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Considerations for the assessment of the safety of genetically modified animals used for human food or animal feed☆

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Abstract

Genetically modified food and feed crops have entered the Western market, and genetically modified animals may follow in the near future. The issues that are commonly addressed in the assessment of the safety of genetically modified crops are discussed, as well as the analogous issues that may arise for genetically modified animals. For safety assessment, the degree of substantial equivalence of the novel food- or feed-organism to an appropriate counterpart should be established. Based upon the differences thus found, a further strategy for the safety assessment is chosen. This may, for example, take the testing of a novel food or feed for its potential toxicity and allergenicity. Another issue is that of the possible transfer of genes from the genetically modified organism to others. This would be a concern, for example, if the introduced DNA comprised genes coding for resistance against clinically important antibiotics. Unanticipated long term health effects of the genetically modified food or feed can be monitored by postmarket surveillance. National regulations for food and feed derived from genetically modified organisms may differ, but they are based upon the same underlying principles. The regulatory status of genetically modified animals may differ from that of genetically modified crops, as the foreign gene in some animals will be regarded a veterinary medicine. National regulatory experience with transgenic food animals has been gained in a few cases so far. The FAO/WHO has initiated the harmonisation of the food safety evaluation of genetically modified organisms.

1. Introduction

The safety of genetically modified organisms (GMOs) was discussed more than 20 years ago, long before any genetically modified (GM) plant or animal came on the market. GM crops have been commercially cultivated since the mid-1990s with the acreage of GM crops now standing at approximately 45 million acres, mainly in the USA, Argentina, Canada, and mainland China. The main GM crops are soybean, cotton, maize, and canola (James, 2001). The safety of these crops for food and feed use was assessed in various nations prior to their release on the market, not only in the countries cultivating these crops but also in importing nations, such as in the EU.

If we disregard GM animals that have been modified for non-food purposes (including pharmaceutical purposes), GM food animals have not been introduced yet to the Western markets. In addition, published data on the food safety of GM animals are

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scarce. Given the state of research on experimental GM food animals, market introduction of GM food animals can be anticipated in the near future. Therefore we will highlight the main issues in the assessment of the food- and feed-safety of GM crops and compare these issues to similar issues that we envisage for GM animals.

2. General

2.1. GM crops

Most of the GM crops that are on the market have been modified to enhance agronomic performance or to facilitate plant breeding. These crops contain one or two foreign genes, coding for proteins that are expressed in rather low quantities in plant tissues. Examples of introduced traits are

- Herbicide resistance, enabling GM crops to sustain application of herbicide on their leaves contrary to weeds, which perish under the action of the herbicide.
- Insect resistance, by the introduction of insecticidal proteins from bacteria.
- Male sterility, which facilitates hybrid breeding.

It is expected, however, that the range of traits will become diversified in future. In addition, some future GM crops will have undergone more profound genetic changes. Whole new metabolic pathways, for example, may be introduced by the introduction of multiple genes. One example is the 'golden rice', which has been modified to produce provitamin A in its kernels, which naturally do not contain this provitamin (Ye et al., 2000). These new developments in crop plant biotechnology are reviewed in more detail elsewhere (Kleter et al., 2000).

The foreign DNA in these crops is commonly introduced by two methods. First, plasmids of the bacterium *Agrobacterium tumefaciens* are employed, which are integrated into the plant genome. Second, DNA is introduced by 'bombardment' with accelerated DNA-coated particles. For both methods, cells or tissues from plants are cultured in vitro and regenerated into whole plants after genetic transformation with the foreign DNA.

2.2. GM animals

Many of the GM animals for food purposes that have been modified to enhance performance, have been transformed with growth-related genes, such as those for growth hormone (somatotropin), growth hormone releasing factor, and insulin-like growth factor (Pinkert and Murray, 1999). In addition, GM animals have been created with novel enzymes in their intestinal epithelium to increase the efficiency of feed utilisation as an alternative to the use of feed additives. Examples include animals expressing phytase to increase the uptake of organically bound phosphorus (Golovan et al., 2001) and animals expressing bacterial enzymes catalysing the synthesis of the essential amino acid cysteine (Ward et al., 1999).

