.01 in rows to the west. Combined data for east and west border rows beyond row 9 gave total out-crossing of 0.0012. To the north and south, detections were totaled for each 12.5 meter block and gave figures of 0.0053 and 0.0047 for north and south inner block and 0.0015 and 0.0021 for north and south outer block.

For soybean there is very little chance that pollen will escape from plots. Soybeans are almost completely self pollinated, and honey bees are responsible for the occasional cross-pollination. US Certified Seed Regulations (7 CFR {201.67 - 201.78}) recognize this cross-pollination unlikely in the safeguards set up for Foundation, Registered, and Certified seed. For Foundation seed, the most stringent category in the Certified Seed Regulations Table 5, soybeans are permitted to be grown zero distance from the nearest contaminating source (i.e. other soybean cultivars), as long as the distance is adequate to prevent mechanical mixing. Soybean seed has a short time potential for high germination and vigor, and in commercial operation fresh soybean seed is produced annually for each new season. However, some remaining seed from one crop is capable of germinating the following season, and is therefore able to cause a temporal, if not geographic, dispersal of the soybean plant. The Certified Seed Regulations require for Foundation, Registered, and Certified seed that at least one year must elapse between the destruction of a stand of soybean and a subsequent establishment of a new soybean stand. Vegetative reproduction of soybean plants does not occur under field conditions (USDA on-line information, 1996). This type of analysis is ethically necessary for all GMO species before use in farms, in addition to field trials in limited space.

By the use of traits such as male sterility, it is possible to avoid the risk of transfer of pollen or seeds. The approach taken will depend upon the species in question, and needs of the local community. For example, socio-economic concerns may mean that some farmers prefer to produce seeds for their future use rather than buying hybrid seed each year. Such decisions may not be best left to producers if there is perceived to be serious risks.

The extensive use of monoculture in agriculture has resulted in loss of biodiversity for crop species, not only the previously existing species growing in the space taken over (in land, water or air). The effects may be complex, for example insect species which rely on certain pollen or nectar may be lost if they cannot utilize the newly appearing species. The International Convention on Biological Diversity recognized a value in continued existence of biodiversity. There is no evidence that genetically modified plants will make the situation any worse than current agricultural varieties, but we would urge that methods to preserve biodiversity in agriculture be encouraged, and monitoring studies are done.

III.3.3 Economic issues

Agriculture has always been a major economic force of trade between countries and biotechnology promises to continue to alter the balances of trade (Juma, 1991; OTA, 1991). Much of the new wave in biotechnology research is being performed by private companies. These companies are being encouraged to perform research in their country's national interests, including the hope of more export earnings from the sale of products and/or technology. This association of biotechnology with business means that the primary goal is economic profit, rather than human or environmental benefit. This is not a new phenomenon, and internationally the public is becoming aware of this clash of priorities. In biotechnology we can expect benefits to humanity, but this is not the reason for industrial investment. The human and environmental benefits will come about as a secondary consequence.

It is important to think of the trans-frontier nature of biotechnology. There has been a move by the G7 group of countries to make internationally binding regulations on the use of GMOs, and regulations on import and export have been agreed upon. However some countries also want to include handling and use of GMOs and a clause on compensation for human health or environmental damage, and a clause to assess and possibly compensate for the impact of biotechnology on traditional agriculture (Masood, 1996).

Intellectual property issues are some of the most controversial in modern biotechnology (OTA, 1989; Lesser, 1991). Bioprospecting has been partially controlled by the Convention on Biological Diversity, which regulates collecting of species after 1993 in the wild. It does not regulate the use of samples from botanical gardens that were collected before this, and also it does not regulate the resources found in the oceans of international waters (Tangley, 1996). It covers the country of ownership, but inside countries there are also disputed claims to which community has rights. This new approach contrasts with the practice which still continues among many researchers for free exchange of materials, and there are unresolved ethical questions about whether one country or group can claim ownership of a species. Another approach would be to see them as the common heritage of all species and all humanity.

There are also unresolved legal and practical implications of the ethical issues when someone improves upon a variety that another has developed. Many medicinal plants have been collected and selected by indigenous groups, local farmers and traditional medicinal healers. Modern approaches can identify the active ingredients and several patents have been issued to these companies. These are being challenged, but the issue needs further ethical resolution. The practical issues of royalty sharing also need to be resolved.

