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REPORT

Safe production of farmed Atlantic salmon *(Salmo salar)*

***ΣChain*: Developing a Stakeholders' Guide on the vulnerability of food and feed chains to dangerous agents and substances (EU Strep FP6-FOOD-518451**

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ABSTRACT

This work contains a review of the undesirable substances that may be introduced as contaminants of natural and malicious origin, and of emerging hazards, in the production chain of farmed salmon, from ova to packed fillet.

The work, focused in the supply chain to European countries, contains a brief introduction to general food safety in relation to aquaculture products, followed by an overview of the production chain for salmon with indication of where in the chain the undesirable substances might be introduced.

The review ends with the outlining of best manufacturing practices, the identification of emerging risks and the application of the failure mode effects analysis methodology to the identification of the steps, in the entire production chain, vulnerable to contamination.

KEYWORDS	ENGLISH	NORWEGIAN
GROUP 1	Safe production, food contaminants	Trygg produksjon, kontaminanter i mat
GROUP 2	Farmed salmon, food safety	Oppdrettslaks, matvaretrygghet
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Introduction

On the 28th of January 2002 the European Parliament and the Council adopted Regulation (EC)178/2002 laying down the General Principles and requirements of Food Law. The Regulation establishes the basic principle that the primary responsibility for ensuring compliance with food law, and in particular the safety of the food, rests with the food business. The same principle applies to feed business. The food business operators must therefore take the all the necessary measures to ensure that the food they produce is fit for human consumption. Serious food safety incidents during the 1990's (the most famous of which was probably the 1999 contamination of Belgian with poultry polychlorinated biphenyls and dioxins and their subsequent export to many European countries (Van Larebeke et al., 2002), led to a considerable focus on hazards and contaminants. This focus on safety resulted in the establishment of new maximum limits for dioxins in food (CR (EC) No 2375/2001) and the approval of the Regulation (EC) No 178/2002 laying down the general principles and requirements of Food Law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. It also made mandatory the implementation of traceability - defined as the ability to trace and follow a food, feed, food-producing animal or substance intended to be, or expected to be incorporated into a food or feed, through all stages of production, processing and distribution - in Europe from the 1st of January of 2005 (CR (EC) No 178/2002). The Regulation also establishes the over-arching principles, definitions and requirements on which all future food law in Europe will be based.

Safe food production is supported by the implementation of risk analysis, international standards, guidelines and recommendations such as those developed by the The Codex Alimentarius Commission (FAO, 2004) and the Hazard Analysis and Critical Control Points (HACCP) system (FAO, 1998; Huss et al., 2004), which are obligatory in Western countries. HACCP is a systematic preventive approach to food safety that addresses physical, chemical, and biological hazards from the point of view of preventing contaminations, rather than relying on testing and inspecting the finished products. HACCP is used in the food industry to identify potential food safety hazards. Additional European legislation that applies to food safety includes (EC) No 852/2004, on the hygiene of foodstuffs; (EC) No 853/2004, laying down specific hygiene rules for the hygiene of foodstuffs; (EC) No 854/2004, laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption and (EC) 99/2002 laying down the animal health rules governing the

production, processing, distribution and introduction of products of animal origin for human consumption. In addition, the European Community has had a rapid alert system since 1978: it was first established by a Council decision and later replaced by a specific provision in the Council Directive 92/59/EEC regarding the general safety of products, where Article 8 provides the legal basis for the European Community's rapid alert system for food products and for other consumer products. The Member States have a duty to provide information urgently if a serious and immediate risk to the health of consumers is detected. By this directive the Member States are obliged to report via the Rapid Alert System for Foodstuffs (RASFF) those cases where a dangerous food product could be sold outside the territory of the Member State that has identified the specific risk, but in practice the detection of a dangerous food product it is being notified always.

The EC's concern about the food safety of its citizens is also reflected in financial support to research projects aiming at its improvement. Σ-Chain is one such EU-financed STREP project with one Brazilian and ten European participants (EU Strep project FP6-FOOD-518451) whose objective was to develop a Stakeholders' guide to identify and address the vulnerability of food and feed chains to contamination with dangerous agents and substances. The project addressed the total production chain of four selected food products as case studies (water, poultry meat, milk powder and farmed salmon). Farmed salmon, the case presented in this work, was selected to illustrate a long-geographic production chain.