A common method of genetic modification of animals is the microinjection of foreign DNA into egg pronucleus (mammals) or egg cytoplasm (fish). Another technique involves the genetic modification of mature cells followed by nucleus transfer into eggs.

Recently, the use of autonomous artificial chromosomes complemented these techniques for inheritable genetic modifications. These chromosomes may contain several features common to natural chromosomes, including centromeres, telomeres, and satellite DNA. The target foreign DNA has been introduced into these chromosomes. The advantage of this system is that the randomness and uncertainties inherent to foreign gene insertion are avoided. These artificial chromosomes are replicated as separate entities and passed through the germline to following generations (Co et al., 2000).

In addition to the methods that target germline modification, gene therapy can be employed for the genetic modification of somatic cells within an animal. Different types of vector can be used, including retroviruses, which are integrated into the animal's DNA, and adenoviruses and plasmids, which do not integrate but remain autonomous. Gene therapy was recently employed to target the transient local expression of plasmids carrying the gene for growth hormone releasing factor in pigs (Draghia-Akli et al., 1999). The plasmid DNA containing the gene of interest had been applied by the technique of electroporation to pig muscles. Serum levels of

growth hormone and insulin-like growth hormone were increased in the weeks following the modification.

3. Safety assessment of GM foods and feed

3.1. Substantial equivalence

3.1.1. GM crops

The principle of substantial equivalence encompasses the comparison of the GMO to its conventional counterpart. Substantial equivalence is often mistaken for the outcome of a safety assessment. It is rather the starting point of the assessment, though, and based upon the degree of equivalence, additional safety experiments are undertaken.

The comparison can involve the phenotypic and compositional characteristics of the novel crop. The compositional analysis usually involves the analysis of macro- and micronutrients, antinutrients, and toxins. In addition, the comparison should involve plants harvested at a sufficient number of locations representative for the commercial cultivation during at least two growing seasons. There is, however, no standard recipe for this comparison, because of the divergent nature of food crops as well as the various genetic modifications. The GM crops are therefore evaluated on a case-by-case basis.

For the GM crops that are on the market now, with one or two foreign genes introduced, the principle of substantial equivalence has worked well. It is envisaged, however, that future GM crops will be the result of more intricate modifications, for example by the introduction of multiple genes and/or metabolic routes that are new to the recipient crop. Unintended effects of genetic modification appear more likely for such profoundly altered crops. Further refinement of the comparative approach of substantial equivalence is needed to keep abreast of these developments (FAO/WHO, 2000).

Currently research is carried out to develop analytical methods to analyse the changes brought about in profoundly altered GM crops. Methods are being developed, for example, in EU-sponsored R&D projects within the ENTRANSFOOD network (http://www.entransfood.com). These methods do not focus on singular compounds, but record a whole spectrum of compounds, proteins or RNA present in a crop to screen for possible differences. Examples are liquid chromatography coupled to nuclear magnetic resonance (LC–NMR) to detect metabolites (Noteborn et al., 2000), two-dimensional gel electrophoresis to detect proteins, and cDNA microarray hybridisation to detect RNA (Van Hal et al., 2000). The identity of these differences should then be further explored, and the implications for product safety assessed. These techniques are reviewed in more detail elsewhere (Kuiper et al., 2001).

3.1.2. GM animals

The strategy for the safety assessment of foods derived from GM animals has been discussed within the OECD and the FAO/WHO (Berkowitz and Sarma, 1993; FAO/WHO, 1991, 1996; Kryspin-Sørensen, 1992). In these discussions, it was concluded that the food safety assessment of GM animals should comprise:

- Molecular characterisation of the inserted foreign DNA.
- Safety of foreign gene products.
- Unintended effects of the insertion of foreign DNA, e.g. effects on animal health and carcass composition.
- The effect of disease resistance brought about in transgenic food animals on consumer's exposure to disease-causing agents.