Companies have been responsible for about 80% of the releases of GMOs in the world (Krattiger and Rosemarin, 1994). The risks that companies take include investment in unprofitable products, risks of environmental and/or medical legal claims, and risks of unwelcome legal restraints. As commercial seeds and animals are passed on to farmers, the farmers will assume increasing responsibility for sensible farming practice, which is usually in their long-term interests also, e.g. monitoring of pest resistance to insecticidal proteins. The risks to the farmers include crop failure, unprofitable products, damage to their land or their health, and even possible legal claims against them.

Each of the groups involved in the release of GMOs also has their own set of benefits. Ideally, all may share the goal of human progress, but they also share the benefits for their own progress. All three have economic interests, perhaps scientists less than the other two groups, if the scientists have the luxury of financial support unlinked to research application. The general public also shares these benefits, but may have a longer term economic and environmental framework, and has the benefit of being consumers. Variety or alternatives can give choice, if such a variety is available, and many people may also welcome a variety which is lower cost. In fact, when we consider this factor the public may also have short term economic sights, when it enters the supermarket.

IV. Regulation of Food Safety and Biotechnology

IV.1 *National Regulations and Guidelines*

The World Health Organization (WHO) estimated in 1988 that less than 10% of food-borne disease is reported in countries of the European region, let alone for poorer countries who lack those resources. In that report the food safety guidelines of 32 European countries were reviewed, and there were a number of differences. The impact of food contamination on adverse health is not able to be fully recognized, and one of the basic needs is methods to better detect food contamination, and ways to allow practical regulation of food safety standards. Even if there is a monitoring service, within each country different ministries and levels of government may also have overlapping responsibilities.

For some substances there is broad international consensus, for example, since the discovery of the aflatoxins in the 1960s, regulations have been established in many countries to protect the consumer from harmful effects of mycotoxins that may contaminate foodstuffs. At least 77 countries now have regulations for mycotoxins, though tolerated limits vary (van Egmond and Dekker, 1995). It is quite important to have international approaches and support because food products are sold and transported across borders, and a ban in one country could be circumvented if a neighboring country approved its production.

Conversely, many food additives are accepted in foodstuffs following demonstration that they are safe (Halogen et al., 1995). The demonstrations of safety rely on scientific tests, and the safety issues associated with novel products or organisms can be addressed by essentially the same methods independent of whether genetic engineering has been used (OECD, 1986).

Because many of the GMOs destined for food production were first grown extensively in the United States of America, the decisions of the FDA have been influential in international policy. The FDA opposed systematic labeling of foods made from plant biotechnology in 1992. A description of FDA procedures for approval of foods from genetic engineered organisms is Henkel (1995). The FDA exempts food from case-by-case review unless there are signs that there will be a problem, for example an allergic reaction. This has been criticized by some, especially the decision to leave it up to industry to decide, and also that labels may not be necessary for some products. Chicago passed a local law requiring all foodstuffs made from genetically engineered organisms to be labeled as such (*Nature* 365: 96). There is also regulation by the United States Department of Agriculture (USDA). The USDA Food Safety and Inspection Service (FSIS) is also responsible for ensuring that transgenic animals intended for human consumption are wholesome, unadulterated and properly labeled (Basu et al., 1993).

The UK guidelines on novel foods (Jonas, 1995; ACNFP, 1989-1995) are implemented through the Ministry of Agriculture, Fisheries and Food, and the Department of Health. Voluntary guidelines have been followed since 1989. Each year a public report is issued including the details of each submission, the arguments discussed, data that was presented and recommendations made. The ACNFP actually also considers food treated in novel ways, not only biotechnology. This is quite consistent with the ethical concerns, because there is no reason to single out one method of food preparation.

Product-based assessment is a theme seen in both the United Kingdom and the United States of America and in most international reports on the subject. In both countries labeling and review is not statutory, but the choice to do so is often voluntarily made. The United Kingdom committee does not recommend labeling if there is no viable genetic material in the final food to be consumed, for example in oils (ACNFP, 1995).

