Food and Agriculture Organization

ANIMAL BIOTECHNOLOGIES : STATE OF THE ART, RISKS AND PERSPECTIVES

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INTRODUCTION

Animal biotechnology is an area of scientific research that is under constant evolution. Although no genetically modified (GM) animal is currently on the market, the United States Food and Drug Administration (FDA) is looking into the authorization of a fast-growth transgenic salmon. Some countries are worried about the imminent availability of such animals on the market, given the many diverse uncertainties, and have asked the Food and Agriculture Organization of the United Nations (FAO) and the Codex Alimentarius to determine risks associated with genetically modified organisms and to draw up procedures of analysis and international standards for derived products.

The Codex Alimentarius Commission was created in 1963 by FAO and the World Health Organization (WHO) to establish food standards, guidelines and other normative texts, under the Joint FAO/WHO Food Standards Programme. The basic aims of this programme are to protect consumer health, to promote fair trade in food and to coordinate food standardization by governmental and non-governmental organizations. At its twenty-third session, the Codex Alimentarius Commission set up the Intergovernmental Task Force on Foods Derived from Biotechnology to draw up science-based standards, regulations and recommendations for foods derived from biotechnology and for novel characteristics of foods introduced by biotechnology.

FAO and WHO hold regular consultations of scientific experts to discuss the safety and nutritional value of genetically modified food in support of the work of the Task Force. These consultations seek to provide FAO, WHO and their member countries with scientific advice on the safety and nutritional value of foods derived from biotechnology, on the basis of existing scientific data and research carried out by national authorities, FAO, WHO, and other relevant international organizations or forums. They serve to transmit the advisory opinions of experts, who are independent of the Commission, to specialized committees and task forces. Strategies to assess the safety and nutritional value of foods derived from biotechnology are examined on the basis of increasing public concerns and the outcomes of the many tests carried out to date. Recommendations are also made on the priorities of further research into the safety and nutritional value of foods derived from biotechnology.

It was in this context that I was tasked with carrying out a literature survey in preparation for an expert consultation to be held in 2003/2004 on the subject of foods derived from genetically modified animals. This meant collating recent information on animal biotechnology (including insects) and on the status of GM animals and derived foods, with a special focus on food safety. However, while highlighting safety, the report necessarily had to consider the broader implications of environment, ethics and animal welfare. This survey is based on many (mostly recent) documents and reports, but draws especially upon a report on animal biotechnology, which I believe anyone interested in the topic should read, that was compiled in 2002 by several American scientific committees on behalf of the US Food and Drug Administration.

In 2020, the world's population could amount to 8 billion people, with 6.7 billion living in the developing countries. A problem of food security would thus co-exist with the already manifest problem of soil erosion and resource depletion, notably fishery resources. Biotechnology is championed as a solution to the anticipated food deficit, but also holds promise for crop and animal production, human and animal health, and animal welfare.

What do we mean by biotechnology? There are several definitions, but the most frequent refers simply to *organisms whose genetic material has been modified by a means that cannot be achieved by conventional breeding techniques.* The Codex definitions adopted by the Cartagena Protocol on Biosafety are as follows. A living modified organism (LMO) *is understood as any living organism that possesses a novel combination of genetic material obtained through modern biotechnology.* "Modern biotechnology" is understood as *the application of in vitro nucleic acid techniques, including the recombination of deoxyribonucleic acid and the direct introduction of nucleic acids into cells or organelles,* or *the fusion of cells beyond the taxonomic family*, *that overcomes natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection*. More simply, the term GMO applies to *any biological entity capable of producing or transferring genetic material, this having been modified in a manner that is not effected naturally by propagation and/or by natural recombination.*[1]

[1] Definition of the African Association of Microbiology and Food Hygiene.

Since they were first domesticated, animals have been bred by humans for chosen properties and traits, initially by human selection, and subsequently with the assistance of genetic engineering. The purpose of applying biotechnology to animals is essentially to increase their productivity and yield, to improve their resistance to disease and parasites, and to improve the nutritional and technological qualities of foods derived from these transgenic animals. Related techniques can also be used to control human and animal disease.

This report is divided into three parts. The first deals with the many forms of animal biotechnology and directly resulting problems, which are listed in detail. There is then a chapter on the specific case of transgenic animals to protect human health. While the term biotechnology encompasses many techniques, notably techniques applied to animal production, the focus here is on everything related to genetic engineering and cloning. Genetically modified animals thus include animals resulting from any form of cloning, animals that have been genetically modified to produce meat and other products for human consumption, and animals that have been genetically modified for purposes of human health.

Biotechnology has opened up wide possibilities in many fields: from agriculture to pharmaceuticals. It has also raised increasing concern, with sometimes fierce debate on GM animals involving scientists, food producers, consumers, public interest groups, especially environmental groups, national authorities and decision-makers. The second part of the report looks at environmental concerns, dwelling briefly on transgenic insects, and highlights concerns about animal health and welfare.

The third part looks at concerns about the safety of transgenic animals and derived products. These are closely allied to current with public fears and a complex interplay of political, economic, scientific and social considerations.

PART ONE

Animal biotechnology: Assessment of techniques used and associated problems

I. Animal biotechnology

A. Introduction of novel genes

Transgenesis involves adding, replacing or inactivating a particular gene. A gene can be transferred *in vivo* into single somatic cells, which is referred to as gene therapy. A gene can be transferred into germ cells which produces transgenic animal germlines. Several methods are used:

- manipulation of a fertilized oocyte followed by implantation into the uterus;
- manipulation of the sperm used for fertilization;
- manipulation of the early embryonic tissue;
- use of embryonic stem cells which after *ex vivo* manipulation and selection can be introduced into developing embryos;
- manipulation of somatic cells in culture and insertion of the nucleus into an enucleated oocyte (technique resembling cloning);
- insertion of a gene by microinjection;
- insertion of a gene by viral vector.

There are many techniques of transfection (term designating the introduction of genetic material into a cell) but all present technical problems: the structure of the DNA introduced into a cell varies as do the number of introduced sequences and the transgene insertion sites. The last two techniques appear to be the most common. The method most used appears to be direct microinjection of a foreign gene into the pronuclei of fertilized eggs (mammals) or the cytoplasm (lower vertebrates and invertebrates). The second method used for the insertion of a gene into vertebrate cells is by viral vector. The use of retroviruses and adenoviruses in fact offers interesting prospects.

Retroviruses are used to insert a gene of particular interest into culture cells or into the somatic tissue of trial animals. They are also used to modify the germline of fish, molluscs, chickens, mice and cattle. Under the technique, the RNA sequence in the viral genome transgene associates with a specific construct that permits transcription in the DNA sequence. This DNA sequence will then be randomly integrated into the genome of the target cells. A marker gene is often included in the construct to select cells that contain the desired gene.

Transposons, which are short DNA sequences that can be mobile under certain conditions, can transfer DNA sequences from one site to another. At present, this technique is only used routinely to obtain transgenic insects. Trials, especially with chickens and mice, have suggested that transposons from fish or insects could be used to obtain transgenic mammals, although these lack this type of mobile sequence. These methods require further research but appear to show promise, especially for the generation of transgenic cattle.

B. Direct genetic manipulation

Direct manipulation of a genome serves to modify a specific trait of an animal; the gene responsible for this trait can be suppressed or modified through gene insertion. An embryonic cell is modified then inserted into a developing embryo, one practical example being the suppression of a specific enzyme in order to produce pigs for xenotransplantation. Similarly, direct genetic manipulation could enhance the resistance of transgenic animals to certain animal diseases, such as spongiform encephalopathy. This technique seems to hold out many possibilities, but is not without its difficulties.

The technique is based on the possible recombination of the introduced gene and identical DNA sequences in the cell. Although this does occur, it does so rarely, which limits the efficiency of the method. In addition, numerous stages are required before obtaining the desired transgenic animals and the level of success is poor. These animals then have to be bred to obtain homozygous progeny. Such difficulties could be overcome by using cultured cells and nuclear transfer from these modified cells.

C. Nuclear transfer and cloning

Seven years after Dolly was created, the first cloned horse was born on 4 May 2003 in the United States. It was obtained by transferring an embryonic cell nucleus into a mare's enucleated oocyte. Dolly was the first animal to be cloned by transfer of the nucleus of a ewe's somatic cell into the enucleated oocyte of another ewe – this nuclear transfer technique involves inserting a cell nucleus into the enucleated oocyte of another animal of the same species. The nucleus donor cell can be a somatic cell or an undifferentiated embryonic cell. The term "clone" is now synonymous with the nuclear transfer of a somatic cell. The resulting embryo is then placed in culture and implanted at a specific stage of development into the uterus of a recipient female. This technique has been applied to a wide range of animal species (rodents, cattle, sheep, goats, pigs).

The efficiency of the nuclear transfer technique is limited, with success put at 10% at most, depending on the species. However the level is improving as proficiency in nuclear transfer techniques rises. Limitations relate to problems of reprogramming the donor cell nucleus, development abnormalities and perinatal problems. There are many potentially useful applications (reproduction of animals with high genetic value but low fertility, improved dissemination of high-interest genome, conservation of endangered species), but these methods are costly.

D. Current situation

Animal biotechnology is an active field of research and many successes have been posted. For example, an American company has created a salmon with 200% higher maturation thanks to an "anti-freeze" gene linked to the growth hormone gene. The transgene allows the growth hormone to function throughout the year, including during the cold season, thus permitting continuous fish growth. A lower fat content, of potential interest to consumer health, has also been noted.

The transgenic animal species listed in Table I are taken from reports and documents cited in the bibliography.