The American authorities have formulated additional points that need to be considered in evaluating the food safety of GM animals, particularly the potential risks emanating from the use of retroviral sequences, including the risk of recombination with wild-type viruses (Jones, 1998).

These points for consideration were extended recently in an interim report of the Canadian government in preparation of guidelines for the food safety assessment of transgenic livestock and fish (Health Canada, 2001). This report also considers that the principles for the safety assessment of GM plants can be applied to that of GM animals, although more elaborate guidance may be required.

The Canadian report suggested the inclusion of the following additional items in the safety assessment:

- The well-being of the transgenic animal.
- Compositional ('nutritional') analysis
    - analysis of nutrients and bioactive compounds
    - sampling of raw and cooked material, tissues and the whole-ground carcass
    - meat quality impact of 'large animal syndrome'
- Compositional analysis: novel methods needed in addition to targeted analysis.
- Toxicology
    - screening for unintended effects by molecular profiling techniques and study of the GM animal's behaviour and development
    - attention paid to the possible consequences of under- and over-expression of genes.

The issue of the transgene copy number in homozygous animals versus heterozygous animals called for further consideration. With regard to the well-being of transgenic animals, a recent paper discusses the evaluation of animal welfare in the context of GM technology (Van Reenen et al., 2001).

One of the safety considerations in the assessment of GM crops is the possible effect that the genetic modification may have had on the levels of intrinsic antinutrients and toxins. Although food animals rarely produce antinutrients and toxins, safety evaluators should be aware of exceptions to this general rule. Tetrodotoxin, for example, occurs in puffer fish, which is consumed in Japan. Another, more commonly encountered example is that of the enzyme thiaminase, an important antinutrient that degrades thiamine (vitamin B1). This enzyme is present in viscera of some commercial fish species (Board on Agriculture, 1982, pp. 64–65). Thiaminase has been implicated in massive extinctions of larvae from prey fish both in Northern America and the Bothnic area, known as Cayuga syndrome or Early Life Stage Mortality Syndrome. The larvae would have previously suffered thiamine deficiency during their embryo stage due to maternal consumption of forage fish containing thiaminase (Ketola et al., 2000). Feeding livestock with thiaminase-rich fish has been associated with adverse effects, such as paralysis and mortality in dogs and loss of equilibrium and mortality in salmon (Houston and Hulland, 1988; Saunders and Henderson, 1974). In addition, thiamine deficiency in a Thai human population has been associated with the consumption of raw fermented fish containing thiaminase (Vimokesant et al., 1975). The effect of the genetic modification event on the expression levels of thiaminase in GM fish should therefore be taken into account.

Studies have been reported in literature on the comparative carcass analysis of growth-enhanced GM animals. GM pigs genetically modified with various types of growth hormone, for example, yielded leaner meat (i.e. lower fat content) than control pigs, while meat lipids contained less saturated fatty acids and more unsaturated fatty acids (Solomon et al., 1997).

Scientific literature on safety assessments carried out on GM food animals is scarce. We located only two references on this subject, both dealing with transgenic growth-enhanced fish.

Guillen et al. (1999) tested the safety of growth-enhanced tilapia, which had been genetically modified with tilapia growth hormone. Macaques were administered tilapia growth hormone by intravenous injection of 1 μg/kg daily for 30 days. Blood samples were tested for parameters that are likely influenced by growth hormone activity. No effects of tilapia growth hormone were observed, corroborating the previously observed lack of activity on in vitro cultured rabbit cartilage. In addition, no adverse effects were observed on the blood parameters of human volunteers, who consumed GM tilapia twice daily during 5 days. Zhang et al. (2000) fed carp transgenic for growth hormone to mice, which were subsequently analysed for reproductive toxicology, blood chemistry, and histopathology. No differences were found between the feeding of transgenic and non transgenic carp to the mice.