IV.2 *International Regulations on Food Safety*

The Group of Advisers on Ethical Aspects of Biotechnology to the European Commission (1995) recommended food be labeled to indicate when its composition and characteristics have been substantially modified by genetic engineering techniques, but said that labeling was inappropriate when changes are insubstantial. An earlier draft directive on novel foods opposed systematic labeling to avoid any stigma, also noting that such labels may not provide any useful information to the public (Butler, 1995). However, pressure from consumer groups and the recognition of consumer's right to choose, led this group to recommend (Art. 2.3):

The consumers must be provided with information which, for transparency, should be:

- useful, adequate, and informative;
- clear, understandable, non-technical;
- honest, not misleading or confusing, and which aims to prevent fraud;
- enforceable, i.e., possible to verify.

Basically these labels apply when the product is significantly changed in composition, nutritional value or intended use. Generally they focus on the product rather than the process. European Union Novel Food and Novel Food Ingredient Legislation was passed in 1996 (awaiting decision) and is expected to provide a statutory basis for all European Union countries, and food will only be sold in one country if no other country objects. There are disputes over labeling requirements, seen in 1996 with the proposals to import soybeans. Because these beans are mixed after farming, it is difficult to know which beans are from GMOs and which are not. There are several European Commission Directives on the production of food additives or GMOs (93/114/EEC), on medicinal products (93/41/EEC), and on plant protection products (91/414/EEC).

The Confederation of Food and Drink Industries (Brussels) supports labeling only when there is a change in the food's nutritional value or the way it is metabolized in the body. However, some companies like Zeneca and Calgene which market tomatoes with delayed softening support the idea of labeling because this removes suspicion from the public mind and gives choice (Butler, 1995).

Some professional associations have made statements, such as the American Dietetic Association (1995), or published discussion papers, such as the American Veterinary Medical Association (Kopchick, 1992).

The OECD (1996) has had several workshops on the subject of safety of novel foods, and in 1994 held a workshop in Oxford, United Kingdom, which used the principle of substantial equivalence, and concluded that the same approach could be applied to microbes, plants and animals. Substantial equivalence suggests that existing organisms used as food, or as a source of food, can be used as a basis for comparison when assessing food safety^(**) (OECD, 1993). They considered three situations:

- 1) there is substantial equivalence between the new food and a traditional counterpart (e.g. virus resistant plants produced by insertion of the viral coat protein, or herbicide tolerant plants produced by introducing a protein comparable to one already present in a plant but tolerant to a selective herbicide);
- 2) there is substantial equivalence between the new food and a traditional counterpart, except for the inserted trait (e.g. insect protected plants produced by the insertion of the Bt gene or disease resistant plants produced by the introduction of a new protein); and
- 3) there is not substantial equivalence between the new food and a traditional counterpart (e.g. introduction of a gene or genes that encode a trait that significantly alters the plant for use in food or feed, such as production of a new oil or carbohydrate).

If substantial equivalence is established they considered that the novel food be treated the same as the familiar one. If there was a new trait, then the evaluation should be case-by-case for the product of the gene. The RNA/DNA toxicity is not an issue, though the potential for transfer is. Some of the factors considered important in evaluation are the source, identity, construction, effect, degree of digestibility, allergenicity, stability of the trait, protein and any products of its action (secondary metabolites), site of expression (tissue specificity) and colonization potential for micro-organisms (OECD, 1996). In the case that a novel food does not have substantial equivalence to a current food, then safety testing was called for.

We may not need to apply any additional regulations to those that cover food safety, unless novel components are introduced to the food. This was also the recommendation of a FAO consultation group (WHO, 1991). In 1988, the International Food Biotechnology Council (IFBC, 1990) was formed with the aim of identifying the issues and assembling a set of scientific criteria to evaluate the safety of food derived from plants and micro-organisms resulting from the applications of biotechnology. They did not consider animal foodstuffs. The membership of the Council was comprised of approximately 30 companies, who set up committees to look at scientific, legal/regulatory and policy/public relations aspects. They discussed the variability of composition inherent in foods and food ingredients, such as the nutrients and toxicants. There are several vitamins (A and D), certain trace minerals (Fluorine, Iodine, Copper, Selenium) and other essential nutrients that are consumed safely only within a narrow range. Intake below that range results in deficiency or disease, and above that range in toxicity. There are many food toxicants that are already accepted at low levels in foods. For intentional introductions a safety factor of 100 is commonly used. They surveyed the range of toxicants and nutrients in traditional foods as a basis for comparison with new foods, and as the standard for defining food that is considered safe. They also recommended that the regulation of food from GMOs be directly patterned on the existing law.

