Transgenic salmon, a safe product?

Environmental risks associated with the production of transgenic salmon

COGEM advisory report CGM/031124-01

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Netherlands Commission on Genetic Modification (COGEM)

COGEM's task is to advise the government at their request or independently about the risks of using genetically modified organisms (GMOs) and to inform the government about ethical and societal issues associated with genetic modification. COGEM's task is described in the Environmental Management Act.

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Summary

COGEM has published this advisory report due to the advancing technological developments with respect to genetic modifications, advanced plans for the introduction of transgenic salmon onto the American market and the societal discussion within Europe concerning this. In this advisory report the possible risks for the environment of rearing transgenic salmon have been considered against the current practice of salmon rearing. This means that the possible environmental risks associated with intensive fish farming have not been included in the considerations.

Intensive fish farming, such as salmon rearing, is controversial due to the associated environmental problems. In recent years a new aspect has entered this discussion, namely the rearing of transgenic fish and in particular transgenic salmon.

The environmental risks associated with the rearing of transgenic salmon are dependent on the chance of escape and establishment, the modification made, the chances of and consequences of outcrossing, the consequences for the ecosystem, and the possibilities present for limiting undesired consequences.

If transgenic salmon are reared using the same production methods as for normal salmon rearing then escapes would seem to be unavoidable. A number of factors determine whether the escape of transgenic salmon will be more harmful than the escape of non-transgenic reared salmon.

- Genetic modification provides the possibility of introducing characteristics that are not present in the natural population. When characteristics that are not naturally present in the population are introduced, it is difficult to predict the behaviour of these resulting transgenic fish and their interaction with other organisms.
- Due to the manner in which they have been created and selected, transgenic salmon populations are probably more genetically homogenous than reared salmon. If crossbreeding occurs, this lack of genetic variation could have particularly harmful consequences for the maintenance of the wild salmon population.
- Transgenic salmon have an increased chance of a pleiotropic effect with harmful consequences. Pleiotropy is where one gene influences several phenotypic characteristics. If the transgenic salmon gain a clear reproductive advantage as a result of the pleiotropic effect but have a reduced chance of survival then this can lead to the displacement or even the extinction of the entire salmon population.

Due to the many obscurities and contradictions in the research conducted to date, the consequences of new or improved characteristics cannot be determined in advance. Furthermore, it is unclear whether the behaviour of transgenic salmon under laboratory conditions can be translated to the situation in the sea.

COGEM is of the opinion that based on the current data it is impossible to unequivocally state the situations in which the environmental risks are negligible. In view of the large scientific uncertainty, COGEM calls for as much restraint as possible. On the other hand COGEM is of the opinion that on the basis of scientific arguments it cannot be stated in advance that the rearing of genetically modified salmon will always result in unacceptable environmental risks. If the rearing takes place on land with extensive containment measures or if it can be demonstrated that the gene inserted has no associated additional risks compared to the rearing of non-transgenic salmon then the foreseeable environmental risks of transgenic salmon rearing appear to be small. At the very least, COGEM recommends the adoption of a case-by-case approach. For each case this should include an extensive environmental risk analysis, based on the specific circumstances.

COGEM has appended a report about the ethical and societal aspects, to this advisory report about the possible environmental risks. A key aspect in this discussion about transgenic salmon is the damage to the fish's integrity. Other arguments in the debate are mainly directed towards the animal's health and welfare, food safety, consumer acceptance, dangers for the environment and the economic interests.
COGEM points out that the present European and national legislation cannot prevent the cross border consequences of transgenic salmon rearing for the environment. COGEM also highlights the fact that Dutch legislation concerning the ethical and societal considerations of genetic modification in animals does not apply to the introduction of salmon products to the Dutch market. With respect to this it should be noted that following the introduction of transgenic salmon to the American market, the chance that cross border consequences of transgenic salmon in the European or Dutch environment could occur, or that transgenic salmon products could appear on the Dutch market within 5 to 10 years is realistic under the present circumstances.

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Advisory report

1. Introduction

At the end of 2004 we will know whether salmon will have become the first transgenic animal to be marketed for human consumption. By this time the fish producer Aquabounty (Massachusetts, VS) expects to gain approval from the American Food and Drug Administration (FDA) for the introduction of transgenic salmon to the American market. In November 1996, Aquabounty submitted an application for the commercial rearing of transgenic salmon with an enhanced growth rate. Whether the FDA approves the application and in so doing opens the way for other transgenic fish will to a large extent depend on the assessment of the food safety and also the environmental risks posed by rearing transgenic salmon (Hoag, 2003).

Since the successful production of the first transgenic fish in the mid-1980s, researchers have being trying to genetically modify fish such that they contain characteristics of interest to aquaculture (Zbikowska, 2003). These efforts now seem to be bearing fruit. For example, Aquabounty hopes to submit a second application, for transgenic trout, to the FDA before the end of 2004. Cuban researchers from the 'Center of Genetic Engineering and Biotechnology' in Havanna are working on the production of transgenic tilapia (*Oreochromis spp.*) and expect to be able to market the fish in three years time. A salient detail with respect to this is that the Cuban researchers are testing the food safety by using volunteers who eat the transgenic tilapia (Hoag, 2003). Such experiments are not permissible under European legislation.

In recent years, there has been a lot of public discussion about food safety. Scandals related to dioxin, BSE, salmonella, the use of growth hormones, etc, have resulted in consumers becoming more critical about how food is produced. Furthermore, the European public in particular has a general aversion towards genetically modified organisms (GMOs). This means that introducing the commercial production of transgenic salmon is controversial. Public objections to transgenic animals not only concern the damage to the animal's welfare and integrity, but also the possible consequences for the environment should they escape. A feared loss of genetic variation and biodiversity are frequently stated arguments in this respect.

COGEM has published this advisory report due to the advancing technological developments with respect to genetic modifications, advanced plans for the introduction of transgenic salmon onto the American market and the public discussion within Europe concerning this. In this advisory report the possible environmental risks posed by the rearing transgenic salmon have been considered against the current practice of salmon rearing. Food safety is not one of COGEM's responsibilities and is therefore not included in this advisory report.

COGEM considers it unlikely that the rearing or production of genetically modified salmon will take place in the Netherlands. Due to geographical conditions, Dutch waters appear to be unsuitable for salmon rearing. However, the Dutch environment could suffer adverse consequences following the introduction of transgenic salmon elsewhere in Europe or in the world. Adverse consequences will possibly not be limited to territorial waters but could spread over the entire global marine ecosystem.
Although there are no reasons to assume that the rearing or production of transgenic salmon will take place within Europe in the near future, this possibility is nevertheless still present. At present some of the biggest salmon producers are countries such as Norway, Scotland and Ireland. These countries fall within or are associated with the European Union and therefore fall under European legislation. Due to Dutch national interests and the Dutch contribution to European policy, COGEM is informing the Dutch government about the possible risks of transgenic salmon for humans and the environment. In so doing, COGEM will use this advisory report to provide an overview of the environmental risks for the purpose of the public discussion.

This advisory report has been compiled on the basis of scientific articles, previously published reports concerning the rearing of genetically modified salmon and interviews with Dutch and foreign experts.

2. Aquaculture

Fish farming, also referred to as aquaculture, is a growing industry. Since 1970, the worldwide production of reared fish has grown by more than nine percent per year, varying from intensive production in enclosed areas and on land to extensive rearing in the sea. Since 1995 the fish catch has remained constant. A total of 130.2 million tonnes of fish was produced in 2001, of which 37.9 million tonnes came from aquaculture. In 2001 the fish catch was 92.4 million tonnes (FAO 2003a).