Table I : Examples of transgenic animals and their characteristics

GMO	Genetic modification	Source of gene	Purpose of genetic modification	Main benefits/ beneficiaries
Tilapia	Growth hormone	Arctic flounder/salmon	Faster growth	Fish farmers
Salmon	Growth hormone	Arctic flounder/salmon	Faster growth	Fish farmers
Salmon	"Anti-freeze" gene	Bib/salmon	Faster growth	Fish farmers
Sheep	Expression of an antibody in the milk	*H. sapiens*	Enriched milk	Consumers
Ewe, cow	Synthesis of human proteins in the milk	*H sapiens*	Production of useful molecules	Humans
Cows	Higher β and κ casein content in milk		Enriched milk resistant to heat	Agrifood industry (cheese)
Primate	Gene marker		Experiment technique with primates	Tests for human disease in the future
Pigs	Phytase gene		Reduce the level of faecal phosphorus in the environment	Less pollution from pig excrement

Selected sources

The main reasons for creating transgenic animals are therefore:

- greater resistance to disease;
- improved breeding techniques and yields;
- reduced pollution from livestock waste because of better feed conversion and digestive capability (pigs, fish);
- modified natural components of milk (lactose and humans, allergies to certain caseins, improved technological properties of milk);
- addition of components to milk for human or animal consumption;
- production of proteins of pharmaceutical or veterinary interest.

II. Problems associated with these techniques

A. Technical problems relating to germline modification

Expression of randomly inserted genes

Controlling the expression of the introduced gene seems impossible, as the gene needs to be expressed in the appropriate tissue, at the correct time and at an adequate level. In practice, the transgene either fails to express itself or else expresses itself in a variable and inappropriate manner. These problems arise from the limited understanding and difficult control of the complex system of regulation of transcription (promoters, regulatory elements, etc.). Expression of the inserted gene is influenced by many control elements located

around the integration site. As a result, the transgene is often unexpressed or, more rarely, expressed abnormally, which of course reduces the efficiency of these techniques.

The methylation of certain nucleotides also seems to be linked to the absence of expression of certain genes. Methylation is a very important regulatory mechanism in somatic cells. The absence of specific (unknown) signals to regulate the intervention of this mechanism would appear to prevent the expression of the transgene. Appropriate vectors permitting the insertion of the transgene and the regulatory process are currently under development, in particular certain lentiviruses, such as FIV or BIV, that would appear to have the appropriate properties.

Surplus animals

The problem with these techniques is that many animals fail to present the anticipated properties, do not possess the transgene or display major genetic abnormalities. Also, several animal generations are required to evaluate the stability and effects of the transgene. Failure is high, so these techniques are now turning increasingly towards the culture of modified and selected cells followed by nuclear transfer to create the desired animals, thus reducing "surplus" transgenic animal numbers.

Uniqueness of transgenic animals

One characteristic of GM animals is their considerable variability, which is linked to:

- the number of transgene sequences contained in the cells;
- the variable transgene insertion site(s) and consequences (unique phenotype);
- the level of expression of the transgene;
- the variability of abnormalities and their frequency.

A direct consequence is the extreme difficulty of assessing the risks that are associated with these individuals.

B. Problems linked to germline manipulation

Unexpected genetic side effects

Traditional outcrossings, like the different kinds of mutation (for example, deletion, duplication, insertion, inversion, translocation, transposons, and even aneuploids and polyploids), often cause the involuntary suppression or modified expression of certain genes. If detected, such abnormalities are generally rejected. Depending on the location of the chromosomes into which the modified genes have been integrated, these undesired effects can also occur with genetic engineering.

The insertion of a transgene into a functional gene can cause genetic modification and varying degrees of dysfunction. The insertion of a transgene into a silent gene could activate the expression of that gene. Mammals possess a large proportion of noncoding genome sequences, which lessens the risk of modification/inactivation of genes associated with insertion of the transgene. However, the problem remains, and abnormalities of expression of genes situated near the integration site have been observed. Certain consequences are highlighted in the literature and need to be evaluated:

- abnormalities of immune system (suppression of certain immune mechanisms, sensitivity to disease, abnormal expression of genes and induction of immunity tolerance);
- alterations to physiological mechanisms, fertility, foetal development, etc.

We can also add:

- the passage of pathogens across interspecies barriers;
- the activation of latent viruses.

Gene interaction is too complex to fully appreciate the possible biological consequences of inserting a foreign gene into a genome. Assessing this phenomenon is further complicated by the fact that gene expression is also partly determined by environmental factors and inevitably depends on the genetic make-up of the host.

Unforeseen consequences of modification

Consequences such as changed characteristics of food absorption, fertility and sexual maturity are discussed. The introduction of the growth hormone gene into fish increases their nutritional needs and changes their metabolic and physiological parameters. Behavioural abnormalities are also reported, such as increased aggressiveness among transgenic mice, and the disappearance of maternal behaviour or avoidance of risk among certain transgenic fish. The abnormalities noted among transgenic fish can be transmitted to their offspring.

The insertion of a gene encoding human cell-surface proteins into pigs for xenotransplantation could render these animals susceptible to human diseases, as has been observed with mice, increasing their risk of illness and helping propagate certain human diseases. The possibility that pig viruses could become virulent for human cells also represents a high risk.

Gene markers

Markers are generally inserted into vectors along with the transgene, in order to select the cells that possess the desired transgene. It could for example be a sequence encoding resistance to an antibiotic. While some researchers consider these markers harmless, others point out that these DNA sequences can provoke side effects in both the transgenic animal (acquisition of antibiotic resistance in host bacteria) and the consumer (allergenicity). Although the likelihood of side effects is probably low, it would seem impossible to disprove such a possibility.

Undesired inserts

Additional sequences unrelated to the specific transgene but contained in the vector construct can be introduced into target cells. Such sequences are difficult to detect and remove. In particular, retroviruses are produced by cells possessing a large number of endogenous viruses and viral DNA sequences. The accidental introduction of these sequences when inserting the transgene is therefore possible, and genetic side effects can be foreseen. There could also be a recombination of different sequences leading to the generation of novel infectious viruses.

Creation of new pathogens

Such transgenic animals and derived products could be the source of new diseases or more virulent modified pathogens. The risk is accentuated by the limitations of methods of analysis and detection of new unforeseen pathogens.

The gene for antibiotic resistance used as a marker could pose a problem if integrated into the genome of a virulent pathogen. Retroviruses used as vectors can combine with endogenous or exogenous viruses and generate a more virulent virus. The insertion of regulatory sequences or new genes into a viral genome could thus modify the pathogenecity of a micro-organism.

Mobilization of the transgene/Horizontal transfer of the transgene

Using viruses as vectors carries the risk of transmitting the transgene to other individuals, which would be possible if the viral vector were related to a virus pathogenic to the targeted species. The two viruses could combine to form a virus that could spread the transgene among the animal population. The transgene could also be mobilized through the endogenous retroviruses that normally replicate at low level in the host organism.

Similarly, the presence of moveable transposons in the genome of transgenic animals could facilitate the mobility of the inserted transgene, notably its horizontal transfer. The possibility of transgenes transferring horizontally is however disputed.

C. Problems related to cloning

The two cloning techniques differ according to the type of nuclear donor cell, which can be a (differentiated) somatic cell or an (undifferentiated) germline cell. The somatic cell nuclear transfer technique differs from the latter in two essential respects: the length of the inserted chromosome telomeres which is shorter because of the absence of telomerase but restored among transgenic animals, and the level of DNA methylation of somatic cells. The inappropriate level of methylation and the inability to correct the level are thought to cause developmental abnormalities in embryos produced with this technique. The conditions needed for the reprogramming of the inserted nucleus are disputed. Although nuclear reprogramming is currently a problem, the clear progress made in recent years suggests that it is not insurmountable.

Efficiency of techniques

The somatic cell nuclear transfer technique is not very efficient. High prenatal mortality and abnormal development, perinatal mortality and abnormal placentation among cattle and sheep have been observed, as have respiratory distress, lethargy, cardiomyopathy, pulmonary hypertension and problems of regulation of insulin levels or hypoglycaemia. These problems would appear to stem from the methods and media of embryonic cell culture, the nuclear transfer method or a combination of the two. A reprogramming of inserted genes during fertilization and early embryo development have been observed.

Reduction of the gene pool

Cloning could significantly reduce the gene pool. However, it could also help maintain certain character traits or foster genetic diversity where seemly impossible (sterility, etc.). A reduction in genetic diversity prevents future enhancement of species and homogeneity within animal species could mean greater susceptibility to disease.

III. Transgenic animals and the protection of human health

A. Biopharming

Numerous transgenic domestic animals have already been created for the expression of proteins in their derived products, such as milk, blood or eggs. However, none of these animals has yet been used commercially, although they represent a cheaper means of expressing proteins than other industrial methods. The resulting substances are subject to specific regulatory procedures and their properties are tested in the same way as substances resulting from more "conventional" technology.

Contamination or spread of a novel pathogen

One of the main problems associated with transgenic animals created for the production of biopharmaceuticals is the theoretical risk of micro-organisms acquiring the transgene. This has however not been observed to date.

Another problem is the possible generation of pathogens virulent to humans or animals through the recombination of the transgene vector and nonpathogenic endogenous proviruses in the transgenetic animal. This can be foreseen for retroviruses that efficient vectors for inserting genes into germline cells and for adenoviruses. It would be possible for many species and has in fact been observed among pigs. There is therefore significant risk of generation of a pathogenic recombinant virus.

A similar risk arises with the use of lentiviruses, notably BIV and FIV, as gene vectors. Recombination with a virus such as HIV is however considered highly unlikely because of the large genetic distance that exists between them. However, the use of a lentivirus could also lead to the generation of a pathogenic recombinant.

Disposal of animals and prevented entry of unwanted animals into the food chain

Animals used for the expression of proteins should not enter the human or animal food chain, at least not without authorization. Animals that do not contain the product of the transgene would not pose any risk to human health, but should nevertheless be totally segregated in the absence of specific, appropriate regulation. Transgenic animals without appropriate expression of the desired trait, unwanted male animals and animals at the end of their service life should not be used, advertently or inadvertently, as food or feed.

B. Xenotransplantation

This biotechnology would help solve the sometimes serious problem of insufficient supply of human organs or tissue for transplantation. Trials with the transplantation of pig cells and tissue to humans have been carried out in several countries, including the USA, Russia and those of the European Union.