** special thanks to Mr Mark Cantley of the OECD for his comments on the Draft Report.

The IFBC (1990) recommend that the following types of genetic elements be considered acceptable for use in food:

- uncharacterized genetic material presently consumed in food, that was introduced from non-food species used as sources of genetic variation in developing and improving foods using traditional methods of genetic modification and for which documentation of safe food product is available;
- fully characterized genetic material derived from non-toxic, non-pathogenic micro-organisms that are not intentionally consumed as food but are commonly found in or on food and accordingly have an established record of safe use;
- fully characterized non-coding DNA from sources that are not traditional foods. Since non-coding DNA can not encode any protein, then only the intrinsic properties need be considered. The only concern is a quantitative one: large quantities of nucleic acids can cause gout;
- coding DNA from non-food species that have already been used as sources of genetic variation in developing and improving foods using traditional methods of genetic modification and for which documentation of safe food product use is available.

In conclusion, a balance must be found between the right of consumers to information and the imposition of unnecessary information which may confuse people over what the major facts relevant to their diet are, e.g. containing allergens, phenylalanine for sufferers of phenylketonuria, fat content, sugars, etc.. An article in the conclusion is made regarding this. Whether the information should be in the form of a label or an information sheet, and what should be in that information (e.g. this product has undergone safety assessment or this product contains X gene), are matters of debate.

IV.3 Regulations on Environmental Safety

A review of international biosafety guidelines was prepared by the United Nations Economic Commission of Europe (ECE, 1995). The ECE began involvement in the collection of biosafety guidelines following the concluding document of a 1986 meeting of the Representatives of the Participating States of the Conference on Security and Cooperation in Europe (CSCE), held in Vienna. This work allows exchange of information on biosafety and is already well underway. They include submissions from 30 governments, the United Nations Industrial Development Organization (UNIDO), the Commission of the European Community and the OECD. In July 1991, a Voluntary Code of Conduct for the release of organisms into the environment was prepared for the informal UNIDO/UNEP/WHO/FAO working group on safety. The OECD issued safety guidelines on genetic engineering earlier, in 1986, which have been used as a basis for regulations in many countries, not only those of the OECD.

Countries which have passed specific laws on the regulation of genetic engineering include Austria (1994), Denmark (1986), Finland (1995), France (1993), Germany (1990), New Zealand (1996), Norway (1993), Russian Federation (1996), Spain (1994) and the United Kingdom (1989). Most other industrialized countries have Ministry guidelines on genetic engineering. There are critics of legislation which was aimed at the process of manufacture, not the product (Tzotzos, 1995).

A major impetus for European countries to enact laws on genetic engineering was the European Commission Directives 90/219/EEC of 23 April 1990, which covers the contained use of genetically-modified micro-organisms, both for research and commercial purposes; 90/220/EEC of 23 April 1990 on experimental and marketing-related aspects of GMOs, which covers any research and development release of these organisms into the environment, and contains a specific environmental risk assessment for the placing of any product containing or consisting of such organisms onto the market; 90/679/EEC of 31 December 1990 and 93/88/EEC of 29 October 1993, which provide a minimum requirement designed to guarantee a better standard of safety and health as regards the protection of workers from the risks of exposure to biological agents. Competent authorities for the first two directives are appointed in all Member States.

The United States of America regulates through government departments or agencies. The USDA has the greatest number of applications and has deregulated various GMOs since 1992. Crops approved for open release (Petitions under 7 CFR Part 340 of the USDA GMO release guidelines) include (note, for some, several companies have approval): Phosphinothricin tolerant soybean; PRV resistant papaya; CMV resistant/WMV2 resistant/ZYMV resistant squash; Colorado potato beetle resistant potato; Fruit ripening altered tomatoes; Sulfonylurea tolerant cotton; Male sterile/Phosphinothricin tolerant cotton; European Corn Borer resistant corn; Phosphinothricin tolerant corn; Lepidopteran resistant corn; Lepidopteran resistant cotton; Coleopteran resistant potatoes; Oil profile altered rape; Glyphosate tolerant soybean; Bromoxynil tolerant cotton; WMV2 resistant/ZYMV resistant squash.