Over the past three decades, aquaculture has become the fastest growing food-producing sector in the world. The production of both Atlantic and Pacific salmon has increased from a few thousand metric tonnes in 1980 to about 1,9 million tonnes in 2004 (FAO, 2006). Farmed salmon is a recognized nutritious source of protein and it is also rich in long-chain polyunsaturated omega-3 fatty acids (PUFAs): eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA are known to have many positive effects on human health. Probably the most known are their effects on prevention of coronary heart disease and support of cardiovascular health (Siddiqui et al., 2008) but additional studies have shown that these fatty acids may also support human health by improving brain function (Boudrault et al., 2009) and brain development (Innis, 2007), they have been proposed as effective diet components in cancer prevention and treatment (Berquin et al., 2008) and have been shown to be effective in therapies for diseases characterized by immune dysfunction (Calder, 2001).

However, during the production of any foodstuff there is a potential danger of contamination with hazardous substances, and farmed salmon is no exception. Hazards of concern in the production of farmed salmon include mainly pathogenic bacteria, chemical contaminants and residues from veterinary treatments. Parasites, toxins and malicious contaminations must be taken into account although the probability of their occurrence is very small. Thus, although Europe has had a low incidence of food safety incidents from farmed salmon (80 cases in 2006 and 58 in 2007) (RASFF, 2008) and the benefits of consuming fish seem to greatly surpass its potential risks (Mozzafarian and Rimm, 2006), the hazards must be examined, addressed and eliminated from the production chains. The following sections of this review present the most relevant potential contaminants in the production chain of farmed Atlantic salmon together with methodologies suitable to identify weaknesses in its production in order to that make the product safe for human consumers. It must also be noted that during the preparation of this manuscript an excellent book was published on the subject of farmed fish quality and safety (Lie, 2008).

1 Production chain of farmed salmon

The production chain of Atlantic salmon consists of five main steps: (1) brood stock and ova production, (2) fry and smolt production, (3) on-growing, (4) slaughtering and processing to produce fillets of salmon and (5) distribution of the fish products to the market. In addition there is transport of live eggs and fish between the different production units which can cross regional and national boundaries, and fish feed production and distribution. All salmon species are carnivorous and eat other live aquatic animals such as smaller finfish, crustaceans and invertebrates. In the farmed environment, the feed consists almost exclusively of formulated dry pellets, with about 10% water content, which are produced most often by extrusion technology. A large proportion of salmon feed is made from aquatic, marine raw materials, namely fishmeal and fish oil (Hardy, 1996) but lately new formulations are being introduced with a larger proportion of vegetable oils (Bell, 2008). The feed formulations, optimized for each of the breeding steps, change depending on the phase of growth in the production chain.

2 Potential contaminants in the farmed salmon chain

Potential and emerging contaminants may be introduced at any of the above listed steps in the salmon production. Contaminants that accumulate in the edible part of the fish, such as dioxins or heavy metals, are usually considered a higher risk than those than can be eliminated or washed out during the rearing of the fish (veterinary treatments, bacterial contaminations) so that the fish may be made free of these contaminants by the time of slaughter. Persistent contaminants are usually introduced together with the feed and include toxic metals such as methyl-mercury, inorganic arsenic, cadmium, phosphorated and halogenated organic compounds, polychlorinated biphenyls (PCBs), dioxins and pesticides (Berntssen and Lundebye, 2008). More recently new hazards have been detected, notably melamine and cyanuric acid (Andersen et. al., 2008; Brown et. al., 2007; Reimschuessel et al., 2008). Several other hazards can enter the chain through veterinary treatments (antibiotics such as chloramphenicol or the forbidden antiparasitic drugs malachite and leuco-malachite green and crystal violet), from the natural environment (*Listeria*, spp) or from the post harvest handling (*Costridium Botulinum, Staphylococcus aureus*). Some of the most important contaminants in the farmed salmon production chain are listed in Table 1.

2.1 Virus

Viruses only multiply in susceptible host cells. Human enteric viruses may become a problem only if seafood is contaminated and transmits the infection to the consumer. Infected people may excrete the virus particles and therefore sewage discharges into farming and harvesting water pose a problem. Viral infections are most relevant in shellfish grown in contaminated waters (Lees, 2000), but there have also been outbreaks caused by infected food handlers and infected wash water or ice supplies (Carter, 2005). Fish, and farmed fish, do not seem to be a source of foodborne viral infection, although viruses cannot completely be disregarded as an emerging risk in farmed salmon production, since the main problem to discover and link viruses to diseases lays in the difficulty to detect them (Svensson, 2000). Improved detection techniques may change this perception. Control measures consist of ensuring clean water and ice supplies and ensure all food handlers follow good hygiene practices and medical screening practices- especially return to work after sickness (Regulation (EC) No 852/2004).