3.2. Allergenicity

3.2.1. GM crops

As all food allergens are proteins, the potential allergenicity of newly introduced proteins has been a consideration in the safety evaluation of GM crops. A decision tree has been drawn up to aid the evaluation for potential allergenicity of a transgenic protein (Metcalfe et al., 1996). This decision tree

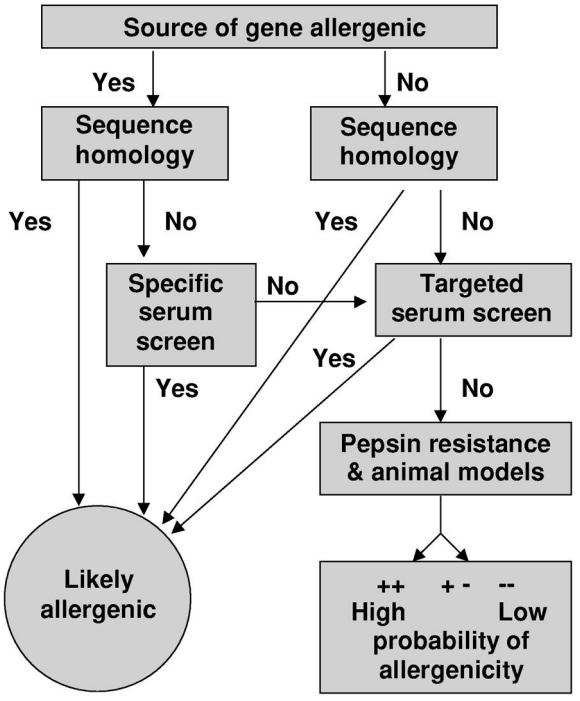

Fig. 1. Decision tree for the assessment of potential allergenicity of proteins introduced in GMOs (FAO/WHO, 2001a).

was recently refined (Fig. 1; FAO/WHO, 2001a). The first step in this refined tree comprises the comparison of the novel protein's structure with the structures of known allergens by computer-assisted alignment of their amino acid sequences. The direction following the first step through this decision tree depends on, among others, the source of the foreign gene. If the gene source is a known allergen, than its reaction with sera from patients that are allergic to the specific source should be tested. In case of a negative result, or if the gene source has no history of allergenicity, (further) testing involves sera from patients that are allergic to organisms broadly related to the gene source. Depending on the outcome, further testing may be required, involving in vitro digestion with the stomach protease pepsin (as most food allergens are stable to digestion) and in vivo animal testing. If any of these steps yield a positive outcome, the GMO should be considered likely to be allergenic.

Another consideration that may also arise from the modification, is that of the changes brought about in the properties and occurrence of allergens that are intrinsic to recipient organism. Experimental crops have been created, for example, with decreased levels of intrinsic allergens (Tada et al., 1996).

3.2.2. GM animals

Allergenicity is also an issue of concern in GM animals. Animal products, such as shrimp and cow's milk, contain a number of well known and lesser known intrinsic allergens, e.g. tropomyosin (shrimp). The effect of the genetic modification on their (allergenic) properties and tissue levels should therefore be determined.

Another point of consideration is the apparently incomplete digestion—and intestinal uptake—of orally administered proteins and peptides with hormonal activity in fish (McLean et al., 1999). This accounts for the fact that fish growth is enhanced by experimental feeding of, for example, animal pituitaries containing growth hormone. As fish and animals can be turned into feed for cultured fish, the possible effects of ectopic expression of protein hormones in GM animals warrants further consideration.