V. Conclusions and the Role of UNESCO

If we were asked whether the overall effect of biotechnology on environmental and food safety will be positive or negative, the answer given the current technologies would be unequivocally positive. This is because biotechnological methods already allow better monitoring of both environmental and food safety, and we can also hope for overall benefit in production.

The goal of regulations is the promotion and protection of human health, so that burdens on particular approaches should not be used, rather benefit/risk evaluation of all alternatives.

There is a right for consumers to be informed about the content of the foods made from organisms modified by genetic engineering. The information should be available for consumers at the site of sale. Such information should include any relevant health information, especially the possibility for allergies, and any information that may be important for religious or specific diets, e.g. animal gene products.

Local socio-economic conditions vary, and there may be both positive and negative effects of plant biotechnology on different communities and countries. There is not a consensus on whether biotechnology will favor international trade or not, nor whether it will have net positive or negative effects on national economies, though it should have advantages in environmental sustainability and in food production.

Some of the specific roles of UNESCO (and/or other UN organizations) could be:

1. Promotion of research into the socio-economic implications of plant biotechnology upon different cultures and countries, by encouraging broader study of bioethics.
2. There is a need for an independence and credibility of information, where people may trust the information on safety that is provided. Organizations that promote industrial activity may be more suspect than those which are independent of it. There could be a role specifically for UNESCO in provision and storage of safety information.
3. There is a need for education of the public, experts and government officials, of the benefits and risks of biotechnology. This should include workshops on risk assessment and biosafety, and public meetings to inform people on biotechnology. In general we should think how to best stimulate research and teaching in bioethics in member countries, supporting local workshops and visits by experts.
4. Training of food scientists in use of current biotechnological methods, including assays and toxicity tests.
5. Promotion of research into areas of plant technology thought to be applicable to developing countries to supplement the well-funded industrial research.
6. Specific areas of research could be promoted such as identification of traits that influence weediness (the competitive behavior that leads to undesired effects on the position and impact of a plant in the environment); identification of any problems of sizing up to commercial scale harvests from field trials; identification of genes or genotypes that convey competitive advantage on plants possessing them that would in turn result in the spreading of leaked genes.

7. Supporting global data-sharing on food safety, environmental safety, and technical methods for improving crops, some of which is already underway by the ECE and UNIDO. However, the compilations are not complete or up-to-date, and they do rely upon the submissions by Member States. The USDA maintains an on-line information server which is accessible by all persons, and relays the latest information on each application for a field permit or safety studies. An international version of this service would be valuable, and could be spread through the United Nations Internet sites.

8. There is a need for research on intellectual property protection for both traditional and new genetics. How do we distinguish inventions from discoveries. The impact on vulnerable developing countries and groups should also be studied.