Table 1. Potential contaminants of natural, malicious and emerging contaminants that might be a risk in the farmed salmon chain.

Group of Substances		Names of contaminants
Drug residues	Antibiotics, antihelminthics and antiparasitic	Chloramphenicol, florfenicol, nitrofurans, oxolinic acid and flumequine, florfenicol, sulfonamides, quinalones, tetracylines, diflubenzorone, cypermethrine, praziquantel, fendendazole, emamectin, ivermectin, delthamethrin, emamectin benzoate, malachite green and leuco-malachite, crystal violet, teflubenzuron
Inorganic compounds	Salts and ionized compounds and toxic elements	Caustic soda, phosphates, carbonates, and silicate salts, sodium hypochlorite, arsenic, cadmium, flourine, lead and mercury
Biological	Virus, bacteria, moulds and parasites	Hepatitis A and Norwalk virus, *E. coli*, *L. monocytogenes*, *Enterobacteriacea* bacteria of the genus *Bacillus*, *Campylobacter, Clostridium, Leptospires, Salmonella, Shigella, Staphylococcus, Vibrio, Yersina*, moulds, *Anisakis simplex, Cryptosporidium parvum* and *Diphyllobothrium*
Toxins	Mycotoxins and neurotoxins	Aflatoxins, fumonicins and others, *C. botulinum* toxin
Organic compounds	Alcohols, aldehydes, antioxidants, mineral oils, nitrogenous compounds	Coloured dyes, alcohols, glycol ethers, formaldehyde, butylated hydroxytoluen (BHT) and butylated hydroxyanisol (BHA), ethoxyquin, mineral oils, diesel, nitrosamines, melamine
	Organobrominated compounds	Polybrominated diphenyl ethers (PBDEs)-28, 47, 99, 100, 153 and 154
	Organochlorinated compounds	Aldrin, camphechlor, chlordane, heptachlor, DDT and related compounds, dieldrin, dioxins (PCDD/PCDF) and dioxine-like PCBs), endosulphan, endrin, isothiazalones, lindane (gamma-hexachlorocyclohexane (HCH), benzene hexachloride (BHC), polychlorinated biphenyls (PCBs)
	Phtalates	Phtalates
	Polyaromatic Hydrocarbons (PAH)	Bromodiolone
	Surfactants	Quaternary ammonium compounds, other surfactants
	Solvents	Kerosene, white spirits, turpentine
	Synthetic pyrethroid	Cypermethrin and deltramethrin
Others	Forbidden animal species, GMOs and derivates, radionuclides	Forbidden processed animal protein (meat-bone meal and blood meal), antibiotic resistance genes (GMO), technetium
	Physical contaminants	Glass, metal pieces, plastics and poly balls

2.2 Mycotoxins

Mycotoxins are secondary metabolites produced by fungi; they enter the production chain through feed contamination and have the potential to reduce growth and seriously affect fish and shrimp health, although we are not aware of cases where humans have become affected after ingestion of fish fed with contaminated feeds. The most relevant mycotoxins in aquaculture are aflatoxins, ochratoxins, cyclopiazonic acid, fumonisins and trichothecenes produced by the genera Aspergillus, Pencillium and Fusarium (Encarnação, 2007). Mycotoxin contamination of aquaculture feeds may increase due to the fact that feed ingredients of plant origin, which are more susceptible to contamination than ingredients of animal origin, are increasingly being used in fish feed manufacture (Santacroce et al., 2008). The potential for

contamination is higher under tropical and subtropical conditions than in temperate or arctic zones (CAST, 2003). Mycotoxins also appear to be very heat stable and the pelleting and extrusion process of fish and shrimp feeds do not seem to effectively reduce their levels (Manning, 2001). Problems caused by mycotoxins can be reduced or eliminated by using only high quality feeds and by screening the oils and other ingredients used in their manufacture. Maintaining good storage conditions and the use of mycotoxin deactivators (binders) or biotransformation of the toxins (using microorganisms or enzymes that specifically degrade the toxic structures to innocuous metabolites) will help to improve the safety of fish feeds (Encarnação, 2007).

2.3 Neurotoxins of bacterial origin

Toxins produced by *Clostridium botulinum* types A, B, E and F cause human botulism. The symptoms develop after 12-72 hours of ingestion and consist of nausea, vomiting, fatigue, dizziness, headache, dryness of the skin, mouth and throat, constipation, paralysis of muscles, double vision and finally respiratory failure and death (Jay, 2000). At high doses the toxins may be fatal within 24 hours. Botulism outbreaks are usually associated with the consumption of home-prepared undercooked foods, including seafoods. Control of *C. botulinum* in fishery products can be achieved by heat inactivation of the spores or by inhibiting the growth of the bacterium during processing of products intended to be consumed without a final heating step, for example controlling the salt concentration in the smoking of salmon (Martens, 1999).