3.3. Gene transfer

3.3.1. GM crops

Antibiotic resistance genes are employed as markers used in the development and selection of genetically modified plants. Their purpose may be twofold. First, the DNA vector carrying the DNA of interest needs to be produced in sufficient quantity prior to the genetic modification. To this end, plasmids containing the gene of interest and an additional antibiotic resistance gene are introduced into bacteria. The antibiotic resistance allows the bacteria harbouring the plasmid to grow on antibiotic-containing media, which ensures production of the plasmid. The plasmid can subsequently be purified from the bacterial culture for use in the transformation of plants. Secondly, plant cells that have successfully been transformed with DNA containing both the gene of interest and an antibiotic resistance gene are able to survive on antibiotic-containing media, whereas non-modified cells perish. This facilitates the selection of successfully trans-

formed plant cells, which subsequently can be regenerated into plants.

Antibiotic resistance genes have no purpose in the GM crops, but are used only in the initial selection process. Safety concerns have been expressed, however, over the risk of transfer of these genes to micro-organisms residing in the gastrointestinal tract of humans and animals consuming GM crops. Although the probability for such a transfer appears low, no data to date have been published on transfection rates in vivo. Consequently, a precautionary approach has been taken by various governments with regard to the use of antibiotic resistance genes. The target antibiotic, for example, should not be clinically important. In addition, the naturally occurring resistance to the antibiotic should be taken into account. Based on these considerations, the kanamycin resistance gene *npt*II was approved and has since then become the most common antibiotic resistance gene in commercial GM crops (FDA, 1998). Recently adopted EU legislation, however, prohibits the use of antibiotic resistance genes.

3.3.2. GM animals

The documented use of antibiotic resistance genes in GM food animals appears rare and may therefore be less of a concern. It can be envisioned, though, that in the production of DNA vectors for the transgene, 'contaminating' bacterial antibiotic resistance genes may originate. The question then arises how the accidentally introduced antibiotic resistance genes may come into contact with pathogenic micro-organisms that might subsequently be transformed with these genes. Intestinal epithelial cells, for instance, may shed into the lumen, degrade and thereby expose their DNA to the intestinal microflora.

Another concern that has been raised specifically over GM animals is the use of retroviral sequences. This may especially pertain to transgenic poultry, because (disabled) retroviruses are employed to successfully transform eggs, whose blastoderms contain numerous cells, which precludes the use of nuclear micro-injection or nuclear transfer. It has been reported that inserted retroviral sequences in animals recombine with wild type viruses giving rise to new retroviruses (reviewed by Mikkelsen and Pedersen, 2000). Recombination of wild type retroviruses with endogenous retroviral sequences containing the transgenes may pose an increased risk over recombination with naturally incorporated latent retroviruses. Novel methods can help circumvent this risk of recombination by the use of artificial retroviruses, in which the retroviral genome has been replaced by DNA vectors lacking sequences that are prone to recombination (Health Canada, 2001, p. 6). In addition, the insertion of DNA (retroviral and non-retroviral) may hypothetically lead to the activation of adjacent latent viruses, although it has been argued that animal cells are capable of suppressing the activity of endogenous viral sequences (Heidmann, 1999). The targeting of foreign DNA to specific integration sites in the animal genome, as recently demonstrated in sheep (McCreath et al., 2000), would circumvent this hazard.

3.4. Postmarket surveillance

3.4.1. GM crops

The EU recently adopted legislation on the cultivation of GM crops that requires the post market surveillance of the GM crops for any unanticipated adverse effects appearing in the long term (EU Directive 2001/18). Applicants seeking to introduce GM crops to the EU market are required to submit a draft monitoring program for approval (EU, 2001, Annex VII). In addition, new legislation on novel food and animal feed (including GM food and feed) has been drafted by the European Commission, which envisions the same postmarket surveillance for GM food and feed. Traceability of the GM food and feed should be warranted by the labelling of the specific GM components throughout the entire production chain.