This technique is thus of particular interest to human health, and extensive research has been – and is being – carried out to overcome the inherent immunological and physiological problems. The only animal currently taken seriously for xenotransplantation is the pig. Primates present serious problems of health safety and ethical concerns.

Introduction of exogenous infectious agents into the receiving organism

Xenotransplantation provides a new pathway for the transmission of existing or new human pathogens. Of main concern are viruses, including exogenous viruses and porcine endogenous retroviruses, as bacteria and parasites are generally easy to eliminate. Some viruses can be eliminated through strict management (vaccination, isolation, close epidemiological surveillance, caesarean section), but comprehensive elimination is rendered difficult by the large number of possible viruses (Table 3.3 of the FDA Report, p.58) and inadequate methods of virus detection. It is however suggested that such problems equate with those of allotransplantation, where human pathogens can also be transferred during the transplant of human organs or tissue.

Given the potential benefits of these emerging techniques, the public would however seem to be willing to accept the attendant risks.

Introduction of porcine endogenous retroviruses

Pigs possess a number of retroviruses in their genome which, depending on their subtype, can affect human cells to varying degrees. No transfer of disease or dissemination of the virus in the tissues have been observed in humans receiving transplants. Nor has any tested porcine endogenous retrovirus caused disease in species involved laboratory trials. It is stressed that the virulence of porcine endogenous retroviruses among mice could be limited by genetic defects. However, these viruses represent a high risk because of their adaptability, variability and resemblance to known human pathogenic viruses. The risk of a nonpathogenic retrovirus becoming virulent is mooted but disputed. Some scientists argue that a series of consecutive events would be needed for this to happen, lessening the chances of such a pathogenic virus emerging. Others call for further information.

C. Conclusion

Animal biotechnology is a field that is under constant evolution. Many transgenic animals have been successfully created for a variety of purposes, and the prospects are enormous. Many techniques exist for the insertion of genes into host cells. They all have advantages and drawbacks, and most have limitations linked to the difficulty of controlling the expression of transgenes inserted at random into the genome of cells; the variability of resulting genomes and unexpected side effects; the population of "surplus" animals; the possible mobilization of genetic sequences; and the possible emergence of new pathogens. Maintaining genetic diversity is another problem. With regard to human health, further research is required into the risks associated with introducing animals created for biopharmaceuticals into the food chain and the risks of generating new human diseases from xenotransplantation.

I. Environmental concerns

A. Background and context

Environmental concerns are often considered by far the most important, because of the difficulties of identifying them and of resolving them, once identified. Such concerns have intensified since the Rio Declaration on Environment and Development (adopted at the United Nations Conference on Environment and Development in 1992) whose Principle 15 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."

The Cartagena Protocol was adopted in early 2000 with the following objective:

"In accordance with the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements… The Parties shall ensure that the development, handling, transport, use, transfer and release of any living modified organisms are undertaken in a manner that prevents or reduces the risks to biological diversity, taking also into account risks to human health."

A distinction is made between transgenic animals deliberately released into the environment and those released by accident. The problems of introducing transgenic animals into the environment concern their impact on the environment and possibilities of vertical and horizontal gene transfer.

B. General principles of risk analysis

Risk analysis has three elements: risk assessment, risk management and risk communication. The first two are most important as concerns risk analysis applied to the environment.

In risk assessment, the risk has two components: i) a potential hazard and ii) the likelihood of that event taking place. Thus the risk is the *potential hazard* x *the probability of exposure*. Risk assessment is a process based on scientific data and involving the following stages: i) hazard identification; ii) hazard characterization; iii) exposure assessment; and iv) risk characterization. Potential hazards and the likelihood of their occurrence are studied in this manner and models are built to predict risk.

Risk management, which is distinct from risk assessment, consists of examining policy alternatives with all interested parties, bearing in mind risk assessment and other factors relevant to protection of consumer health and promotion of fair trade, while, where needed, determining appropriate prevention and control options. An environmental hazard is not so easy to quantify as a health hazard, and concerns a public good rather than a private good (health).

When an appropriate risk management strategy is applied to environmental problems and not to safety problems, the problem must first be set out, as must the objectives and values that will serve to seek a solution. All options are then examined to cover the maximum number of solutions, for weighing the advantages and drawbacks of a vast range of possible solutions helps get all parties involved.

Risk communication is the interactive exchange of information and ideas between risk assessors, risk managers, consumers, industry, academia and other interested parties of the risk analysis process. The exchange of information concerns factors linked to the risk, as well as the ways in which the risk is perceived, and includes a presentation of the conclusions of the risk assessment and a justification for the risk management decisions.

Risk assessment relating to the environment is a complex undertaking because it is very difficult to identify and quantify all the potential risks of releasing GM animals into the environment. The risk analysis

procedure needs to be adapted and the animals need to be classified according to their capacity for dispersal in the environment. Proposed stages are:

- identification of potential harms;
- identification of hazards that could cause these harms;
- definition of what exposure means for GM animals and likelihood of exposure;
- estimation of likelihood of risk;
- classification of risks according to their priorities.

As not all potential risks can be identified, the process of risk analysis needs to be ongoing to take account of new information as it arises.

C. Classification of transgenic animals according to risk to the environment

The harm can be partly envisaged: perturbation to ecosystems, reduction or even elimination of wild populations, etc. The hazard is the transgenic animal itself, whose presence in an environment can have direct and indirect consequences for natural ecosystems through the action of various factors.

The risk is not so much that the animal finds itself in the environment but that it finds itself there AND establishes itself. It is therefore a matter of studying the impact of the establishment of transgenic animals on the wild populations. The establishment of a GM animal and thus of the transgene in the environment depends on three factors: its capacity for survival and breeding (which itself depends on five factors: viability of juveniles and adults, age at sexual maturity, fecundity, fertility and reproductive success); capacity of escape and dispersal; and the characteristics of the receiving community. A reduced community of wild animals will be under greater threat from the introduction of transgenic animals than a large community that will be able to withstand the impact of the transgene.

If a transgenic animal is better adapted to environmental conditions than its wild peers, it will establish itself among the wild population, which it might in fact replace. If not, the transgenic animal will disappear. If the fitness of the transgenic animal is the same as that of the wild animal, they might be able to coexist. Fitness can be determined prospectively (evaluation guidelines in Appendix A of the Scientist's Working Group on Biosafety, 1998) or retrospectively. The prospective method studies four factors: heightened adaptability to environmental conditions, traits and characteristics of the GM animal, capacity to produce novel products and animal's aptitude to escape.

Heightened adaptability to environmental conditions

Heightened adaptability to environmental conditions, such as capacity to resist cold or disease, enables GM animals to establish themselves in an environment or to colonize ecosystems in which their wild counterparts cannot survive.

Enhanced existing traits

Enhanced traits often relate to rate of growth, feed efficiency or production performance (e.g. milk or eggs). An enhanced trait can sometimes be countered by physiological imbalance or increased food requirement, as has been observed among some transgenic farm animals.

Genetic enhancement by means of genetic engineering differs from enhancement through the traditional selective breeding of animals with interesting traits, in the sense that the characteristics associated with the interesting trait do not follow the same evolutionary path. A transgenic animal can have a vascular or skeletal system that is completely unsuited to its improved rate of growth, which produces a developmental imbalance of physiological systems and renders the animal less fit for survival. Transgenic animals developed for production and breeding often present an altered characteristic that counterbalances the impact of the improvement and therefore represent a low risk of establishment in the environment.

However, in some cases the improved trait could outweigh the altered characteristic; for example, it has been noted among certain transgenic fish that a 25% increase in size boosted their reproductive success by 400%

as compared to the norm. Such success benefits the transgenic animal and rapidly disseminates the transgene among the wild population, even if the transgene reduces the lifespan of the transgenic animal. In such a case, the aggregate impact favours the establishment of the transgenic animal in the environment, an advantage that is further accentuated if the conspecific wild population is small. Fragile wild communities could be reduced or even disappear.

Production of novel products

Transgenic animals producing more proteins and pharmaceutical substances in their milk, urine, or any biological by-product, have only limited capability of establishment in the environment, because they have not acquired any special advantage in fitness and their added functionality in fact requires higher energy expenditure which makes them less competitive with their wild conspecifics. Such transgenic animals therefore only represent a low risk for the environment.

Production of animals or animal products for human health

Companion animals genetically engineered to reduce allergenicity and animals modified for xenotransplantation only present a low risk of establishment in the environment. Their fitness remains unchanged or perhaps compromised.

Transgenic insects modified to control the spread of a vector-borne human disease such as malaria are meant to establish themselves in the environment.

Capacity for dispersal

The dispersal capacity of transgenic animals is not known but can be realistically assessed on the basis of knowledge about their wild conspecifics. This capacity will depend on their aptitude for escape, for dispersal and for becoming feral. Combining these three criteria indicates the respective risk of dissemination of GM animals in the environment. Table 2 evaluates each criterion to determine the capacity of different species.

Table 2 : Factors contributing to the risk of dissemination of transgenic animals

Animal	Ability to become feral	Likelihood of escape (from captivity)	Mobility	Environmental damage reported	Level of risk of dissemination
Insects[1]	High	High	High	+++	+++
Fish[2]	High	High	High	+++	
Rodents	High	High	High	+++	
Cats	High	High	Moderate	+++	
Pigs	High	Moderate	Low	+++	
Goats	High	Moderate	Moderate	++	
Horses	High	Moderate	High	+	
Rabbits	High	Moderate	Moderate	+	
Dogs	Moderate	Moderate	Moderate	+	
Chickens	Low	Moderate	Moderate	0	
Sheep	Low	Low	Low	+	
Cattle	Low	Low	Low	0	--

[1] Limited to the Gypsy moth and African bee
[2] Not including shellfish or crustaceans

Source : Animal Biotechnology, Science-Based Concerns, FDA, 2002

The more domesticated the GM animal, the lower its fitness in the natural environment. However, hybridization can occur in areas with both wild and GM populations, enabling the transgene to implant and spread among the wild population. Animal confinement is never absolute; while easier for certain mammals, it can prove difficult for insects, rodents, fish, molluscs and crustaceans.