REFERENCES

- ACNFP (ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES). *Report on the Use of Antibiotic Resistance Markers in Genetically Modified Food Organisms*. London: ACNFP, 1994
- ACNFP (ADVISORY COMMITTEE ON NOVEL FOODS AND PROCESSES). *Annual Report*. London: MAFF, Dept. of Health ACNFP, 1995
- AMERICAN DIETETIC ASSOCIATION. Position of the American Dietetic Association: Biotechnology and the Future of Food. *Journal of the American Dietetic Association* 95 (1995), 1429-32
- BASU, P.; MASTERS, B.; PATEL, B. AND URBAN, O. Food Safety and Inspection Service Update on Food Safety of Animals Derived from Biotechnology Experiments. *Journal of Animal Science* 71 Suppl. 3 (1995), 41-2
- BELONGIA, E.A. ET AL. An Investigation of the Cause of the Eosinophilia-myalgia Syndrome Associated with Tryptophan Use. *NEJM* 323 (1990), 357-365
- BERKOWITZ, D.B. The Food Safety of Transgenic Animals: Implications from Traditional Breeding. *Journal of Animal Science* 71, Suppl 3 (1993), 43-6
- BUTLER, D. Panel Offers Compromise on Food Labelling. *Nature* 375 (1995), 443
- CHADWICK, R. ET AL. *BIOCULT. Cultural and Social Objections to Biotechnology: Analysis of the Arguments, with Special Reference to the Views of Young People*. University of Central Lancashire, 1996
- COGHLAN, A. Engineered Maize Sticks in Europe's Throat. *New Scientist* (6 July 1996), 8
- COUCHMAN, P. AND FINK-JENSEN, K. *Public Attitudes to Genetic Engineering in New Zealand*. DSIR Crop Research Report, N°138. Christchurch, NZ: DSIR Crop Research, Private Bag, 1990
- DAY, P.R. Genetic Modification of Plants: Significant Issues and Hurdles to Success. *American Journal of Clinical Nutrition* 63 (1996), 651-6S
- DEMARLY, Y. [Genetic engineering in plants] [French]. *Bulletin de l'Académie Nationale de Médecine* 176 (1992), 1297-304
- ECE (ECONOMIC COMMISSION OF EUROPE). *ECE Inventory of Safety Guidelines in Biotechnology* (ECE/SC.TECH./47). Geneva: United Nations, 1995
- EUROBAROMETER SURVEY 39.1 (and 35.1), *Biotechnology and Genetic Engineering: What Europeans Think About It in 1993*. Brussels: Commission of the European Communities, 1993
- FUCHS, R.L. ET AL. Safety Assessment of the Neomycin Phosphotransferase II (NPTII) Protein. *Biotechnology* 11 (1993), 1543-7
- FUCHS, R.L. ET AL. Purification and Characterization of Microbially Expressed Neomycin Phosphotransferase II (NPTII) Protein and its Equivalence to the Plant Expressed Protein. *Biotechnology* 11 (1993), 1537-42

- GEISOW, M. The Proof of the Cloning is in the Eating. *Trends in Biotechnology* 9 (1990), 5-7
- GOLDBERG, R.J. AND TJADEN, G. Are B.T.K. Plants Really Safe to Eat? *Biotechnology* 8 (1990), 1011-1015; *Biotechnology* 9 (1991), 198
- GROUP OF ADVISERS ON THE ETHICAL IMPLICATIONS OF BIOTECHNOLOGY OF THE EUROPEAN COMMISSION. Ethical Aspects of the Labelling of Foods Derived from Modern Biotechnology' (5 May 1995). Reproduced in: *Politics and the Life Sciences* 14 (1996), 117-9
- GRUZZA, M.; LANGELLA, P.; DUVAL-IFLAH, Y. AND DUCLUZEAU, R. Gene Transfer from Engineered Lactococcus lactis Strains to Enterococcus faecalis in the Digestive Tract of Gnotobiotic Mice. *Microbial Releases* 2 (1993), 121-5
- HAMSTRA, A.M. *Biotechnology in Foodstuffs SWOKA*, Report 105. Institute for Consumer Research, Koningin Emmakade 192-195, 2518 JP's-Gravenhage, The Netherlands, 1991
- HAMSTRA, A.M. Consumer Research on Biotechnology. In: J. Durant (ed.), *Biotechnology in Public*. London: Science Museum, 1992
- HAMSTRA, A.M. *Consumer Acceptance of Food Biotechnology SWOKA*, Report 137. Institute for Consumer Research, Koningin Emmakade 192-195, 2518 JP's-Gravenhage, The Netherlands, 1993
- HARADA, H. Advancement of Plant Breeding Techniques: Scientific, Social and Global Impact. *EJAIB* 6 (1996), 134-5
- HENKEL, J. Genetic Engineering. Fast Forwarding to Future Foods. *FDA Consumer* (April 1995), 6-11
- HERBERS, K. AND SONNEWALD, U. Manipulating Metabolic Partitioning in Transgenic Plants. *Trends in Biotechnology* 14 (1996), 198-205
- HESS, C.E. Biotechnology-derived Foods from Animals. *Critical Reviews in Food Science & Nutrition* 32 (1992), 147-50
- HOBAN, T.J. AND KENDALL, P.A. *Consumer Attitudes About the Use of Biotechnology in Agriculture and Food Production*. Raleigh N.C. North Carolina State University, 1992
- HORSCH, R.B. Commercialization of Genetically Engineered Crops. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences* 342 (1993), 287-91
- HMG ROYAL COMMISSION ON ENVIRONMENTAL POLLUTION. Fourteenth report, *Genhaz. A System for the Critical Appraisal of Proposals to Release Genetically Modified Organisms into the Environment*. London: H.M.S.O., June 1991
- IFBC (INTERNATIONAL FOOD BIOTECHNOLOGY COUNCIL). *Biotechnologies and Food: Assuring the Safety of Foods Produced by Genetic Modification*. Washington D.C.: IFBC, May 1990
- JONAS, D.A. The UK Approach to the Regulation and Evaluation of Novel Foods Produced by Biotechnology. *Archives of Toxicology Suppl.* 17 (1995), 557-61
- JUMA, C. *The Gene Hunters. Biotechnology and the Scramble for Seeds*. Princeton: Princeton University Press, 1989
- KOPCHICK, J.J. Biotechnology and Food Safety. *Journal of the American Veterinary Medical Association* 201 (1992), 228-34
- KRATTIGER, A.F. AND ROSEMARIN, A. (eds.), *Biosafety for Sustainable Agriculture. Sharing Regulatory Experiences of the Western Hemisphere*. Stockholm: Stockholm Environmental Institute, 1994
- KUNG SHAIN-DOW (ed.), *Biotechnology and Food Safety*. Butterworth-Heinemann, 1990