3.4.2. GM animals

The same would apply to GM animals as to GM crops. The tracing and post-market surveillance of any future GM animal products in the EU will be facilitated by two factors:

1. Traceability-systems for animal products are currently being implemented in the EU.
2. Ingredients derived from animals are less generally present in food- and feed-products than some vegetable ingredients (e.g. maize starch and soy-

bean oil). This can be in part accounted for by anti-BSE measures for animal feed.

A difference between GM crops and GM animals is that some GM food animals may be regarded veterinary medicines by some regulatory authorities. An introduced gene that codes for a growth hormone, for example, is comparable to the administration of exogenous growth hormone, which is a veterinary medicine. These GM animals would therefore be subject to 'pharmacovigilance', which is the mandatory post market surveillance for medicines. Frameworks for pharmacovigilance are in place in Western nations and abroad, e.g. adverse reaction reporting systems. Technical requirements for pharmacovigilance of veterinary medicines in Japan, Northern America, and EU will be harmonised in the near future. These requirements include the reporting of adverse effects of veterinary medicines to the authorities, which is mandatory for the manufacturer and voluntary for others (e.g. animal owners, veterinarians) (VICH, 2001, guidelines 24, 29, 30).

4. Regulation of GM foods and feed

4.1. GM crops

The cultivation, trade, and food and feed uses of GM crops are subject to national regulations in most nations and the safety assessment of the GM crop is part of the admission procedure. For cultivation, for example, the environmental safety will be assessed, but this is beyond the scope of this article. Depending on the envisioned purposes for the novel crop, its food and feed safety will also need to be assessed.

Although the national regulations are somewhat different, the underlying principles are the same. For a more detailed treatise of these national divergences, we refer to recent reviews (Kuiper et al., 2001; MacKenzie, 2000). The internationally acknowledged comparative approach of 'substantial equivalence' is an important guiding principle in the safety assessments under these regulations. Initiatives are underway to harmonise the regulations and the inherent safety assessments of GMOs internationally.

The Task Force on the Safety of Novel Foods and Feed of the Organisation for Economic Co-operation and Development (OECD) is developing guidance documents, for example, on which compositional parameters should be compared between the GM crops and appropriate comparators. So far, guidance documents for soybean and canola have been completed, while those for potato, sugar beet, wheat, maize, rice, sunflower, and cotton are underway. These guidance documents serve as minimum recommendations, but are not legally binding.

The FAO/WHO Codex Alimentarius has developed international standards for food safety that its member states should implement into their national legislation. Codex standards, for example, have been developed on residues of pesticides, contaminants, and veterinary medicines in food. These standards are legally binding and can be referred to in the case of international disputes on the food safety of traded foods and commodities. Efforts towards harmonisation of the national food safety assessments of GMOs are made by the Codex Ad Hoc Intergovernmental Task Force on Foods Derived from Biotechnology. Expert consultations on specific items (substantial equivalence, allergenicity) have been organised by a special working group for this task force. Guidance has been drafted for the risk assessment and risk analysis, and special attention has been devoted to detection and traceability of GMOs (FAO/WHO, 2001b). It is expected that within a few years these documents will be completed and adopted.

4.2. GM animals

The regulatory experience with market applications for GM food animals is very limited compared to that with GM crops. To our knowledge there are actually two cases where regulatory approval has been sought for the market admission of GM food animals. These are the Bresatec pig in Australia and the AquAdvantage salmon in the USA.

The GM pig developed by Bresatec (currently Bresagen) is transgenic for a growth hormone gene that can be 'switched on' by adding zinc to the diet, which allows for increased production of meat (muscle tissue) at an increased feed efficiency (Nottle et al., 1999). The Bresatec company provided data to the Australian authorities that its GM pork

meat were substantially equivalent to ordinary pork. At that point in time, however, the Australia New Zealand Food Authority and the Australian Genetic Manipulation Advisory Committee were unable to process Bresatec's application because food safety of GM animals fell outside their regulatory oversight. Subsequently, because Australian supermarkets expressed a reluctance to market GM pork, Bresatec reportedly abandoned this project [ARMCANZ, 1997; L. Kelly (ANZFA), personal communication].