Intensive fish farming, such as salmon rearing, is controversial due to the associated environmental problems. In addition to the advantages associated with intensive fish farming, such as the savings on fuel due to ships not sailing, not having by-catch and the continuous supply of fresh fish, there also disadvantages. The leakage of feedingstuffs and animal waste substances results in eutrophication and oxygen depletion in the surrounding environment. Moreover, intensive fish farming seems to be a source of diseases. The possible risk of infection as well as the use of antibiotics and pesticides can adversely affect the wild population and other organisms in the ecosystem.
The disadvantages associated with intensive fish farming have led to public discussion. Opponents are of the opinion that commercial fish farming causes too much environmental damage. Yet proponents are of the opinion that fish farming should be seen as a means of protecting the wild species. Fish farming enables the demand for fish to be met without the threat of further overfishing. It is also stated that fish farming can make a significant contribution to the world's foods supplies. For example, the United Nations agricultural organisation, the FAO (Food and Agriculture Organisation) is of the opinion that aquaculture can make an important contribution to solving the food problem in the coming years (FAO 2003b).

In recent years a new aspect has entered this discussion, namely the rearing of transgenic fish and in particular transgenic salmon. Proponents point to the enormous advantages that transgenic fish offer, such as a higher food conversion, faster growth, reduced costs and a reduced spread of diseases due to the insertion of disease resistance genes. However, opponents are of the opinion that the rearing of transgenic salmon will lead to unacceptable environmental risks and that escapes could have catastrophic consequences.

Life cycle and rearing of salmon

The salmon (*Salmo salar*) is an anadromic fish species. At the sexually mature age of about four years, wild salmon return from the sea to the upper reaches of rivers to mate. During this journey, the salmon do not eat but live on reserves. In the upper reaches of rivers, the females lay eggs which are later fertilised by the males. When the young salmon have reached the so-called smolting age, they return to the sea to further develop into adult salmon. During this migratory phase salmon are capable of travelling over large distances.

This cycle is simulated during salmon rearing. In the initial stage the salmon are kept in fresh water recirculation systems on land until the smolting age is reached. The further growth up to market size takes place in nets in the sea. These nets are often located in sheltered bays and fjords. The improved quality of the nets, as a result of which these are more resilient to waves and poor weather conditions, also opens up the possibility of fish farming further to sea. An associated advantage of this is that excess feedingstuffs and waste substances disperse faster and therefore cause fewer problems for the surrounding environment (Subasinghe, 2003).

3. Genetic modifications of salmon

When salmon rearing first started several decades ago, the starting material used was a mixture of wild salmon populations (‘strains’). The current population has arisen as a result of many years of breeding for desired characteristics. This conventional breeding was mainly directed towards characteristics which resulted in an increased production, such as growth rate, cold resistance and disease resistance. Due to the possibilities that genetic modification provides for inserting characteristics that cannot be acquired naturally or which are difficult to introduce by means of conventional breeding, fish producers have become interested in creating transgenic salmon. Their efforts have mainly been directed towards the same characteristics as those chosen by conventional breeders. Genes have been inserted from related species, but also from unrelated species and even from other organisms. However, as well as increasing production, the aim of these modifications also seems to be focused on quality characteristics such as flesh colour and flesh quality.

3.1 Enhanced growth rate

The best-known modification in salmon is related to the growth rate. Salmon grow slowly and need three to four years to achieve their market weight. This slow growth is mainly attributable to the low water temperatures in which the salmon live. Low water temperatures result in a lower growth hormone production and consequently a slower growth rate. Furthermore, the salmon's growth rate decreases during the winter months due to the further drop in water temperatures. With an increased and/or continuous hormone production during the winter months, a greater growth rate can be achieved. The most important advantage of this is the reduced time needed to grow to market size with the result that the production capacity can be increased. As well as the economic advantages of an increased production capacity, an enhanced growth rate is also favourable for breeding purposes. The generation time is reduced as a result of which the selection of characteristics can take place more quickly. The producer is also in a better position to respond to changes in the demand for products, because prognoses only need to be made for a limited period of time.

The normal production of growth hormone takes place in the pituitary gland and is regulated by the central nervous system. This production is bypassed by inserting genes which are not under the control of the central nervous system but which contain their own promoter. Promoters regulate the expression of genes. Inserted hormone genes and promoters can be taken from fish but this does not have to be the case. Antifreeze promoters are frequently used as these ensure that a gene remains switched on throughout the entire season. Antifreeze promoters originate from cold-resistant fish species such as the blenny (*Blennius pholis*) or the flatfish 'winter flounder' (*Pseudopleuronectes americana*) and regulate the production of antifreeze proteins during the cold period. This characteristic is essential for the survival of these fish in cold areas. The insertion of this promoter in salmon together with a growth hormone gene, ensures that the salmon continues to produce growth hormone during the cold period.

Several research groups have confirmed that the insertion of a growth hormone gene in combination with a good promoter results in enhanced growth for transgenic salmon (Devlin et al., 1995a and b; Saunders et al., 1998; Stevens et al., 1998; Devlin et al., 1999; Abrahams et al., 1999; Cook et al., 2000; Devlin et al., 2001). They all concluded that the growth rate of transgenic salmon was significantly higher compared to that of non-transgenic (control) salmon.

Enhanced food conversion

It is frequently stated that transgenic salmon with an enhanced growth rate, due to an enhanced food conversion, have an environmental advantage. Transgenic salmon appear to need less food to achieve market size. In addition to the economic advantages for fish farms, this could also lead to a decrease in the demand for fish meal and fish oil. The increasingly intensive nature of aquaculture has led to an enormous increase in the demand for these products in recent years. Fish meal and fish oil are made from various species of small fish which are caught in the oceans. Two to five kilograms of other fish species are needed to produce one kilogram of salmon. The danger of overfishing the oceans as a consequence of the increased demand for fish feed is imminent ('t Hoog, 2003). This enhanced food conversion could lead to a reduced demand for fish meal and fish oil and therefore a reduced chance of overfishing.
Cook (2000) demonstrated that transgenic salmon in the presmolting stage need 10% less food than non-transgenic (control) fish to achieve the same weight. Because the experiment stopped once a body weight of 55 grams had been reached, it is not clear whether such figures also apply to later growth stages. Adult fish achieve market size at a weight of three to four kilograms. More research is needed before it can be concluded that enhanced growth rates lead to enhanced food conversion.

3.2 Tolerance to cold and freezing

In addition to the insertion of the growth hormone gene, research into transgenic salmon is concentrating on the insertion of cold resistance genes. The majority of the bays on the Canadian Atlantic coast are not suitable for salmon rearing, even though the geographical conditions seem to be favourable. Salmon cannot survive in these areas due to the very low water temperatures (around the freezing point) and the formation of ice in the winter. Fish species which can survive in colder waters, such as the previously mentioned blenny and the flatfish "winter flounder", produce antifreeze proteins (AFPs). AFPs lower the freezing temperature of the blood plasma by binding to developing protein crystals, thus preventing their further growth (Fletcher et al., 2001). By providing salmon with AFP genes it is hoped that the production of AFPs will be high enough to make it possible to rear salmon in colder waters. To date, research has demonstrated that salmon injected with AFPs are less sensitive to cold and that the production of AFPs in transgenic salmon is possible. However, the level of transgenically-produced AFPs in salmon does not seem to be high enough to induce cold resistance (Fletcher et al., 2000).