- LESSER WILLIAM, H. *Equitable Patent Protection in the Developing World: Issues and Approaches*. Christchurch, NZ: Eubios Ethics Institute, 1991
- LEVI-STRAUSS, C. *Mythologiques - Le Cru et le cuit* [The raw and the cooked]. Paris, 1964
- LLOYD-JONES, L.P.M. Biotechnology-derived Foods and the Battleground of Labelling. *Trends in Food Science & Technology* 5 (1995), 363-7
- MACER, D.R.J. *Shaping Genes: Ethics, Law and Science of Using Genetic Technology in Medicine and Agriculture*. Christchurch, NZ: Eubios Ethics Institute, 1990
- MACER, D.R.J. *Attitudes to Genetic Engineering: Japanese and International Comparisons*. Christchurch, NZ: Eubios Ethics Institute, 1992
- MACER, D.R.J. *Bioethics for the People by the People*. Christchurch, NZ: Eubios Ethics Institute, 1994a
- MACER, D.R.J. Perception of Risks and Benefits of in vitro Fertilization, Genetic Engineering and Biotechnology. *Social Science and Medicine* 38 (1) (1994b): 23-33
- MACILWAIN, C. Boll-worms Chew Hole in Gene-engineered Cotton. *Nature* 382 (1996), 289
- MARTIN, S. AND TAIT, J. Attitudes of Selected Public Groups in the UK to Biotechnology. In: J. Durant (ed.), *Biotechnology in Public*. London: Science Museum, 1992
- MASON, H.S. AND ARNTZEN, C.J. Transgenic Plants as Vaccine Production Systems. *Trends in Biotechnology* 13 (1995), 388-92
- MASOOD, E. Liability Clause Blocks Talks on Biosafety Protocol. *Nature* 382 (1996), 384
- MEPHAM, T.B. Transgenesis in Farm Animals: Ethical Implications for Public Policy. *Politics and Life Sciences* 13 (1994), 195-203
- MURPHY, D.J. Engineering Oil Production in Rapeseed and Other Oil Crops. *Trends in Biotechnology* 14 (1996), 206-13
- NESTLE, M. Allergies to Transgenic Foods - Questions of Policy. *New England Journal of Medicine* 334 (1996), 726-7
- NORDLEE, J.A. ET AL. Identification of a Brazil-Nut Allergen in Transgenic Soybeans. *New England Journal of Medicine* 334 (1996), 688-92
- OECD (ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT). *Recombinant DNA Safety Considerations. Safety Considerations for Industrial, Agricultural and Environmental Applications of Organisms derived by Recombinant DNA Techniques*. Paris: OECD, 1986
- OECD (ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT). *Safety Evaluation of Foods Derived by Modern Biotechnology: Concepts and Principles*. Paris: OECD, 1993
- OECD (ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT). *Food Safety Evaluation*. Paris: OECD, 1996
- OTA (U.S. CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT). *New Developments in Biotechnology, 3: Field Testing Engineered Organism, Genetic and Ecological Issues*. Washington: U.S.G.P.O., OTA-BA-350, May 1988
- OTA (U.S. CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT). *New Developments in Biotechnology, 4: Patenting Life*. Washington: U.S.G.P.O., OTA-BA-370, March 1989
- OTA (U.S. CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT). *Biotechnology in a Global Economy*. Washington: U.S.G.P.O., OTA-BA-494, October 1991
- PRAKASH, C.S. Edible Vaccines and Antibody Producing Plants. *Biotechnology and Development Monitor* 27 (June 1996), 10-13