➔ Animals that easily become feral, that have high or very high mobility and that harm wild communities are a major problem. These include mice, rats, fish, crustaceans and insects.

➔ Next come animals with moderate mobility that easily become feral and that cause damage, such as cats, pigs and goats.

➔ Then we have animals that are less mobile but easily become feral and have a moderate impact on ecosystems, such as horses, dogs and rabbits.

➔ Finally, posing the least concern, are animals that are not very mobile, that are highly domesticated and that do not therefore easily become feral, such as poultry, cattle and sheep.

The introduction of a new species into a given ecosystem can have a cascading impact on other plant and animal species and cause unforeseeable harm. There are many examples of this, notably the introduction of tortoises from Florida that undermined the tortoise population in France, and the introduction of wild pigs and reduced plant diversity in Australia. Transgenic animals can compete for food or ecological niches and can alter balances within the food chain by upsetting predator-prey relations. This can lead to a decline of

wild communities and the perturbation of ecosystems. The problem of introducing transgenic animals is similar to any problem of incorporation of new species into an environment.

Pleiotropic effects of transgenes or other genes can have significant consequences. For example, if a transgenic animal has a longer lifespan and higher mating success but low fertility, the populations of wild and transgenic animals will risk eventual extinction. The transgene will initially establish itself amongst the population but will also disappear along with the species. Transgenic trout possessing the modified fast-growth gene would appear to be a case in point: these fish are twice the normal size at sexual maturity which could give them an advantage for mating, but their lower viability could threaten the entire trout population.

Natural selection appears to determine the final level of transgene establishment among wild populations, which vary in their capacity to absorb the ecological impact of the introduced transgene. Alleles or allelic combinations poorly suited to environmental conditions could be rapidly eliminated in stable and sufficiently large wild populations. Natural selection could act, more or less rapidly, towards re-establishing equilibrium. Conversely or under special circumstances, this could eventually lead to the extinction of the population concerned.

Thus, given the unique nature of each transgenic animal, any analysis of risk to the environment needs to be considered on a case-by-case basis. The factors to be taken into account are the impact of the transgene on the transgenic animal's fitness, the species concerned and the stability and flexibility of the receiving community. The more fragile the receiving population, the greater the risk. The precautionary principle therefore suggests that risk assessment should be based on the most vulnerable ecosystem that a GM animal might access. In the case of a transgenic animal that could easily become feral, the assessment will focus especially on its capacity for survival and reproduction. This suggests that the risks can to some extent be ranked in order of magnitude.

D. Risks to the environment

Terrestrial vertebrates

Escaped domestic or laboratory mammals with high feral capacity have disturbed the environment in many countries (e.g. rodents, rabbits, cats, pigs.). Any trait of a transgenic animal of these species that increases its fitness (resistance to climatic conditions, resistance to disease, improved feed conversion efficiency, etc.) and its dissemination among wild populations represents a high risk to the environment.

Fish, molluscs and crustaceans

In the fisheries sector, most transgenic animals have higher growth rates as these represent tangible benefits to fish farmers. But transgenic fish can also have a positive impact on the environment as they produce less contaminating waste. Improved feed conversion efficiency means lower feed requirements, reduced feed waste and effluent from fish farms, and thus lower eutrophication.

Environmental concerns apply more to the "faster growth" characteristic, which can impact on predation, competition and genetic contamination: transgenic fish can eat larger quantities of prey species; their higher environmental tolerance enables them to invade new territories and possibly displace extant natural populations; finally, interbreeding could alter the genetic composition of the natural population.

Four factors influence the ability of transgenic fish to escape into the environment: high mobility, the relative proximity of transgenic and wild species, the fact that ecosystems are often shared, and finally the fact that aquaculture animals are usually marketed live. Advocates of transgenic fish argue that, as they are heavily domesticated, they will find it difficult to survive in natural conditions.

However, studies on transgenic fish suggest otherwise. Transgenic Atlantic salmon have a higher energy and oxygen requirement than their wild counterparts. They lose their juvenile markings at a younger age and show early mobility, which reduces their status as prey, despite their larger size. Pacific salmon present more or less the same characteristics. Their age at sexual maturity is lower but they are not so mobile, no doubt because of an imbalance or delay in the development of their muscular, vascular or nervous systems. Yet these transgenic species compete directly with wild species for food. As highlighted earlier, greater fish size

combined with earlier sexual maturity but reduced juvenile viability can eventually lead to the reduction or disappearance of the receiving population.

The risks posed by transgenic fish culture should be assessed in the same way as for any other aquatic species coming from another ecosystem, under trial conditions that resemble the natural environment as closely as possible. Dispersal in the ecosystem and the impact of each species need to be studied.

Species should be kept in close confinement, but this is not easy for molluscs and crustaceans which have highly mobile larval stages, especially as they are cultured under extensive and thus dispersed systems. Similarly, transgenic fish reared in ecosystems shared with wild populations can escape from the culture zones.

Chromosome manipulation in molluscs and fish to render them infertile would be one way of solving the problem of dispersal in the environment, and is a technique used to reduce the risk to wild native populations. However, it presents a technical challenge and the low proportion of fertile individuals coupled with the so-called "mosaic" individuals resulting from sterilization techniques represent a risk of dissemination of the transgene among wild populations.

E. Conclusion

Not all the risks can be anticipated. Crucial information is still needed to assess the environmental risk from the presence of transgenic animals. For example, the growing body of empirical studies on risk from transgenic fish does not provide practical data to determine the level and impact of transgene establishment in a wild population, even though it draws attention to the need for serious risk analysis. Transgenic animals need to be monitored after their commercialization to discern unexpected impacts and attendant risks, and to adjust risk assessment and management. Further information is required.

In view of current uncertainties, many scientists call for the precautionary principle to be applied, especially for transgenic fish, molluscs and crustaceans. No transgenic fish has yet been exploited commercially, but countries involved in salmon fishing in the North Atlantic and adjacent areas have agreed to apply a number of precautionary measures. It is perhaps on account of the virtual disappearance of populations of fish species of economic importance to the region that decision-makers appear to be inclined to apply the precautionary principle, according to which *the absence of scientific certainty should not be used as an excuse to postpone management efforts*.

Other important principles are that priority should be given to maintaining the productive capacity of a resource or ecosystem, that any impact should be reversible over a period of two to three decades, and that decisions should be taken on the basis of risk and benefit. Finally, benchmarks need to be established to identify areas of greatest uncertainty on which monitoring, research or study needs to concentrate.

II. Genetically modified insects

A. Transgenic insects

Insect biotechnology is used to create genetically modified insects that are useful for pest control, especially in agriculture, and for the control of vector-borne animal or human disease. One of the major objectives of transgenesis is in fact to control the transmission of vector-borne diseases such as malaria. The vectors can be controlled by the usual methods, involving insecticides, actions against vector home environments or means of protection, such as mosquito nets, but these methods are only relatively effective because of growing resistance to insecticides and the physical limitations of the methods themselves. The only course of action is then to eliminate the vector itself.

Biotechnology can be used to reduce or even eliminate vector insect populations, or to reduce the capacity of an insect to carry and disseminate a parasite or pathogen. Various methods have been proposed: the use of sterile males, the introduction of a lethal gene or the introduction into the insect vector population of a gene that gives resistance to infestation by human or animal pathogens.

Use of sterile males

Sterile males are used to reduce vector population density and sterilization can be done by chemical or physical irradiation. However, such methods reduce mosquito viability as the irradiation causes lesions in all

insect tissues. Biotechnology can improve the sterility of males without damaging their viability and can therefore improve the effectiveness of control programmes and reduce the number of released insects.

The use of sterile males requires sexing so that females are not released. Distinguishing male from female is easy in species that permit visual sexing on the basis of size of pupae, but can be a real challenge in others. Proposed methods include the use of a dominant gene associated with a female-specific promoter which would render the females dependent on a high concentration of tetracycline for survival and would therefore render them unviable in a natural environment. The males would simply carry this gene which they would introduce into the wild population (RIDL system of Thomas et al. 2000). Such a gene could however be a major problem if it were to establish itself among wild communities of non-targeted insects.

The use of sterile males is effective if the females mate with them. However, the females of some species of mosquito are monogamous so this system would lose effectiveness under the massive inflow of already fertilized females. Depending on the target species, it would therefore seem best to combine methods, notably with another genetic technique.

Particular characteristics

The production of Anopheles mosquitoes resistant to *Plasmodium* infection (malaria) is an interesting concept, but the gene in question has to be closely linked to the dissemination mechanism. However, the "resistance" trait would appear to depend on several genes. It has also been shown that 100% effective resistance is needed in areas with high prevalence and dissemination of the pathogen. The problem is that the creation of selection pressure based on *Plasmodium* could eventually lead to the emergence of resistant *Plasmodium*, which has led to the idea of introducing several independent genes resistant to the pathogen. This is a major problem as biotechnologies are used for traits that are regulated by a single gene and cannot be used where a trait stems from a complex set of genes. Linking and transferring the set of genes is also complex.

Another example is the sterilization of male ephemera larvae infesting cotton bolls using irradiation, which has not been 100% effective despite the high cost. Scientists have thought of inserting a gene capable of blocking the development of fertilized eggs, to help reduce the wild populations.

B. Direct problems

Stability and effectiveness of the inserted gene

Insertion needs to be stable and effective. Once the desired trait has been identified, the responsible gene needs to be defined and the inserted transgene needs to express itself at the right time and in the appropriate tissues. The resulting insect is then studied and can be reproduced in large volumes if observations are satisfactory. Dissemination models need to be prepared and trials conducted in confined areas.

Cost of biotechnologies

The control of insect vectors of animal and human disease is a controversial subject. Traditional methods need to be seen to be ineffective if biotechnologies are to be introduced, and this for two basic reasons: the high cost of obtaining transgenic insects and the time and resources needed to conduct GMO risk analysis. A cost-benefit study is required.