3.3 Disease resistance

Fish which live in large numbers close together are susceptible for infectious diseases. In salmon rearing, diseases such as the contagious and fatal salmon anaemia, infectious haemopoietic necrosis, viral haemorrhagic septicaemia and the sea louse, are responsible for large yield losses. Control is being hindered by the occurrence of pesticide and antibiotic resistance. In addition to this, vaccines are only available for a limited number of diseases and vaccine treatments can lead to stress in fish (Jia et al., 2000). In addition to the economic disadvantages for the fish farmer, sick stocks can form a threat for their wild counterparts. Furthermore, antibiotics and pesticides can enter the environment and have a negative impact on other organisms within the ecosystem.

Researchers are attempting to create disease-resistant salmon to prevent these problems. In so doing, a distinction is drawn between genes which bring about resistance to a single disease and genes which have a broader application. For example, several research groups are focusing on the control of bacterial infections. Hew (1995) inserted a lysozome gene from the rainbow trout (*Onchorhynchus mykiss*) into the Atlantic salmon and Sin (1997) provided transgenic salmon with the magainin gene from the frog (*Xenopus laevis*). The potential of this means of modification has been confirmed by Jia et al. (2000).

These researchers showed that antimicrobial proteins can protect salmon against the fish pathogen *Vibro anguillarum*.

3.4 Flesh colour

Wild salmon have a pink flesh colour due to eating shrimps. Salmon farmers add the colouring agent canthaxanthine (E161) to the fish feed to give reared salmon the same pink colour. In the absence of this colouring agent the flesh of reared salmon would largely be grey in colour. However, the colouring agent has side effects. A high intake by consumers can lead to the pigment accumulating in the retina which can result in impaired vision. As a result of this the European Commission has decided to reduce the quantity of canthaxanthine permitted in the feed (Commission Directive 2003/7/EC).
Despite rumours, there are no indications that efforts have actually been undertaken to provide salmon with a gene that would enable them to produce this pink pigment (Komen, 2001).

3.5 Flesh quality

When salmon become sexually mature their weight and flesh quality decrease. Producing sterile fish is one way of preventing fish from maturing into adults. A frequently used method is the production of triploid fish. Triploidy is induced in fish by means of temperature shocks, hydrostatic pressure shocks or by using chemicals. The eggs are treated shortly after fertilisation which results in the cell having three sets of chromosomes. The disadvantage of this method is that triploidy results in slower growth and a reduced survival chance of the fish.
Other attempts to obtain sterile salmon are directed towards the insertion of anti-sex hormone genes. The aim is to inhibit the production of the sex hormone in these transgenic salmon, so that the salmon do not become sexually mature (Uzbekova et al., 2000). After the administration of sex hormones, the transgenic salmon still become sexually mature so that reproduction remains possible. An important advantage of this method is that the sterility is inherited and can therefore be controlled. Moreover, the fish possess the normal number of chromosomes. Therefore, the disadvantages of an extra set of chromosomes do not appear to play a role in these transgenic fish.

4. Risks of cultivating genetically modified salmon

The environmental risks associated with the rearing of transgenic salmon, are dependent on the chance of escape and establishment, the modification made, the chances and consequences of outcrossing, the consequences for the ecosystem, and the possibilities present for limiting undesired consequences. In this advisory report the possible environmental risks posed by rearing transgenic salmon have been considered against the current practice of salmon rearing. This means that the possible environmental risks associated with intensive fish farming have not been included in the considerations.

4.1 Escape

Fish regularly escape under current salmon rearing methods. Nets break due to wear and tear, weather conditions and incidental accidents. Also a considerable number of salmon escape when the nets are being hauled in. Several examples indicate that large numbers can be involved. In 1988 700,000 salmon escaped on the Norwegian coast due to storms and in 1989 184,000 salmon escaped on the Scottish coast (Webb et al., 1991). In July 1996, seven nets were destroyed at high tide in the vicinity of Cypress Island, Washington, United States, and as a consequence of this more than 100,000 salmon could escape (McKinnel en Thomson, 1997). A considerable number of fish still escape despite the efforts of fish producers to limit this. In its Social and Environmental Report for 2002, Nutreco, the largest salmon producer in the world, states that 0.03% of all fish reared escaped from their nets in 2002. This is equivalent to 15,000 to 16,000 fish. There is no reason to assume that these figures will be any lower for other fish producers.
In view of the aforementioned data it does not seem that escapes can be avoided. If the rearing of transgenic salmon takes place in a similar manner then transgenic salmon will end up in the environment.

If the conditions inside the nets are substantially different from those outside, it is conceivable that escaped salmon will not be capable of establishing or will experience difficulty in adapting. However, aquaculture makes use of nets in the sea to simply and cheaply simulate the environment in which the salmon normally grow. Furthermore, as salmon have a relatively short history of domestication, they have a good chance of surviving and establishing in the wild (Knibb, 1997; McGinnity et al., 1997). Several research groups have demonstrated that escaped salmon are capable of successfully reproducing in

Canadian and Scottish rivers (Volpe et al., 2000; Webb et al., 1991). Studies on the wild salmon population in Norway from 1989 to 1996, demonstrated that 34-54% of salmon from the Norwegian coast, 10-21% in the fjords, 4-7% in the rivers and 21-38% in the pairing places, originated from salmon farms (Directorate for Nature Management, 1999). Furthermore, extensive research carried out between 1966 and 1971 revealed that salmon are capable of travelling large distances. They can cover distances of thousands of kilometres in search of food-rich areas.

4.2 The effects of modification

Whether transgenic salmon are capable of establishing in the wild is in part determined by the modification made. The establishment of transgenic salmon and the environmental risks associated with this depend on the effect of the characteristic on the reproductive and/or survival chance of a salmon.
A better competitive position in terms of food, being a better predator, being a less attractive prey, or having an improved resistance to disease, can increase the transgenic salmon's survival rate. Characteristics which provide a mating advantage or result in the earlier onset of adulthood, also seem to be advantageous for transgenic salmon. In addition to the adverse consequences for wild salmon, increased reproductive and survival rates of transgenic salmon can also adversely affect other organisms in the community.

The limited data as well as the many obscurities and contradictions in the research conducted to date, make it far from easy to determine which consequences the renewed or improved characteristics will bring. Furthermore, it is unclear whether the behaviour of transgenic salmon under laboratory conditions can be translated to the situation in the sea.

4.2.1 Enhanced growth rate

The insertion of the growth hormone gene with the resultant enhanced growth rate seems to affect both the reproductive and survival rates of transgenic salmon. The survival rate is affected by abnormal foraging behaviour, external characteristics and behaviour with respect to predators. Accordingly these abnormalities are also of indirect importance for the mating behaviour of transgenic salmon. The survival rate in part determines the number of transgenic salmon which swim up the river and are capable of mating. Abnormal body size and the earlier onset of adulthood also seem to affect the reproductive rate.

Competition for food

As a result of overfishing the natural quantity of salmon in a number of areas has declined strongly over the past few decennia. The increase in salmon numbers due to escapes of reared salmon and reared transgenic salmon, does not necessarily have to result in competition for food with the wild salmon. However, the consequences for other fish species and other organisms must also be examined in a risk assessment. The niche which has arisen due to the overfishing of salmon has almost certainly been filled. The increase of the salmon population could therefore result in the displacement of the 'newly' established fish species or organisms.