- ROTHENBURG, L. AND MACER, D.R.J. Public Acceptance of Food Biotechnology in the United States of America. *Biotechnology & Development Monitor* 24 (Sept. 1995), 10-3
- RUDELSHEIM, P. ET AL. *Safety Assessment of Deliberate Field Use of Genetically Modified Plants*. European Commission BRIDGE Programme, 1992-1994
- SAMPLES, J.R. AND BUETTNER, H. Corneal Ulcer Caused by a Biologic Insecticide *Bacillus thuringiensis*. *Amer. J. Ophthalmology* 95 (1983), 258-260
- SANCHIS, V. [Applications of Molecular Biology Techniques for the Control of Aflatoxin Contamination] [in Spanish]. *Microbiologia* 9 (Feb 1993), Spec No. 69-75
- SASSON, A. *Biotechnologies and Development*. Paris: UNESCO, 1988
- SMITH, J. New Opportunities in Food Biotechnology. *Australasian Biotechnology* 4 (1994), 285-91
- SMITH, R.E. Food Demands of the Emerging Consumer: The Role of Modern Food Technology in Meeting that Challenge. *American Journal of Clinical Nutrition* 58 (1993; 2 Suppl), 307S-312S
- STRAUGHAN, R. AND REISS, M. *Ethics, Morality and Crop Biotechnology*. London: Biotechnology and Biological Sciences Research Council, 1996
- TANGLEY, L. Ground Rules Emerge for Marine Bioprospectors. *BioScience* 46 (1996), 245-9
- TIEDJE J.M. ET AL. The Planned Introduction of Genetically Engineered Organisms: Ecological Considerations and Recommendations. *Ecology* 70 (1989), 298-315
- TZOTZOS G.T. (ed.), *Genetically Modified Organisms: A Guide to Biosafety*. United Kingdom: CAB International, 1995
- UMBECK, P.F. ET AL. Degree of Pollen Dispersal by Insects from a Field Test of Genetically Engineered Cotton. *J. Econ. Entomology* 84 (1991), 1943-1991
- VAN EGMOND, H.P. AND DEKKER, W.H. Worldwide Regulations for Mycotoxins in 1994. *Natural Toxins* 3 (1995), 332-6; 341
- WAHLQVIST, M.L.; TRUSWELL, A.S.; SMITH, R. AND NESTLE, P.J. *Nutrition in a Sustainable Environment: Proceedings of the XV International Congress of Nutrition: IUNS Adelaide*. London: Smith-Gordon/Nishimura, 1994
- WEISBURGER, J.H. Does the Delaney Clause of the U.S. Food and Drug Laws Prevent Human Cancers? *Fundamental & Applied Toxicology* 22 (1994), 483-93
- WHO (WORLD HEALTH ORGANIZATION). Regional Office for Europe, *Food Safety Services*, 2nd edition Public Health in Europe 28. Copenhagen: WHO Regional Office for Europe, 1988
- WHO (WORLD HEALTH ORGANIZATION). *Strategies for Assessing the Safety of Foods Produced by Biotechnology*, Report of a Joint FAO/WHO Consultation. Geneva: WHO, 1991
- WOOD, M. Can Better Barley be Bred? *Agricultural Research* (Feb 1994), 4-7
- ZEMANEK, E.C. AND WASSERMAN, B.P. Issues and Advances in the Use of Transgenic Organisms for the Production of Thaumatin, the Intensely Sweet Protein from *Thaumatococcus danielli*. *Critical Reviews in Food Science & Nutrition* 35 (1995): 455-66

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