The AquAdvantage salmon developed by Aqua Bounty is transgenic for a salmon growth hormone gene under control of a promoter from the ocean pout's antifreeze protein gene. The transgene is expressed in the salmon liver and provides for year-round secretion of growth hormone. The growth of the young AquAdvantage salmon is 4–6 times as high as for ordinary salmon, yet mature AquAdvantage salmon at harvest are the same size as ordinary salmon, weighing approximately 3 kg (Fig. 2). Furthermore, the size of the GM salmon at sexual maturity did not increase above that of typical salmon after four generations of breeding [E. Entis, personal communication]. Growth hormone levels in edible tissues are reportedly within the range found within non-GM counterparts (Entis, 1997).

Aqua Bounty has submitted an application to the American authorities for the market approval of the AquAdvantage salmon. Contrary to agronomically enhanced GM crops, GM animals with improved agronomic traits are regarded 'new animal drugs' by the Americans, comparable to exogenous growth hormone administered to animals. The application was therefore filed to the Center for Veterinary Medicine of the Food and Drug Administration as a 'new animal drug application (NADA)'. The safety assessment will include many aspects, including the environmental risks associated with the different options for fish cultivation (open pens, closed tanks), risks of waste discharge from the fish farms, and food safety. The environmental risks are discussed elsewhere (CEQ/OSTP, 2001).

Fig. 2. Second generation transgenic Atlantic salmon containing the antifreeze protein promoter linked to a salmon growth hormone gene (AquAdvantage salmon). The large (transgenic) and two control siblings are shown for comparison. Despite the increased growth rate of the GM sibling, both GM-and non GM-salmons will reach the same size at sexual maturity (Hew and Fletcher, 1997).

Food safety studies that have been carried out in preparation of the NADA-application for the AquAdvantage salmon include [E. Entis, personal communication]:

- Level of expression of the introduced gene.
- Serum levels of peptide- and steroid-hormones.
- Bioavailability of the salmon growth hormone to humans.
- Comparison of the composition [macronutrients, micronutrients (vitamins, minerals), amino acids, fatty acids] between GM and non-GM salmons.
- Potential allergenicity of the GM salmon compared to ordinary salmon.

Several papers on the AquAdvantage salmon in their presmolt phase have been published, including data on metabolic activity (Cook et al., 2000b), body composition (Cook et al., 2000a) and body composition as influenced by food deprivation (Cook et al., 2000c). It has been noted, for example, that the presmolt transgenic fish bodies contained more moisture and less protein, lipid, and ash than controls of the same weight (Cook et al., 2000a).

As noted above, the FAO/WHO Codex Alimentarius Task Force is preparing guidance documents for the safety evaluation of GMOs. In anticipation of future developments in food biotechnology, an Expert Consultation will be convened on the topic of genetically modified fish (FAO/WHO, 2001b).

5. Conclusions

The first genetically modified crop foods were introduced in the mid-1990s and others have followed. Prior to these market introductions, safety assessments were carried out. Genetically modified

animals probably will enter the market within the near future. With regard to the safety assessment of these animals, we conclude that:

1. Little experience has been gained so far with GM animal/animal product safety evaluations. To expand this experience, it may be useful to examine cases that are currently in their experimental phase. The following parameters are of interest with respect to the assessment of safety and functionality: test parameters, the effects of food/feed processing, unintended effects (hormonal imbalances and natural variations) and appropriate test models. An Expert Consultation on this matter is urgently needed!
2. Some of the genetic modifications of agronomic importance can be considered 'animal drugs'. It is therefore worthwhile to take notice of the safety assessments carried out with the conventional counterpart of these animal drugs, e.g. recombinant bovine somatotropin.
3. The experience gathered with the assessment of GM crops and the new profiling techniques that are currently developed to facilitate the safety assessment of future GM crops may be applicable to GM animals.

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