Transgenic salmon with an enhanced growth rate require more food in a short period of time. For example, in experiments in enclosed basins, Abrahams and Sutterlin (1999) found that transgenic salmon consumed five times as much food as salmon from the control group. Cook (2000) and Devlin (1999) demonstrated a consumption two to three times as high. If similar figures apply under natural conditions, this increased food intake could lead to a food shortage for the entire salmon population. An increased food intake can also adversely affect the ecological balance. Overgrazing can lead to the extinction of species. In addition to this, competition with other fish species and organisms dependent on the same food sources can occur.

It is not realistic to assume that transgenic salmon will always be a better competitor. For modifications which lead to a continuously enhanced growth rate, the competition for food during the winter months would seem to disadvantage the transgenic salmon. During the winter months, wild salmon have a period of fasting due to a reduced food supply. In contrast to this the transgenic salmon with their continuous feeding motivation will need food throughout the winter months. The lack of food will lead to debilitation and in the most extreme cases to the death of the transgenic salmon. If despite a limited food supply, the transgenic salmon are capable of finding enough food during the winter then this could cause a serious disruption to the ecological balance (Reichhardt, 2000).

The insertion of a growth hormone gene can also have adverse effects for the salmon. In transgenic salmon the growth rate seems to be correlated with skull and jaw deformities. Overproduction of cartilage in the skull and jaw has been found in transgenic salmon with a strongly enhanced hormone production.

Salmon with these serious deformities are not capable of feeding themselves and will not survive after escaping (Devlin et al., 1995a; 1999).

Predation

The question of whether transgenic salmon with an enhanced growth rate will be better hunters or an easier prey defies a simple answer. Efficient predation depends amongst other things on swimming behaviour. For transgenic salmon, different research groups have demonstrated the presence of improved (Abrahams and Sutterlin, 1999), reduced (Devlin et al., 1999) and comparable (Stevens et al., 1998) swimming performances. Furthermore, the researchers disagree about the behaviour of transgenic salmon as the prey of predators. Devlin (1997; 1999) found that transgenic salmon had a reduced swimming speed and suggested that this reduced capacity resulted in salmon having a reduced capacity to avoid predators. Stevens (1998) was of the opinion that the swimming performance was probably only reduced if the transgenic salmon had an extremely enhanced growth rate. He came to this conclusion after research demonstrated that transgenic salmon with a moderately enhanced growth rate had an enhanced metabolic activity but demonstrated no difference in swimming speed compared to the control salmon. However, all of this does not explain the results of Abrahams and Sutterlin (1999), who for transgenic salmon found a positive correlation between growth rate, swimming capacity and behaviour with respect to predators. According to them, transgenic salmon with an enhanced growth rate are faster swimmers that dared to take more risks in the vicinity of a predator in order to obtain food.

Whether or not transgenic salmon are an easy prey is not just determined by the salmon's swimming speed and anti-predation behaviour, but also perhaps by the salmon's colour. Transgenic salmon with an enhanced growth rate achieve the smolting age earlier, loose their camouflage colours more rapidly and therefore earlier assume the silver grey colour of an adult salmon which departs for the sea (Devlin et al., 1995a; Devlin et al., 1999). If the disappearance of the camouflage colour is not associated with the departure to the sea then these salmon are in a disadvantageous position. Not having a camouflage colour renders them more visible and thus makes them an easier prey (Abrahams and Sutterlin, 1999).

Mating

Transgenic salmon with an enhanced growth rate reach the smolting age (Saunders et al., 1998) and sexual maturity sooner (Devlin et al., 1995). The

generation cycle is reduced from four to two years. As a result of this transgenic salmon are capable of reproducing more quickly than wild salmon.
Although enhanced growth results in an earlier onset of sexual maturity, it seems that the mating season of the transgenic salmon does not differ from that of the wild salmon (Devlin et al., 1995). This means that in addition to matings between transgenic salmon, matings between transgenic and wild salmon are also possible.

It is not clear whether transgenic salmon with an enhanced growth rate are bigger upon reaching sexual maturity. Devlin et al. (1999; 2001) found that transgenic salmon provided with a growth hormone gene were two to three times bigger than salmon from the control group upon reaching sexual maturity. This research was carried out under laboratory conditions. It is unclear whether such figures also apply to natural, less ideal conditions. On its website, Aquabounty (2003) states that despite ten years of experience with transgenic salmon there is no evidence that these are larger upon reaching sexual maturity. Unfortunately this claim is not supported with data. However, the fact that an enhanced hormone production in transgenic fish does not necessarily have to result in large adults is apparent from the study by Muir and Howard (2002). For transgenic medaka (*Oryzias latipes)* they found a final body size identical to that of non-transgenic fish from the control group. Also transgenic rainbow trout were not bigger upon reaching sexual maturity. Interestingly in salmon provided with the same growth hormone gene, larger adult specimens were observed (Devlin et al., 2001).

If upon swimming up the river transgenic salmon have a body size comparable to or greater than that of reared salmon then this will probably result in mating behaviour which deviates from that of wild salmon. According to the data presented below, this deviation will probably benefit the wild salmon. As a result of this the chance of transgenic salmon mating with wild salmon would seem to decrease.
Due to the increase in body size, the mating behaviour found in reared salmon deviates from that found in wild salmon in several respects (Webb et al., 1991; Jonsson, 1997). For example, just like wild salmon, reared salmon return to the river to pair, but in general they do so at a later point in time. As well as the lack of river experience, the body size of reared salmon plays a role. Reared salmon are larger and therefore low water levels early in the season hinder them from swimming upriver. In addition to this it would seem that due to the abnormal body size, wild salmon and reared salmon mate at different locations. Although reared salmon are also found next to wild salmon in the upper river reaches,

wild salmon generally swim further upriver than reared salmon. This reduces the chances of reared and wild salmon mating.

Females seem to prefer larger fish. Muir and Howard (1999) discovered that large male medakas were more successful in mating. However, if the difference in body size between wild females and transgenic males is extreme, it is unlikely that wild and transgenic salmon will recognise each other as members of the same species and crossbreed (Muir and Howard, 2002). Furthermore, body size seems to be linked to aggression. Large males are more aggressive and therefore more successful in the competition for females. However, it is an unclear whether transgenic males also exhibit such aggressive behaviour with the associated mating advantage. For reared salmon, aggression under rearing conditions does not generally provide any mating advantages. Furthermore, salmon with aggressive behaviour are not suitable for rearing conditions. Selection by breeding has resulted in salmon with a large body size and reduced aggression. From the data available it is not clear whether the size advantage transgenic males have in the competition for females, compensates for their reduced aggressiveness.

4.2.2 Tolerance to cold and freezing

The insertion of a cold resistance gene enables salmon to survive under colder conditions. Transgenic salmon which can establish in a new niche due to a new characteristic are considered to be an invasive, exotic species. There is much concern about the associated possible risks for the environment that invasive, exotic species could cause. In the past, the introduction of new species has led to the unwanted displacement of native species. In the 1960s the introduction of Nile perch to Lake Victoria resulted in a reduction in the local fish population. Within 10 years about half of the native fish species had disappeared.