The problem in human health terms

In the case of the control of certain vector-borne diseases, the elimination of the parasite within the vector population could result in an increase in population, which could foster the propagation of other vector-borne human or animal diseases. For example, mosquitoes rid of *Plasmodium* could become more susceptible to other human or animal pathogens. Tests are therefore required, especially for parasitic worms (Anopheles mosquitoes are vectors for filaria) and numerous viruses, including HIV. For the time being, mosquitoes do not seem to be carriers of the HIV virus, but it would be disastrous if they were to become so. Virologists see this as totally inconceivable but public opinion appears to see it as a major concern. Data need to be found to prove that this is not possible.

Problem of "driver" mechanisms

Three mechanisms are proposed:

- The use of transposable elements (which replicate and disseminate): present know-how renders this mechanism too uncertain, and the risk of horizontal transfer of an uncontrolled transgene means that it is forbidden.
- *Wolbachia* infection in mosquitoes: this mechanism is still under development and thus untested.
- The use of complex mechanisms using two complementary lethal genes that counteract one another. Hybrids only possessing one of these genes would be unviable which would benefit the animals carrying the two genes. Bonding the gene for resistance would enable it to implanted among the target population.

Without a driver mechanism for dissemination, the method would be seriously restricted by the migratory movement of vectors, notably female mosquitoes. Combining these methods with the use of sterile males would be more effective as they would eventually lead to a reduction in the wild population.

Problem of bonding

This is a major problem, for it is impossible to envisage creating insect resistance to infestation by a pathogen if there is no guarantee of complete bonding between the driver mechanism and the transgene. There would be crossings and hybrids, without bonding, and those with the driver mechanism would not be effective for control.

C. Risks to the environment

Problems of insect confinement and release

Insects have high mobility and considerable potential for colonization of new environments. They must therefore be confined to permit study without risk to the environment. This is important to avoid the propagation of a transgene in a wild population, especially in the case of biopharmaceutical insects. Transgenic insects should be confined in a laboratory, as there is no way they can be detected after release into the environment, especially if they proceed develop in an unexpected manner.

Two guides with differing emphases have been drawn up for insect confinement:

- A classification of risks to the environment and of GMOs, with specific procedures for each. A distinction is made between different kinds of GM insect and corresponding levels of confinement.
- Recommended practices of the US Animal & Plant Health Inspection Service (APHIS) which constitute a single standard procedure without distinction between transgenic insects, and highlighted by the OECD in 1998.

At present, each laboratory develops its own procedures for the confinement of GM animals, without uniformity. The thorny problem of insects created for biopharmaceuticals is not taken into account.

Some observers argue that confinement requires time and investment at the expense of pure research, but the release of genetically modified insects could feasibly have damaging and more or less irreversible consequences for the environment.

Horizontal transfer of a transgene

The risk of horizontal transfer of a transgene is regularly emphasized and, if this were to happen, could have significant consequences for the environment. The insertion of genetic material into wild populations, such as genes resistant to antibiotics (markers) or to insecticides, is highly undesirable.

Such an occurrence is impossible to evaluate as we lack information on horizontal transfer mechanisms and related frequencies. There has been very little study, but horizontal transfer would appear to be possible between conspecifics. The underlying mechanism is unknown, but this phenomenon has been known to occur with small fruit flies. High plasmid exchange is also possible between insects and intestinal bacteria, which are then found in faeces and thus the environment.

The impact of such gene transfers is unknown, but close links exist between insects and other organisms (pollinizers, preys or predators, vectors, etc.) which means negative impact on an insect population could have a major impact on all ecosystems.

Control and regulatory body

National regulations often tend to forget transgenic insects. No regulations or international recommendations exist for the confinement of transgenic insects. However, their release is subject to authorization in most countries. There are sometimes several regulatory bodies at national level and control procedures can be complex.

In the US, several different federal and national institutions need to be consulted before GM or non-GM insects can be released. Some commentators would also like to see the health agencies involved.

So far, the only releases of transgenic insects that have taken place in the US have been for short duration trials. Their subsequent destruction, or at least total recovery, are prerequisites for authorization to conduct such trials.

Need for risk analysis

Risk analysis should be conducted prior to any release of transgenic insects and should include studies on:

- the stability of the transgene
- the possibility or not of horizontal transfer of the transgene
- the present and potential geographic distribution of the GM insect
- the different traits transferred to the GM insect and their impact on the ecosystem
- possible unforeseen side effects on the environment.

The traits and fitness of a transgenic insect appear to be easily verifiable. On the other hand, the horizontal transfer of the transgene and short-, medium- or long-term side effects on the environment are more difficult to determine. A large number of scientific uncertainties need to be cleared before transgenic insects can be released into the natural environment.

Determining the level of risk

There are three possible scenarios:

- A field or controlled-environment trial permitting the recovery or destruction of all the insects;
- The release of sterile insects for biological control; this poses less risk than insects meant to establish themselves among the wild population as they cannot breed.
- Insects for permanent establishment in the environment and crossbreeding between GM insects and wild insects to disseminate the transgene.

We can identify the risk but assessing the likelihood of risk is virtually impossible.

Domesticated insects are virtually incapable of surviving alone in the environment (e.g. silk worms). The risk of dissemination of these insects is thus very low. Sterile insects represent the same low risk of dissemination because horizontal transfer is very rare. The case of bees would appear to be more uncertain as bees are half domesticated, so have higher potential for survival and dissemination in the environment.

Risk analysis models for transgenic insects do exist, but have limitations as designed on the basis of possibly biased theoretical data. There are too many known and unknown interactions between the different factors (population dynamics, genetics, environment and space, etc.)

D. Conclusion

Transgenic insects require proper risk analysis if reliable risk-benefit analysis is to be conducted. The possibility of finding alternatives to the costly and time-consuming production of GMOs needs to be looked into, as do the objectives of producing transgenic insects and the achievements to date. Negative impacts

need to be studied and reduced, which will mean standardizing the risk analysis to be carried out before any release of GM insects. Retrospective studies following the introduction of these animals will also be needed.

III. Animal health and welfare

A. Reproductive biotechnologies and techniques

All reproductive manipulations, including semen collection, repeated artificial insemination, embryo collection and transfer, or the inducement of superovulation can cause stress to animals during constraint and handling. These methods are not specific to GM animals and few have been studied from the perspective of animal welfare.

The intensity of violation during artificial insemination and embryo collection varies according to the species. These two techniques are relatively uninvasive for cattle and are done with local anaesthetic. On the other hand, for smaller species such as sheep, goats and pigs, they entail invasive surgical intervention (laparotomy or laparoscopy) and thus cause operative and post-operative pain. Cows carrying an embryo are subject to amniocentesis to check the genotype. Cows carrying nontransgenic embryos or male embryos are aborted and have another embryo inserted. This limits the number of recipient females used to give birth to transgenic animals, but it also raises welfare concerns as these animals are regularly exposed to stress and pain. At the same time, they can be prone to slow or difficult calving (dystocia) requiring increasingly frequent caesarean sections.

Abnormalities in the offspring can also raise concern for an animal's welfare.

Alternatives to such methods causing stress and pain are sometimes suggested, such as the removal of ova in the slaughterhouse, non-invasive embryo collection or techniques of cloning and in vitro culture to reduce the number of recipient animals.

B. In vitro culture

In vitro culture tends to extend the gestation period and to produce higher birthweights, resulting in difficult deliveries and frequent surgical intervention. These animals have more congenital malformations (skeletal malformation, incomplete development of the vascular system or urogenital tract, immune system dysfunction, brain lesions) and high perinatal mortality.

The mechanisms responsible for these abnormalities are not known, but chromosomal anomalies, abnormal regulation of gene expression during embryo development and problems of communication between foetus and mother have been implicated. Culture conditions also appear to be directly associated with the level of developmental abnormalities and perinatal mortality.

C. Efficiency of biotechnologies

Efficiency varies according to technique. Microinjection is particularly inefficient, with reported successful transgenic offspring of only 1%. Embryo mortality stands at 80% to 90% and there is high perinatal mortality. In addition, few animals possess the inserted gene at birth and many show anatomical, physiological or behavioural abnormalities. The efficiency of methods used also depends on the species modified.

Efficiency has a direct bearing on the number of attempts needed for success and the number of animals used. While several embryos can be implanted into mice and pigs to offset embryo mortality and thus considerably reduce the number of recipient females, this does not seem possible with cattle because of the phenomenon of freemartinism.

Transgenic animals do not necessarily pass the transgene to their offspring. It has also been reported that offspring can have a limited lifespan, a variety of malformations and general or specific malfunctions. This is attributed to so-called "mosaic" transgenic animals that do not carry the transgene uniformly in all their cells.

D. Gene expression

The random insertion of transgene sequences in the genome of a target cell can have major consequences, especially in the expression of certain genes. Numerous abnormalities have been noted among transgenic animals, depending on the function of the transformed gene. Recessive silent abnormalities can be expressed

during breeding between transgenic animals, and their homozygous offspring could present a number of abnormalities.

Controlling genetic expression is variable and difficult requiring the use of appropriate promoters and regulatory sequences. Many abnormalities are still observed among resulting animals, both mammals and fish (physiological and morphological problems, sensitivity to disease and stress, behavioural problems, etc.). These will undoubtedly lessen as techniques improve.

E. Benefits to animal welfare and integrity

Biotechnologies are also promoted as improving animal welfare and health, with reduced mortality and morbidity because of greater resistance to disease and parasites; the elimination of phenotype characteristics such as horns; the adaptation of animals to intensive production; a reduced sensitivity to suffering and stress. They also help control the sex ratio among animal populations, especially chickens, thus avoiding the slaughter of male chicks.

Others also argue that animals with greater genetic value receive better care which can only enhance their welfare.

However, a problem of animal health does arise. The shrinking gene pool and the uniformity of genomes could weaken animal populations and make them more susceptible to disease.

F. Nuclear transfer

The method of somatic cell nuclear transfer is relatively new and inefficient. The failure rate is high, as is prenatal and postnatal mortality, and there are many abnormalities causing problems of health and welfare from the immediate postnatal period: respiratory distress, lack of suckling reflex, physiological and morphological abnormalities, behavioural problems. The cause of these problems has not been identified with any certainty (stages of the technique itself, difficulty in genetically reprogramming the inserted nucleus, etc. See Part One). Study findings do however vary considerably and many transgenic animals have been successfully produced. Further studies are required.