If escaped transgenic salmon are capable of establishing themselves in a new ecological niche, this will inevitably affect the current ecological balance. The salmon will have to compete with other fish species and/or organisms for food and space. Other fish species or organisms which serve as prey or feed upon the same food as the transgenic salmon could be seriously threatened as a result of this. In the worst scenario this could result in the extinction of species. Furthermore, the salmon could in turn serve as a source of food. If the transgenic salmon fail to establish due to reduced fitness then their presence could still influence the ecological balance. How detrimental the disruption to the current ecological balance will be is in part determined by the resilience and adaptability of the current species in the ecosystem.

4.2.3 Disease resistance

The possession of a disease resistance gene does not necessarily have to affect the survival and/or reproductive rates of the transgenic salmon. The transgenic salmon will only have an increased survival and/or mating chance in the event that a disease breaks out for which it has a resistance gene. During a disease outbreak the transgenic salmon will have a competitive advantage. This advantage can result in an improved competitive position for food and/or mating locations. Selection in favour of the transgenic salmon will then take place and this could lead to the displacement of the wild salmon population.

4.2.4 Other modifications

To the best of our knowledge, experiments with modifications other than those mentioned have not taken place. This does not mean that salmon will not be furnished with other characteristics in the future. Such a modification could be the insertion of a gene for the pink flesh colour. Modifications such as flesh colour which are not externally visible would seem to be neither beneficial nor harmful. These characteristics do not result in a demonstrably higher or lower reproduction capacity or an improved or reduced survival rate. In comparison to reared salmon, the escape and establishment of transgenic salmon with such characteristics will probably not give rise to any additional risks.

4.3 Outcrossing

Transgenes can disperse though the wild salmon population due to outcrossing between transgenic salmon and wild salmon. Whether or not the transgene disperses through the population following outcrossing is determined by the effect of the modification on the fitness of the transgenic salmon. A decrease in the prevalence of the transgene can be expected for characteristics which have a detrimental effect on fitness. An increase in the prevalence can be expected if the salmon seems to benefit from the characteristic inserted. This can result in a displacement or even the extinction of the wild salmon population.

4.3.1 Outcrossing model

No data are available about outcrossing between wild and transgenic salmon. Muir and Howard (2002) built a model to estimate which characteristics will or will not disperse through the population and could result in displacement or extinction. No single model can contain all of the complexity present in the natural environment and provide a guarantee that the outcome predicted will actually happen. That also applies to this model. However, it does offer the possibility of seeing which potential dangers could lie in outcrossing transgenic salmon with their wild counterparts.
The effect of the invasion of transgenic salmon on the wild salmon population is predicted using six fitness parameters:

- Survival rate of the immature salmon; the chance that the young salmon will reach adulthood.
- Survival rate of the mature salmon; chance of surviving to matable age.
- Fertility of the female salmon; number of eggs laid by female salmon.
- Fertility of the male salmon; percentage of eggs that are successfully fertilised.
- Mating success; the degree of successful mating.
- Speed with which the mating age is reached.

The six fitness parameters are used to estimate the extent to which the reproductive and foraging behaviour of transgenic salmon deviates from that of their wild counterparts. The fate of the transgenic and wild salmon is predicted by subsequently entering these estimates into a mathematical simulation model.

∗ **Reduced fitness**
A strongly reduced survival rate, infertility or a mating disadvantage due to the inserted gene are factors which result in a reduced fitness of the transgenic salmon compared to the wild salmon. A reduced fitness of the transgenic salmon will, in the ideal case, result in a reduction in the prevalence of the transgene in the incrossed population.

∗ **Comparable or increased fitness**
According to the model, modifications which give the transgenic salmon a comparable or enhanced fitness compared to the wild salmon result in the transgene dispersing through the wild population. Muir and Howard investigated which parameters most enhanced the transgenic salmon’s fitness. Modifications that reduced the age at which the fish reached sexual maturity,

most strongly resulted in an increased fitness, followed by survival rate, mating advantage, fertility of female salmon and the fertility of male salmon. The shorter generation time as a consequence of the earlier onset of sexual maturity means that the gene is dispersed more rapidly. The earlier onset of sexual maturity or an enhanced fertility of the salmon can even negate the effect of a reduced survival rate.

∗ Extinction of the salmon population

Modifications which give the transgenic salmon a comparable or enhanced fitness compared to the wild salmon, but for which at the same time one or more of the six fitness parameters are strongly reduced, can result in the extinction of the salmon population. Unlike reared salmon, the most important characteristic in transgenic salmon is determined by just a single gene. Genes (including transgenic genes) are often pleiotropic in nature. Pleiotropy is where one gene influences several phenotypic characteristics. If the transgenic salmon gain a clear reproductive advantage as a result of the pleiotropic effect but have a reduced survival rate then this can lead to the displacement or even the extinction of the entire salmon population.

The model reveals which pleiotropic effects can result in the extinction of the salmon population. (1) The transgene has an enhanced mating advantage but a reduced viability in the adult stage, (2) the transgene has an enhanced viability in the adult stage but a reduced male fertility and (3) the transgene has an enhanced mating advantage as well as an enhanced viability in the adult stage but a reduced male fertility. With this transgenes that provide a mating advantage for both male and female salmon will more rapidly result in extinction than transgenes which only affect the male sex.

The occurrence of a pleiotropic effect is often associated with transgenic fish with an enhanced growth rate (Hedrick, 2001). The reduced survival rate of transgenic organisms due to the absence of a history of natural selection on the one hand and the mating advantage due to increased body weight on the other, means that many expect that these transgenic fish upon escaping will cause the salmon population to become extinct. This highly disadvantageous effect is sometimes referred to as the ‘Trojan gene effect’. Research into the effect of outcrossing reared salmon with wild salmon seems to support such expectations. McGinnity et al. (2003) demonstrated that a reduced survival rate in combination with a competitive advantage in the production of offspring had detrimental consequences for the salmon population and would probably lead to the extinction of the wild salmon population after several generations.

4.3.2 Consequences of outcrossing for the wild salmon population

Reared (transgenic) populations are less adapted to their environment than their wild counterparts. The wild salmon population is the culmination of thousands of years of natural selection as a result of which the population has adapted to the environment (Directorate Nature Management, 1999). Transgenic salmon populations which have arisen after a relatively short selection procedure have not been selected for survival rates in the wild but for the desired gene. A reduced fitness compared to wild salmon is therefore likely.

Transgenic salmon with a reduced fitness, as a result of which the transgene will not disperse through the population, seem to be relatively safe. However, if there is a repeated influx of transgenic salmon or if the number of escaped transgenic salmon is much higher than the number of wild salmon, natural selection will not occur. The transgenic salmon will be part of the population and could therefore adversely affect the wild population.

The wild salmon population consists of a large number of stocks. These are the local and genetically diverse populations which have adapted to the conditions of their local habitat (Directorate for Nature Management 1999). These populations are genetically diverse and therefore less sensitive to external influences such as diseases, pollution and bad weather conditions. Reared populations on the other hand have a homogenous composition. The selection of characteristics and the fact that the population originates from a select group of parents has resulted in a population with little genetic variation (Gross, 1998; McGinnity et al., 1997). This genetic variation is even less in the case of transgenic populations, as they are genetically more homogenous due to the manner in which they have been created and selected. The outcrossing of transgenic salmon with wild salmon will result in a more homogenous and therefore more vulnerable population.

The second factor which makes transgenic salmon more of a risk for wild salmon than non-transgenic reared salmon, is the increased chance of any harmful pleiotropic effect. In reared salmon, the characteristics selected are determined by several genes (polygenetic characteristics) and therefore characteristics can be inherited independently from each other. A harmful characteristic will disappear due to outcrossing, whereas beneficial characteristics will be retained. A strongly detrimental pleiotropic effect can cause the displacement of the wild population and can even lead to the extinction of the wild salmon population.

The changed genetic composition and the disappearance of the wild salmon population could lead to a loss of unique genes which would be highly desirable at a later stage, for example, in the case of a new disease which can spread among salmon or in a breeding programme.

4.3.3 Consequences of outcrossing for the ecological balance

Both the substitution of the wild salmon population by the reared population and the extinction of the salmon population could be detrimental for other species in the ecosystem of which the salmon is a part. Communities, in which other fish species and organisms besides salmon play a role, have a resilience which allows them to recover after extreme external influences, such as pollution by humans or extreme weather conditions. It is difficult to predict whether they have sufficient resilience to cope with the changed characteristics of the salmon population or the disappearance of the salmon population. New or improved characteristics of the salmon population could mean that they compete more effectively for food and space, or that they are a better predator or a less desired prey (section 3.2). The consequences might not only adversely affect the wild salmon population but could also adversely affect other organisms which are dependent on the same type of food. The disappearance of the salmon could have serious consequences for organisms that use salmon as a food source and which cannot switch to a different type of food. In the most extreme case the characteristics of transgenic salmon could result in them becoming a plague species that causes a loss of biodiversity.

5. Containment measures

With present rearing methods, in which use is made of nets in the sea, it is not possible to take containment measurements that would make the risks of escape acceptably small. The transfer of salmon rearing to land and the production of sterile fish are two methods frequently mentioned as possibilities for containing the risks for the environment.

5.1 Preventing escapes

The present rearing methods in which use is made of nets in bays and fjords, cannot guarantee the containment of the salmon. However, this guarantee can be offered if the rearing is transferred from the sea to the land. If the appropriate containment measures are used, it would seem that salmon could be reared on land without risks for the environment. The entire rearing can take place on land if both salt water and fresh water recirculation systems are used. However, the setting up of such salmon farms is a costly investment and needs to be considered against the economic advantages that a producer thinks he will achieve by rearing transgenic salmon. Despite the high costs, producers are considering a switchover to such systems. The resistance of society to current salmon rearing practices and the advantages which salmon rearing in basins provides are possible reasons for producers to switch over (Reichhardt, 2000). More easily manageable conditions simplify the control of diseases and facilitate an improved control of nutrient and waste substances possible. Land rearing makes it possible to rear salmon in a more sustainable and environmentally friendly manner (Fletcher et al., 2003).

5.2 Sterile fish

A second frequently stated method is the production of sterile salmon and this certainly seems possible from an economic perspective. The rearing of sterile fish species could be an important means of protecting wild species against the possible effects of escape. The production of sterile salmon on a commercial basis is currently being investigated (Reichhardt, 2000).

Triploidy

A currently much used sterilisation method in fish rearing, producing triploid fish, does not guarantee a 100% chance of success. For the most successful treatment, the high-pressure method, 80% to 100% triploid fish are found (Boudry and Chatain, 1999). Furthermore, the statement that triploid salmon are not a threat to the wild salmon population only seems to apply to female salmon. In triploid females, the reproductive organs do not develop, the development of the ovaries is inhibited and the hormone production remains low. As a result infertile triploid females only return to the river in very limited numbers. These characteristics mean that triploid females cannot reproduce (Cotter et al., 2000). Triploid males, however, do develop reproductive organs and have testosterone levels comparable to those of diploid males (Cotter et al. 2000). Should triploid males reach the mating locations and exhibit behaviour that is identical to that of diploid males then this could result in the mating of triploid males with diploid, wild salmon females. The competition between diploid and triploid males for the females present can suppress the reproduction of the wild species (Boudry and Chatain, 1999).

Triploid males do not produce sperm or produce sperm of very poor quality. Despite this poor quality, Cotter et al. (2000) obtained offspring following the artificial insemination of eggs from a diploid female with sperms from a triploid male. These offspring were severely debilitated and had no chance of survival. Due to the strongly depleted number of triploid males which swim back to the rivers the chance of offspring is even smaller still.

Transgenic sterility

An alternative method is to create sterile transgenic fish by inserting anti-sex hormone genes. With this method an effort is made to induce sterility by blocking the production of the sex hormone, gonadotrophin-releasing hormone (GnRH). Results from a project financed by the European Union, ‘Assessment of biological containment and gene flow in transgenic sterile fish’ demonstrated that the method works and can result in sterile transgenic salmon. Research groups from several European countries, under the leadership of the Irish coordinator Smith (2000), indicated in their final report that the insertion of anti-GnRH has produced sterile transgenic rainbow trout. Further publications concerning these sterile fish have yet to appear. However, in the same year a publication appeared co-authored by researchers who were also represented in the aforementioned EU project. They published that attempts to insert the anti-GNRH gene to obtain sterile rainbow trout had not led to the desired result (Uzbekova et al., 2000). The gene was successfully inserted into the genome and could be transferred to following generations and was expressed, but the fish were not sterile.

With sterile salmon the danger of outcrossing seems to be negligible. Either no offspring or no viable offspring are produced. However, sterility does not provide a guarantee that escapes of these salmon will result in no risks or only very limited risks. Escaped sterile transgenic salmon can still survive for many years and disrupt the ecological balance as a result of the new or improved characteristic (see section 3.2). The insertion of a sterility gene does, however, offer the possibility of limiting the adverse effects. If the rearing is stopped, no new influx will occur and eventually the transgenic salmon will disappear from the sea.

6. Conclusions

The environmental risks associated with the rearing of transgenic salmon, are dependent on the chance of escape and establishment, the modification made, the chances and consequences of outcrossing, the consequences for the ecosystem, and the possibilities present for limiting undesired consequences.

If transgenic salmon are reared using the same production methods as for normal salmon rearing then escapes would seem to be unavoidable. A number of factors determine whether the escape of transgenic salmon will be more harmful than the escape of non-transgenic reared salmon.

- Firstly the possibility of its genetic modification provides to insert characteristics which do not occur in the natural population. Inserting characteristics that are not naturally present in the population makes it difficult to predict the behaviour of these fish. Furthermore, the changed characteristics of the fish or the fish population could have an unpredictable effect on other organisms in the community and lead to a disruption of the ecological balance. Moreover after escaping, genetically modified salmon are considered to be an exotic variety in a certain area, as the new characteristics enable these salmon to establish themselves in new environments.
- The second factor is the expectation that transgenic salmon populations will have a more homogenous composition than the reared salmon population, due to the manner in which they have been created and selected. With crossbreeding this lack of genetic variation could have particularly harmful consequences for the maintenance of the wild salmon population and lead to a loss of unique genes that might be very useful in later breeding programmes.
- The third factor which makes transgenic salmon more of a risk for wild salmon than non-transgenic reared salmon, is the increased chance of any harmful pleiotropic effect. Pleiotropy is where one gene influences several phenotypic characteristics. If as a result of the pleiotropic effect the transgenic salmon clearly have a reproductive advantage but a reduced survival rate, this could result in the displacement or even the extinction of the salmon population.