G. Biomedical applications

There are fewer welfare problems with biomedical applications as there are few secondary modifications (although phenotypic problems can still occur). Also, as these animals have high value, their care is undoubtedly better than that of farm animals.

Biopharmaceuticals

The proteins or substances secreted in the physiological products should not have any effects on the organism of the secreting transgenic animal. If the substance is carried in the circulation and is biologically active in the animal's organism, it can cause certain physiological dysfunctions which can cause pain and discomfort. Secretion of the substance should be confined to the expressing tissue, but this is difficult to control. It has been reported that the early expression of a transgene can cause the premature development of the mammary gland and render any subsequent lactation painful.

Xenotransplantation

No phenotypical abnormality has been noted in pigs produced for xenotransplantation, so there are no problems of animal welfare, even though the efficiency of the microinjection technique used to obtain such transgenic pigs is low.

As regards animal health, modification of their cell structure could render pigs susceptible to infection from human viral disease.

The special conditions of husbandry also raise concerns about the pigs' welfare. The isolation needed for pathogen-free pigs and while awaiting organ donation causes abnormal behaviour among pigs which are extremely sociable animals.

Other

Problems of welfare (and ethics) arise in connection with genetically engineered farm animals that are created to study human diseases or the toxicity of medical drugs or other substances. Standard testing procedures need to be drawn up to avoid all stress and suffering.

H. Conclusion

The impact of genetic engineering on the health and welfare of animals is a major public concern. Perception of animal welfare varies widely because determined by cultural attitude to animals, and involves ethical judgements.

Biotechnologies can cause suffering, physical and psychological stress, behavioural and physiological abnormalities and/or problems of health among animals, whatever their intended use or function. On the other hand, they also have the potential to reduce or eliminate such problems, which also arise under intensive animal production practices.

PART THREE

ANIMAL BIOTECHNOLOGY: FOOD SAFETY CONCERNS, REGULATION AND SOCIETY

I. Safety of food of transgenic animals and derived products

A. Background

Concern about the quality and safety of food products has been growing since the early 1980s. Many hazards have been identified, studied and handled by instituting national regulations and international standards and by setting up regulatory and inspection systems in processing plants, livestock farms and slaughterhouses. These hazards can be biological (bacteria, parasites, viruses, prions), physical (metals, etc.) and chemical (residues of pesticides or veterinary drugs, toxic substances, etc.). New hazards are now perceived in relation to the use of transgenic animals.

Transgenic animals include those obtained through nuclear transfer, those with improved production traits and those developed for biomedical purposes. Animals for xenotransplantation are barred from the food chain by national regulations.

B. Products derived from cloned animals

In 2002, some 1400 Holstein cattle produced by blastomere nuclear transfer (not somatic cells) were raised in the US. They and their subproducts (animal and milk) are marketed and enter the food chain. No result of analysis of products derived from these transgenic animals is so far available, nor is there any information on abnormalities of gene expression in these adult cloned animals or analytical information on the composition of milk or meat derived from them or their offspring. The animals are considered perfectly safe and no apparent ill effects have been noted among consumers. However, caution and risk analysis are recommended for such derived products, especially in the light of the problem of reprogramming the inserted nucleus.

The safety of food from offspring of cloned animals is a controversial subject. Some see no risk as they originate from natural mating, while others point out that the offspring of a cloned animal has one half of the latter's genome.

The cloning of animals from somatic cells is a recent technique, so it is difficult to make a firm decision on the safety of related milk or meat. Genetic variations appearing with nucleus differentiation and possibly causing modified genome expression are not known. The findings of studies on products of cloned animals will no doubt be available soon.

C. Genetically modified animals

Allergenicity and hypersensibility

Most food allergens are proteic, well known and identified. As regards the safety of new proteins in foods derived from transgenic animals, the possibility that a new protein could cause an allergic reaction among certain individuals needs to be assessed. FAO has published an approach for assessing the potential allergenicity of new proteins extracted from foods derived from transgenic animals, using the decision tree reproduced in Figure 1 below.

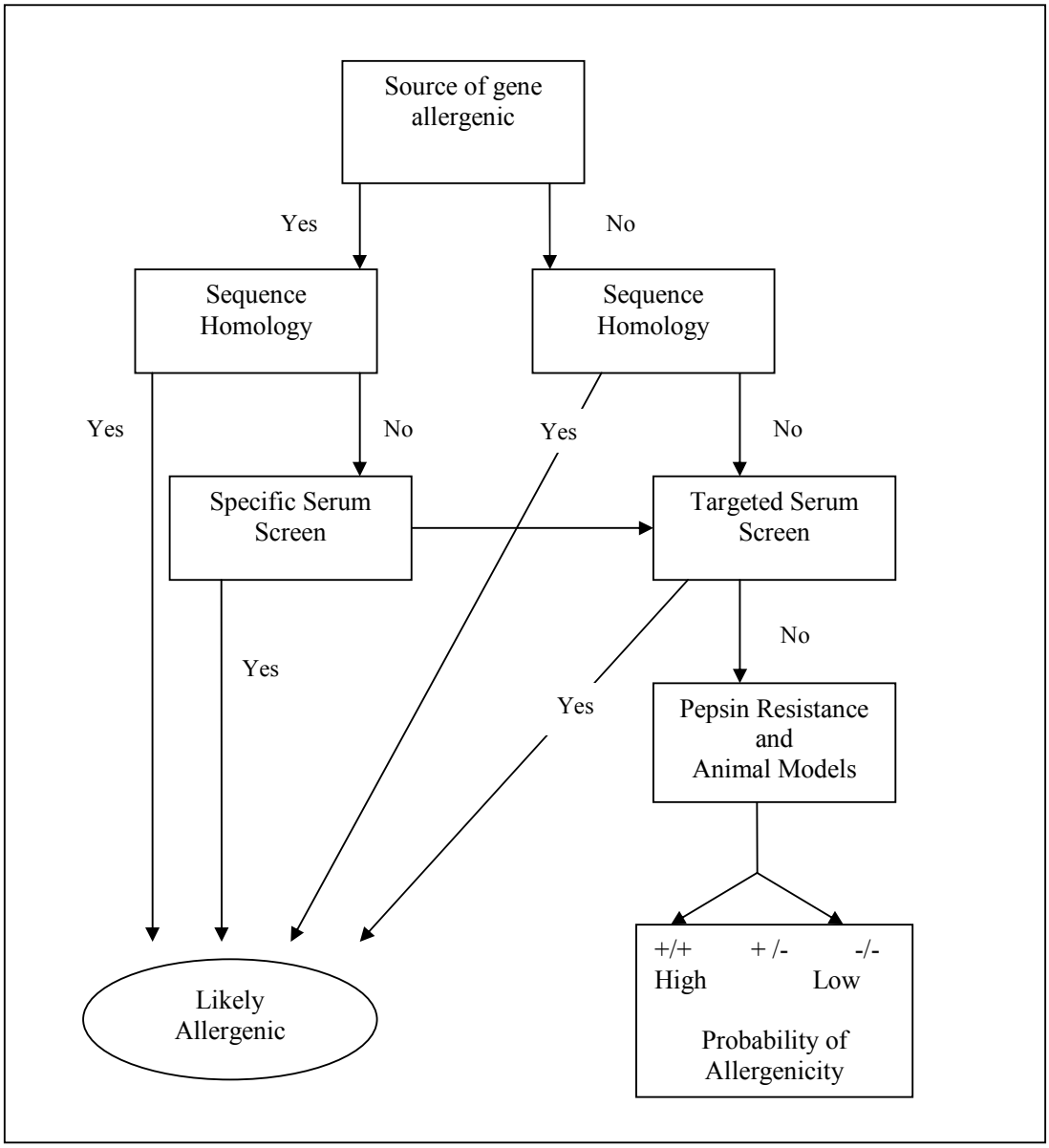

Figure 1 : FAO/WHO 2001, decision tree to assess the potential allergenicity of foods derived from biotechnology.

If the new protein is produced from a transgene that is known to have allergenic potential, or if the animo-acid sequence is similar to that of a known allergenic protein, then the allergenic potential of the new protein can be tested with the serum of individuals with known food allergies. The problem arises for proteins with unknown allergenic potential which cannot be easily assessed, as there is no existing human immunoserum.

The problem is further compounded when the new protein derives from an existing protein that has no known allergenic potential. Thus, assessing the potential allergenicity of a protein from a transgene remains one of the major difficulties in the overall safety assessment of transgenic foods.

Assessment of allergenicity requires an understanding of several factors, including the source of the transgene protein, its level of expression, its chemical and physical properties, and its similarities to any

known allergen. All these factors have to be considered together to have an idea of the potential allergenicity of the new protein.

The absence of appropriate and effective methods of analysis is a major problem, as is the feasibility of performing adequate assessments for an increasing number of transgenic products. In this connection, WHO and FAO are working on the development of a standardized protocol for the assessment of allergenicity.

The animal model for allergenicity tests of products derived from transgenic animals is recognized as effective. In vivo allergenicity tests among humans would be the best option but raises ethical problems. Post-market surveillance of a product is also advocated, but modalities for doing this are difficult to determine.

Other bioactive compounds

Some transgenic animals are designed to express biopharmaceuticals. That these products could retain their bioactivity in the organism after consumption of the food is a safety concern.

All proteins and polypeptides are normally broken down in the digestive tract, thus destroying their bioactivity. Only small peptides pass the barrier of the digestive epithelium. The problem remains, however, for people whose digestive epithelium has been compromised by disease or injury. Similarly, the digestive epithelium of young children is permeable to proteins for a period of a few weeks to a few months, during which these proteins could enter the bloodstream. This poses a real problem for bioactive peptides contained the milk.

The peptides or proteins could have a negative impact on the digestive system. The production of bactericidal proteins in milk to reduce cattle susceptibility to mastitis from *Staphylococcus aureus* or to control bacterial disease in fish could upset the bacteriological equilibrium of the intestinal flora of consumers. It could also lead to pathogens resistant to these antimicrobials.