On the basis of the limited data available it is not possible to unequivocally state in which cases the risks for the environment following the escape of transgenic salmon are or are not acceptable. Due to the many obscurities and contradictions in the research conducted to date, the consequences of new or improved characteristics cannot be determined in advance. Up until now no experiments have been carried out in which transgenic salmon or other fish species have been released into the sea. Furthermore, it is unclear whether the behaviour of transgenic salmon under laboratory conditions can be translated to the situation in the sea. The sea is still a largely unknown and complex ecosystem. The consequences of an invasion of transgenic salmon are therefore difficult to predict. A good environmental risk analysis is further hindered by the fact that characteristics which are inserted in the transgenic salmon do not naturally occur in the salmon population.

The use of an environmental risk analysis is based on the precautionary principle. If on the basis of available scientific data it is likely that potentially negative effects for the environment will occur, even if this risk has not been demonstrated, then the precautionary principle must be adopted and steps must be undertaken to avert such a danger.

COGEM is of the opinion that on the basis of current data it is impossible to unequivocally state in which cases the environmental risks are so small as to be negligible. In view of the considerable scientific uncertainty, COGEM calls for as much restraint as possible. On the other hand COGEM is of the opinion that on the basis of scientific arguments it cannot be stated in advance that the rearing of genetically modified salmon will always result in environmental risks. If the rearing takes place on land under extensive containment measures, or if it can be demonstrated that the inserted gene does not entail any additional risks compared to the rearing of non-transgenic salmon then the foreseeable environmental risks of transgenic salmon rearing appear to be small.

At the very least, COGEM recommends the adoption of a case-by-case approach. For each case this should include an extensive environmental risk analysis, based on the specific circumstances. The analysis described in this advisory report could be useful in this respect.

Transgenic salmon, a safe product?

Ethical and societal aspects

7. Transgenic salmon; ethical and societal aspects

Genetic modification of transgenic salmon, and of animals in general, elicits both ethical and societal questions and results in strong emotions. COGEM is not in a position to issue an ethical-societal judgement about the problems posed by transgenic salmon. This is the task of society, the government and parliament. However, COGEM has a monitoring task with respect to genetic modification and with the addition of this chapter it seeks to highlight the arguments in the ethical-societal debate and the legislative problems with respect to transgenic salmon.

7.1 Legislation

COGEM considers it unlikely that genetically modified salmon will be reared or produced in the Netherlands. Due to geographical conditions, Dutch waters seem to be unsuitable for salmon rearing. However, the introduction of transgenic salmon elsewhere in the world could also have consequences for the Dutch environment and Dutch consumers. COGEM draws attention to the fact that the present European and national legislation cannot prevent such cross border consequences for the environment. As a result of this undesirable situations might arise. COGEM also draws attention to the fact that national legislation with respect to the ethical and societal considerations of genetic modification in animals, is not applicable in the case of the introduction of salmon products to the Dutch market.

Environmental risk assessment

Although there are no reasons to assume that the rearing or production of transgenic salmon will take place within Europe in the near future, this possibility is nevertheless still present. At present some of the biggest salmon producers are countries such as Norway, Scotland and Ireland. Before genetically modified salmon can be introduced to the European environment, an environmental risk assessment as established in Directive 2001/18/EC should be carried out. This directive enables European member states to assess the possible risks to their own environment and to verify proposed measures.
However, COGEM draws attention to the fact that if a request is submitted outside of the European Union, it would not appear to be possible to assess the risks for the European environment and to verify the measures proposed. Living organisms such as transgenic salmon can disperse, and are capable of travelling

considerable distances. This means that the possible consequences of the presence of salmon do not have to be limited to the bay or sea in which the escape occurs. Furthermore, indirect effects of the transgenic salmon could affect European waters. For example, the effect of the transgenic salmon's abnormal foraging behaviour on the food chain could be extensive enough to affect European waters. Therefore the environmental consequences of introducing transgenic salmon are probably not limited to territorial waters but could extend to the global ecosystem. COGEM points out that only good international agreements and transparent decision and assessment procedures can guarantee an optimum protection of ecosystems at a global and European level. The Biosafety Clearing House (BCH) set up by the Cartagena protocol could fulfil an important role in this respect. Unfortunately, not all of the countries potentially involved have signed the Cartagena protocol yet.

Ethical acceptability

The genetic modification of animals is an issue which raises a broad range of ethical and societal objections. Therefore under Dutch legislation, it is forbidden to use biotechnological techniques on animals without a licence. The Dutch Animal Health and Welfare Act decrees that without a licence it is not permitted to (1) change the genetic material of animals in a manner which circumnavigates the natural barriers of sexual reproduction and recombination and (2) to apply biotechnological techniques to an animal or embryo. Licences are only granted if in the opinion of the Minister of Agriculture, Nature and Food Quality there is a clearly substantial societal interest and there are no overriding ethical objections to the undertakings. Furthermore, the undertakings are not allowed to have any unacceptable consequences for the health or welfare of animals. Therefore this policy is also referred to as the ‘no, unless policy’. The National Committee on Biotechnology in Animals (Dutch acronym: CBD) provides advice with respect to the request for licences. For genetic modification the CBD weighs up the advantages, scientific interests and societal interests against the disadvantages and the damage to the animal's health, welfare and integrity. It also examines whether realistic alternatives are available. Many people are of the opinion that the genetic modification of animals for production purposes is not substantially in the interests of society. However, this does not seem to be the case with respect to genetic modifications for medical applications.

At present the aforementioned Dutch Animal Health and Welfare Act, does not provide a framework for the ethical and societal assessment of importing genetically modified animals for which the modification has not taken place in the Netherlands. The Ministry of Agriculture, Nature and Food Quality is therefore working on the introduction of an import test for such cases. This test, to be carried out by the CBD, will be on a voluntary basis.

COGEM considers it unlikely that an ethical societal assessment of genetically modified salmon for the purpose of rearing and/or production in the Netherlands will take place on the basis of the Dutch Animal Health and Welfare Act or the import assessment. No salmon are reared or produced in the Netherlands and no change in this situation seems likely for the time being. Moreover it seems that Dutch policy does not consider the genetic modification of salmon for production purposes to be substantially in the interests of society.
Under the present circumstances there is a realistic chance that transgenic salmon products will be introduced to the Dutch or European market within 5 to 10 years of transgenic salmon being permitted on the American market. This could be in the form of the whole fish or fish products, but also as an industrially processed product in which the fish is no longer recognisable as such. COGEM draws attention to the fact that the voluntary import test provides the possibility of making an ethical-societal assessment for the import of living fish, but that such an assessment is not possible for the import of processed fish. If the fish producers satisfy the food safety rules laid down in the European legislation (Regulation 2002/178) then there appear to be no legal frameworks which can hinder this introduction of transgenic salmon products to the Dutch market. This is irrespective of the possible ethical and societal objections which such a product elicits. In view of the public discussion concerning the genetic modification of salmon, this could lead to an undesirable situation.
However, in relation to this it should be noted that the acceptance of the product by consumers will to a significant extent determine how long the product remains on the market following its introduction.

7.2 Ethical and public discussion

The discussion surrounding the production of transgenic salmon goes beyond the consequences for the salmon and also covers the manner in which the rearing and production of salmon takes place. The arguments presented with respect to this mainly concern the integrity, health and welfare of the animal, food safety, consumer acceptance, the dangers for the environment and the economic interest.

Integrity, health and welfare of the salmon
A key aspect in this discussion about transgenic salmon in the damage to the fish's integrity. Changes to the genetic material of the fish are considered to be an infringement on the integrity. The nature of the modification and the manner

in which this modification is realised are subordinate issues in this respect. In addition to the integrity of the fish, the integrity of the species can also be infringed upon. Changes to species-specific characteristics lead to an infringement of the species' integrity. For example, modifications which result in the consumption of plants instead of animals will affect the salmon's predatory behaviour. Species-specific characteristics, such as the manner in which salmon hunt living prey, will disappear as a result of this.
Physical abnormalities and behavioural changes can affect the salmon's health but also its welfare, ability to fend for itself and its integrity. In transgenic salmon with a strongly enhanced growth rate, jaw deformities that prevent the salmon from feeding have been found. Such abnormalities are regarded as harmful to the salmon’s health and welfare as well as to its ability to fend for itself. Also in salmon with a continuously higher feeding motivation due to an enhanced growth rate, the welfare and ability to fend for itself seem to be harmed. These salmon will need to eat more food in less time in order to satisfy their hunger.
Whereas the aforementioned modifications clearly seem to have consequences for the salmon, the consequences for a number of other modifications will be less clearly visible. Modifications which result in a pink flesh colour or an improved flesh quality do not have to result in physical abnormalities or behavioural changes. With such modifications aspects, such as health, welfare and the animal’s ability to fend for itself seem to play a less important role in the public discussion.

Food safety

Food safety scandals such as those involving salmonella, growth hormones and dioxins have led to a loss of consumer confidence in food. A term such as ‘Frankenstein food’ clearly indicates society's negative feelings and anxiety with respect to genetically modified food.
In direct contrast to this is the assertion from producers that the product they eventually market is safe. Prior to a market introduction of transgenic food all possible safety requirements in the area of food safety as established in European legislation (Regulation 2002/178) must be satisfied. In Europe, these food safety assessments are carried out by the European Food Safety Authority (EFSA). All stages in the production and processing process are considered in the assessment of the safety of the food for humans and animals.

Consumer acceptance

European consumers are extremely cautious about genetically modified food (Eurobarometer 58.0, 2003). There is often a strongly dismissive attitude towards the genetic modification of animals. A large group within the population will only accept the modification of animals if it is substantially important. The modification of animals for medical applications elicits relatively little resistance but the production of transgenic animals for food production seems to be accepted to a much lesser extent. Furthermore, European consumers want the freedom to be able to choose whether or not they eat transgenic fish. The acceptance of food is directly proportional to the freedom of choice that consumers have. This requires clear labelling so that the consumer can see if a GMO is involved or if the product contains GMOs. An ongoing issue in relation to this is the unforeseen presence of GMOs. Products which contain traces of or unintended contamination by GMOs but fall below the boundary value of 0.9% set by the European Commission, do not need to be labelled.

Companies in the fish sector recognise the consumer feelings and are fairly cautious when introducing new products. Consumers have accepted the reared "natural" fish and trust the sector. The fish sector has a reputation of being 'healthy' and is careful to maintain this image. The production of genetically modified fish could harm the sector's image as well as its turnover and profitability. This is one of the reasons why some companies have decided not to pursue the rearing of transgenic salmon.

Environment

Potential risks such as the loss of biodiversity and genetic variation as well as the displacement and extinction of the salmon population are not only aspects included in the scientific environmental risk assessment but are also arguments raised in the public discussion. These objections to transgenic salmon are boosted by the harmful effects associated with the intensive production of non-transgenic salmon. The leakage of feedingstuffs and animal waste substances results in eutrophication and oxygen depletion in the surrounding environment.

Conversely there are arguments which emphasise the importance of transgenic salmon for the environment. As salmon with an enhanced growth rate have an enhanced food conversion, the demand for fish oil and fish meal could decrease, thus counteracting the depletion of natural fish supplies. In addition to this, providing salmon with a disease-resistance gene could lead to a reduced use of pesticides and antibiotics. Also if trawlers no longer have to set sail the reduced use of energy could lower the environmental impact. The claim that the rearing of transgenic salmon could counteract overfishing also applies to the rearing of non-transgenic salmon. However, in the public discussion this is often presented as advantage of producing transgenic salmon.

Economic interest

Proponents of transgenic salmon also use the economic interest as an argument. Genetic modification allows salmon to the developed with characteristics that they could not acquire by means of conventional breeding. For example, larger salmon can be reared or the salmon rearing can be extended to areas that were previously unsuitable in terms of climate. This provides economic advantages for the producer and can, for example, result in increased employment. Furthermore, the production of transgenic salmon could help to solve the food problem and lead to greater food certainty. Also economically important aspects such as technological innovation, the increased technological advantage and cooperation in technological areas are presented as advantageous aspects in discussion. However, a number of these arguments are also presented as disadvantages in the discussion. The use of transgenic salmon and the associated economic advantages are only reserved for large capital-rich companies. These could leave small businesses at a competitive disadvantage.

Other aspects

The discussion is not limited to the aforementioned arguments, as cultural and religious viewpoints equally play a role. Elements such as the cultural appreciation of food, religious opinions and respect for animals and the environment also have a place within the discussion. However, these elements apply not only to transgenic salmon but also to the public discussion about GMOs in general.

7.3 Assessment framework

New developments in biotechnology require a continual adjustment of the ethical-societal viewpoint. There is no general consensus about what is ethically acceptable. This means that for each new request, all aspects relevant for the formation of an opinion need to be itemised and considered.

COGEM recently presented the monitoring report 'Naar een integraal ethisch-maatschappelijk toetsingkader voor moderne biotechnologie [Towards an integrated ethical-societal evaluatory framework for modern biotechnology] (CGM/030618-02)' to the State Secretary for Housing, Spatial Planning and the Environment. This monitoring report has outlined a model for the integral ethical assessment of biotechnological developments. The evaluatory framework contains, for example, a step-by-step plan that can be used to systematically consider all aspects relevant to the assessment and the formation of an opinion. The model contains a checklist of the values, objectives and interests involved. Both the ethical justification and the ethical consequences are

considered, as is usually the case under current policy (Letter from state secretary Van Geel to the Dutch Lower House, 2003).
The evaluatory framework can be helpful in an ethical-societal assessment of new technological innovations, such as the genetic modification of salmon. The framework can be used to itemise and highlight relevant elements. It is an instrument which can help the government in assessing ethical-societal questions and forming policies with respect to this. It can also help producers as they aim to realise sustainable and socially-responsible business practices. The framework can play a facilitatory role by providing the producer with insights into the issues that might play a role in the public discussion about his product.

Using the checklist to itemise the arguments for and against genetic modification provides the following positive and negative aspects. As this is not a case study about one specific modification, all of the general points for consideration are stated. If only one specific modification is involved, a number of aspects will not be relevant.

Positive aspects	**Negative aspects**
Economic interest: cheaper production, better competitive position	Loss of biodiversity and genetic variation
Environmental benefit: reduced use of antibiotics or pesticides	Damage to the salmon's integrity, health and welfare
Enhanced food conversion: less environmental pressure due to reduced use of fish meal and fish oil	Damage to the integrity of the species.
Expansion of rearing areas: increased production	Damage to the salmon's ability to fend for itself
Technological innovation	Cultural appreciation of food
Increased technological advantage	Unintended consequences for third parties, industry, producers, consumers, freedom of choice, animals
Technological cooperation	Respect for the environment and the animal
Increased employment	
Positive contribution to food problem	

If the decision is taken to introduce transgenic salmon to the North or Central American markets, there is a real chance that a policy response will be required within the next 10 years. A further positioning in a Dutch and European context can prevent policy lagging behind new developments.

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Ethical and societal aspects

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