Many transgenic fish express a growth hormone gene, which is usually of fish origin. Can this growth hormone cause problems among consumers? The FDA reports that studies have shown that non-human growth hormones, whether of bovine, ovine, porcine or whale origin, are not biologically active among humans. Nor are digested peptide fragments or insulin-like growth factors I secreted in response to GH administration. Moreover, the IGF-I is destroyed by heat along with the active growth hormones. In the (unlikely, given their age) case of young children being fed transgenic fish or milk containing GH, this would be destroyed during heating. The problem however remains for individuals whose digestive tract has been impaired by disease, digestive ulcer or age and which therefore absorbs proteins that have not been broken down and introduces them into the organism. So the risk varies according to the individual. For a susceptible individual, the hazard could have severe consequences, while for a healthy individual of any age, the risk is thought to be low to moderate.

Toxicity

Because proteins are partly broken down in the digestive tract, their direct toxicity (except in the cases mentioned above) is only a mild food safety concern. Moreover, any direct toxicity of proteins would normally be detected during pre-market assessment. The risk is therefore minimal.

The problem arises in connection with unintended and unanticipated effects of products derived from GM animals, linked not only to the proteins that are directly expressed by a transgene but also to any unintended by-products. For example, the insertion of a transgene could disturb a specific metabolic process and cause the expression of metabolites with some toxicity. What we need to know is whether there are effective methods of analysis and screening that can detect a toxic substance or a change in metabolism that introduces toxicity. Whole foods can have a tiny concentration of proteins expressed by a transgene or arising as a by-product of the transgene. Such toxicity can be very difficult to detect given the sensitivity limits imposed by laboratory animal numbers, the small quantities of substances tested in whole foods, and the possibility that any negative effect will seldom occur.

Methods include:

- Analysis of the structural/functional relationship of the substance and of its physical and chemical properties and comparison with existing databases of toxic agents to see if the molecule has similarities with a known toxic agent.

- *In vitro* method: testing the stability of molecules under different conditions or the ability of the molecule to act on other molecules with specific functions. Few *in vitro* tests have been validated and extrapolated *in vivo* as this is difficult, for the method is still fraught with uncertainties.
- Animal model: the best indicator of possible toxicity. However, extrapolation remains uncertain, hence the use of safety factors. This model serves to determine acute, subchronic or chronic toxicity. The problem is that the dietary regime needs to be balanced if parallel side effects are not to be caused (high possibility of bias). A precise diet, specific doses and clear protocols are required.

D. Institutions, scientific expertise and international standards

International agencies have been charged with establishing international standards for GMOs and derived products. Codex is developing principles for risk analysis applied to foods from GMOs. The first principle is to have a pre-market assessment involving case-by-case study of the direct and indirect consequences of inserting a new gene (toxicity, allergenicity, properties of compounds, stability of genome, nutritional effects and other impacts). Codex principles are however for reference only and not binding.

E. Evaluation of safety of foods derived from genetically modified animals

As concerns examination of the safety of GM foods, the risks associated with genetic engineering are the involuntary modification of the host genetic substance, which can induce changes in food components, including the toxic substances. Evaluation of the safety of GM foods should therefore include the following procedures:

- Identification of the organism that has been modified and of the source organism(s) of the inserted gene(s). The origin and nature of all the genetic elements that have been introduced into the modified organism need to be identified, including the structural and regulatory sequences and all other parts of the vector sequences. The possibility of horizontal transfer of genes and related consequences also needs to be studied. If the transfer of genes resistant to antibiotics is intended, the possible health implications of concentrations of micro-organisms in the human digestive tract or other parts of the body need to be considered.

- Identification of primary and secondary genetic products, including a description of the characteristics of the inserted gene. Identification of hazards requires an understanding of the expressed inserted genes, the characteristics, concentration and location of expressed food products and the consequences of expression. For each protein resulting from genetic modification, the factors taken into account include possible toxicity and allergenicity from exposure to the expressed protein.

- Evaluation of the safety of new substances anticipated in the foods (i.e. proteins, glucides and lipids).

- Assessment of unanticipated effects on the composition of foods, including assessment of changes in the concentration of nutritive or toxic substances occurring naturally, identification of anti-nutritional factor compounds significantly altered in GM foods and assessment of the safety of compounds showing significant modified concentration.

- Evaluation of any toxin produced directly by modification.

- Evaluation of type of treated food, assuming normal manufacturing procedures.

- Evaluation of food consumption patterns, including identification of potential human population consuming GM foods and probable consumption levels, and evaluation of possible consequences if the consumption of modified foods differs from that of equivalent traditional foods.

- Assessment of allergenicity of new foods.

Current approaches to assessing the toxicity of specific proteins are based on internationally approved, acute or chronic testing on laboratory rodents or on fast-growth domesticated species, such as chickens. However, no repeated dose testing with GM foods or food products has yet been published.

As regards allergenicity, most scientists now base their evaluations on a decision tree that has been designed to evaluate the potential allergenicity of foods from GM plants, in the light of current knowledge of what is defined as an allergen and how to better identify an allergen.

Concept of substantial equivalence

The OECD's principal contribution to the evaluation of safety of foods from genetically modified animals has been its publication *Safety evaluation of foods derived by modern biotechnology: concepts and principles* (OECD, 1993). According to this report, the most practical way of determining the relative safety of a new food product is to determine whether it is substantially equivalent to its conventional counterpart, where this exists. This concept was initially applied to organisms of terrestrial origin but, with certain qualifications, was then also applied to products of aquatic biotechnology (OECD, 1994).

Substantial equivalence recognizes that the purpose of evaluation is not to guarantee absolute safety, but to determine whether the transgenic food presents more risks than its conventional counterpart, should this exist. It is generally agreed that such evaluation requires an integrated, specific and gradual approach. The factors taken into consideration when a transgenic food is compared to its conventional counterpart are (as detailed in the previous chapter on the evaluation of safety of foods derived from transgenic animals):

- its identity, source and composition; its characteristics in relation to the "natural" product;
- the effects of processing and cooking;
- the processing stage, the DNA itself and the products of protein expression of the introduced DNA; its nutritional qualities;
- the effects on its function;
- its potential toxicity and allergenicity, as well as possible secondary effects;
- consumption of the transgenic food and the nutritional impact of its introduction.

Interactions between environmental factors and animal genotype also need to be taken into account. These variations can influence the phenotype and composition of the modified animal and need to be studied during the evaluation of equivalence.

If the food derived from a GMO is judged to be substantially equivalent to its conventional counterpart, it is then considered to present the same level of risk. Otherwise, further tests are needed.

Confirmation of substantial equivalence does not mean that the product of a genetically modified animal is identical to the conventional product. Comparison does not take all elements into account and substantial equivalence only provides assurance that the appropriate components of safety of the product will be present in equivalent quantities. As the comparative approach links the composition of new foods to existing products with a history of safe use, the consequences of introducing new foods into a diet can be foreseen. The concept means that all similarities between foods from genetically modified animals and conventional foods can be judged to be safe. Differences noted during comparison are subject to further meticulous examination which includes the testing of traditional nutritive elements and toxicological or immunological testing or long-term studies, depending on the differences noted.

Foods from transgenetic animals might not have any conventional equivalent or the differences between these foods and their conventional equivalents may not be sufficiently characteristic. The history of safe use of the conventional product could not therefore be used to assess the safety of the new food under study. Substantial equivalence cannot be used to determine the safety of foods for which there is no comparator. However, that a novel food does not bear much resemblance to its counterpart does not necessarily make it dangerous. Its safety needs to be determined by using traditional food safety approaches, with supplementary testing on the consequences of modification.

F. Post-approval monitoring of foods derived from transgenic animals

It is widely accepted that foods and food products need to be thoroughly evaluated before being placed on the market, if consumers, animal health and the environment are to be protected. If the assessment raises

safety concerns, the product will not be approved for commercial release. Some countries therefore fail to see any scientific justification for the post-approval monitoring of these products.

Other countries, on the other hand, see the monitoring of possible negative or positive impacts of novel foods as a logical follow-up to the initial science-based risk assessment. They argue that post-approval monitoring should be mandatory to consolidate the initial pre-market risk assessment, which was based on the then state of scientific knowledge. This could apply to any pre-market assessment. It is recognized that it is sometimes difficult to draw clear conclusions from epidemiological studies, especially when applied to food compounds. Post-approval monitoring is advocated as the only feasible way of demonstrating the absence of possible long-term or unexpected consequences of consuming a novel food. Implementing this strategy is not easy, however.

II. Science, institutions, society and policies

A. Problems linked to scientific uncertainties

There are many scientific uncertainties relating to animal biotechnology. Current understanding is considered to be inexact, uncertain and insufficient as regards technique, methodology and epistemology. There are too many factors, variables and interactions to accurately assess the level of risk. These interactions are not always known or understood. Genetic engineering has unexpected secondary consequences and the aggregate impact of these consequences on intended transgene impact cannot be anticipated. Similarly, genes have pleiotropic effects that are impossible to foresee.

It is therefore clearly impossible to envisage all the potential risks. Some of these may not be identified and therefore not studied. On the other hand, analysis of a non-existent risk is a waste of time and resources, and can result in unnecessary costly management measures. In addition, estimating potential risk by using inherently biased methodology must necessarily lead to error.

Regulatory bodies make their decisions on the basis of science-based risk assessment. Scientific uncertainties should therefore be priority research areas in both the private and the public sector. A process of consultation with all stakeholders is required to establish agreed and validated risk assessment protocols and to share results and experiences. There are at least four direct consequences of existing scientific uncertainties: application of the precautionary principle in certain national regulations; extreme precaution in risk analysis; stated need for post-approval monitoring of transgenic animals; and the need for further research.

B. Policy context, national and international agencies

Animal biotechnology raises a number of policy problems. Which standards apply to biotechnology products? A major problem is that the risks concern a variety of areas: human and animal health, animal welfare and the environment. How can these different areas be integrated into the decision-making and regulatory process?

The welfare of transgenic animals is usually covered by legislation on animal welfare in general. Is specific regulation on the welfare of transgenic animals required? Another problem is the absence of regulation on transgenic insects.

There is clear need to clarify the scope and limits of different regulatory and control agencies, and national and international organizations as regards the different areas that affected by biotechnology. Should their remit be extended beyond public health and environment to include social and economic aspects, given that these are also relevant? Many different agencies are involved: those responsible for the environment (field releases and trials), food and human health, imports and exports, and animal protection and health. It is important to define individual responsibilities, legitimacy and role.

A list of national regulatory experiences and institutions in each OECD country can be found on the organization's web site:

http://www.oecd.org/oecd/pages/home/displaygeneral/0,3380,EN-document-531-14-no-no-9598-0,00.html

Transgenic animals and derived food products are governed by regulation on novel foods (Novel Food Regulation introduced in 1997 by the European Commission) in Europe and (Novel Food Regulation part of the Food and Drugs Act of October 1999) in Canada. For Canada, the concept of novel food includes any food from plants, animals or micro-organisms that has been genetically modified in such a way that new traits have emerged, or are no longer observed, or are observed at unusual levels. In Canada, protocols are drawn up by Health Canada to assess the safety of novel food. In the USA, the US Federal Drug and Cosmetics Act has been amended to include GM food.

To summarize, approaches differ in many respects:

- Basic legislation: some countries (Canada, USA) have incorporated GMO legislation into existing legislation; others (Australia, Japan) have issued specific legislation for biotechnology, resulting in a mass of sometimes extremely complex regulations.
- Transparency of decision-making: some countries do not consider public opinion (Canada) and only provide a summary of information once a decision has been made, without prior notification. Conversely, others announce their intentions, consult public opinion and issue reports that summarize positions and decisions (EU, USA).
- Approach to risk assessment and in particular to the principle of precaution: some countries seek to eliminate all risk and only decide once every aspect has been assessed; others decide on the basis of existing rather than potential risks.
- Conceptual approach: for some, the risk to be assessed concerns the product (Canada), while for others it concerns biotechnology in general (Japan, EU, Australia)
- Independence of decision-making: Are all links between governments, scientists, industry and expert committees legitimate? In the USA, there is sometimes a close link between decision-makers and assessors.

Good practices often advocated include greater transparency and public involvement, standardized risk assessment concepts, uniform understanding of the principle of substantial equivalence, and distinction between technique and product. According to the British Better Regulation Task Force, regulation should be transparent, accessible, targeted, complete and proportionate to cost and risk.

C. Convergence of policy, science, ethics and public opinion

Concerns that are not science-based should not guide scientific examination. However, such concerns do inherently influence the scientists' mindset, the way they address questions to policy-makers and their presentation of scientific response to public health and environmental concerns. At the same time, government agencies are influenced in their priorities and decisions by the issues raised by public opinion.

D. Public perception of transgenic animals and derived products

The consumers' perspective

Recent events regarding the application of modern biotechnology to animals and food production have received considerable attention and raised serious public concern. The introduction of new characteristics into food that differ significantly from those of traditional foods could accentuate these concerns in the future. It therefore seems necessary to keep the public informed of safety assessment procedures applied to novel foods.

Another difficulty is the differing consumer needs and expectations in the world regarding food quantity and quality, and the differing nutritional values and cultures. These factors need to be taken into account when examining food production, trade and recent events such as crop enhancement and functional foods. Food safety is a universal concern of consumers who need reassurance that marketed transgenic products have been properly tested for deficiencies and checked for safety.

The five eurobarometers conducted in the European Union since 1991 (the last in 2002) give a certain idea of how the European public perceives GMOs. In many countries this perception is in fact increasingly negative, with concerns relating to:

- the unexpected effects and consequences of GMOs on human health and environment;
- the potential irreversibility of negative effects;
- the ethical acceptability of GMOs;
- the usefulness of GMOs;
- animal welfare;
- relational imbalances between producers, farmers and consumers;
- the equality of peoples in the face of biotechnology.

There is a clear distinction in the way GMOs are perceived according to their intended application. On the one hand, we have biomedical applications which are considered useful, morally acceptable and are encouraged, while, on the other, we have agrifood applications which are considered redundant and hazardous to society. Public reaction varies according to familiarity and preoccupation with the subject. However, some observers report a difference between what the public says and what the public does or is. People *think as citizens and not as consumers*.

The perception of risk differs between the experts and the public. The way the experts estimate risk does not appear to coincide with the public's perception of risk. There appears to be a lack of trust in regulatory bodies and scientific experts, which in part explains the increasing consultation of public opinion, the greater emphasis on transparency and the release of public information.

Assessors have identified three categories of public opinion: unconditional supporters, those who accept the risks and opponents. Acceptance of GMOs is conditioned by four factors: material values, optimism, confidence and preoccupation with issues linked to GMOs and derived products.

Survey responses vary according to connotations underlying related terms, such as "genetic" and "biotechnology", so depend directly on the social and scientific climate at the time of the survey.

Consumers believe they have a right to be informed on the products they purchase. However, the question of whether the labelling of transgenic foods is the most appropriate and realistic way of enabling consumers to make enlightened choices is a matter of fierce debate in many countries. The Codex Alimentarius Commission is currently examining this issue. Several governments have adopted policies and procedures on GMO labelling, and significant differences exist. Provisions for labelling from production to consumption can pose insurmountable problems for countries with limited capacity but anxious to enter international markets.

Public opinion in the USA appears to be less animated, and opinions seem stronger on genetically modified animals than on genetically modified crops. The American people appear to be aware of and encourage the potential benefits of biotechnology, with one survey revealing that 62% believe biotechnology will produce additional benefits over the next five years. Such benefits include improved quality, taste and diversity of food, improved human health and nutrition, reduced use of pesticides and insecticides, lower food costs and improved yields. The current use of GM crops does not seem to be a problem for the US population. Do they feel the same way about GM animals?

Survey data reveal inadequate methodology, with the use of closed questions and an interpretation of results that needs to be shorn of the deep-seated mental prejudices of both assessors and the public. Questionnaires often focus on GM plants, while it might be illuminating to distinguish between GM plants and GM animals to gauge the level of public concern about genetically modified animals.

Communication between the public, assessors and decision-makers

The OECD countries and intergovernmental organizations are seeking new ways of sharing their experience. They are seeking to boost the dissemination of information and real consumer understanding of the safety issue. Some countries have adopted measures for the public exchange of information on the safety assessment of GM foods. The public are invited to comment on the reports and proceedings of safety

assessment bodies. Some regulatory bodies actively consult the public on food safety and regulations. Some make all information supporting an application available to the public, except confidential commercial information. The Internet is increasingly used to inform the public of safety assessment and approval procedures, and is a good source of information on approved foods and food products. Some countries are looking into the possibility of using the Internet to make application details accessible to the widest possible audience, in order to make the assessment process as transparent and understood as possible.

The OECD's on-line BioTrack site is a useful source of information on regulations in member countries, with information on ministries and agencies, and details of laws, regulations and guidelines. It also has two important databases: one on products that have been marketed; the other on GM field tests carried out in OECD countries. Other approaches adopted with huge success in selected countries include the appointment of consumer representatives to safety assessment committees. Consensus conferences have also been attempted with varying degrees of success.

E. Ethical considerations

Up until now, the idea of food products from transgenic animals has not been well received by consumers. Surveys have constantly shown that the public is better disposed towards transgenic plants than transgenic animals. There is greater reluctance towards trials involving animals and changes in animal make-up and therefore broader possible implications. Various cultures and religions limit or forbid the consumption of certain foods of animal origin. The public seems however to be more disposed to consume by ingestion or injection pharmaceutical products derived from transgenic animals. Various ethical issues have been raised.

Distribution of benefits

One preoccupation is the possible impact of biotechnology on agricultural structure, especially the potential elimination of small livestock farms in the face of the cost of producing transgenic animals. People are worried about the impact of a dismantled agricultural society on the environment, sustainable agriculture and quality of life. The public points to the concentration of production and its direct consequences on markets and consumers, and is wary of the dependence of livestock farmers and food producers on multinationals. There is mental conflict between the law of the market and the traditions, cultural identities and needs of society.

Nutrition and food safety

There seems to be general consensus among scientists that the consumption of food derived from transgenic animals is no more hazardous than the consumption of conventional products. However, the public thinks differently. Some people refer to specific diets based on cultural or religious considerations. For example, the consumption of an animal or a food from a transgenic animal that contains proteins or genes of animals whose consumption is forbidden by culture or religion could pose a problem. Another point often stressed is the social divide from different levels of access to biotechnology in developing and developed countries.

Respect for life and the unnatural nature of GMOs

Some people do not believe that technical and economic pressures justify the commercialization of life and the patenting of living organisms.

Overstepping of the species barrier and the large-scale industrial production of genetic animals are seen as contrary to nature. This argument is frequently refuted by biologists who stress that the continuous natural evolution or the human selection of animal genotypes has favoured certain genes and eliminated others.

Finally, biotechnology and conventional livestock practices might seem to pose similar problems, in that both seek maximized productivity and both cause animal dysfunctioning and welfare and health problems. However, such problems seem to be magnified (some would say disproportionately) in the context of biotechnology.

III. Conclusion

Animal biotechnology is a recent science and therefore difficult to view in the light of experience. Many uncertainties and many doubts exist. Information currently available will have to be constantly updated with data and results of analyses and trials of transgenic animals and derived food products, so that techniques, regulations and public opinion can evolve and adapt; so that doubts can be clarified and problems resolved; and so that agreed protocols of analysis and international standards can be determined.

Given the rapid progress being made and the prospects of animal biotechnology, it is almost certain that improved techniques will boost benefits. However, the trade-off between risk, cost and benefit will always have to be examined. Ongoing oversight, greater transparency of results from scientific trials, greater transparency of regulatory and decision-making processes and closer cooperation among all stakeholders are required for the safety evaluation of products derived from transgenic animals.

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