2.4 Bacteria

Foodborne illnesses caused by bacteria may arise from the ingestion of live bacteria, and subsequent infection, or by intoxications due to the ingestion of toxins formed in the foodstuff prior to consumption, as mentioned above for botulism (Lee and Rangdale, 2008). Some pathogenic bacteria may contaminate the fish in its natural environment (*L. monocytogenes, Bacillus cereus, Vibrio* spp) and others contaminate the product during processing (*Clostridium botulinum, C. perfringens*, see above section). Human workers can also contaminate the product due to deficient hygienic practices (*E. coli, Staphylococcus aureus, L. monocytogenes, Salmonella* (Dorè, 2008). Human pathogenic bacteria can also contaminate the fish in its natural environment if the water where the fish is farmed is contaminated with sewage water. The most common seafoodborne pathogenic bacteria are *L. monocytogenes, Salmonella* spp *and Vibrio* spp while the most common intoxications are due to *C. botulinum, C. perfringens, B. cereus* and *S. aureus* (Dorè, 2008). *L. monocytogenes* has often been

isolated from ready-to-eat products such as shrimp, cold and hot-smoked salmon and trout (Ben Embarek, 1994; Espe et al., 2004; Jørgensen and Huss, 1998; Martinez et al., 2003), although listeriosis outbreaks have seldom been traced back to fishery products or farmed salmon (Martinez et al., 2003 and references therein). The potential sources of contamination for *L. monocytogenes*, in particular in smoked salmon products, are many and include the tools, workers and environments of the processing companies (Martinez et al., 2003), although contamination levels are usually low and consumers are probably seldom exposed to risk concentrations (Rorvik, 2000; Lee and Rangdale, 2008). In any case, it is important to identify the sources of contamination and the factors that permit to control the growth of *L. monocytogenes* in salmon and salmon products in order to develop suitable control measures and corrective actions to avoid infections and eliminate them. Strict attention must always be paid to cleaning and disinfection to avoid the occurrence of *L. monocytogenes* and the in-plant colonization (Autio et al., 1999).

Curiously, and probably due to the similarity of the names, *Salmonella* was identified during Σ-chain, as the zoonotic pathogen that consumers most often were concerned about in farmed salmon (Frewer and Kher, University of Wageningen, personal communication). This bacterium can induce diarrhea in humans and the infection source is usually through contaminated is probably via carrier workers or contaminated environments. The risk of transmission of this bacterium from contaminated feeds to consumers is extremely low and no direct association has been found between isolates from feed and from human patients (Lunestad and Rosnes, 2008). We are aware of only one incident, in China in 2007, where frozen salmon filets were infected with *Salmonella* (RASFF, 2007). Most producers of farmed salmon should follow very strict regulations, routines and controls (Nesse et al., 2005; Lunestad et al., 2007) including a 1-2 weeks prior to slaughter starvation period to prevent contamination of the fillet with bacteria from the gut. In any case, Salmonella spp have not been shown to be able to establish or multiply in the intestine of cold water fish (Lunestad and Rosness, 2008).

Vibrio species have been associated with intestinal or extra-intestinal infections in humans (e.g. *V. cholerae, V. parahaemolyticus*) but most often these infections have been associated with consuming raw shellfish and seafood (Lee and Rangdale, 2008), not with salmon products.

2.5 Parasites

There are two parasites that may be of concern in farmed salmon: *Anisakis simplex,* that may cause anisakidosis (Inoue et al., 2000) and *Diphyllobotrium latum*, that causes dyphyllobothriosis (Cabello, 2007). Anisakidosis curses with epigastric pain, nausea, vomiting, diarrhoea and urticaria and dyphyllobothriosis by epigastric pain, abdominal cramps, vomiting, loss of appetite, dizziness and weight loss; but both infections can also be asymptomatic (Jay, 2000). A parasitic infection requires that the parasite be alive when ingested, which may be the case when one consumes dishes of raw (sushi, sashimi), semi-raw (ceviche) or undercooked fish. In Europe, the Council Directive of 22 July 1991 laying down the health conditions for the production and the placing on the market of fishery products (EU CEC Directive 91/493) requires that fish to be consumed raw must previously have been frozen to -20C or lower for 24 hours or longer to kill potential parasites, and this makes these infections rare in Europe. However, cases of anisakidosis and diphyllothriosis after the consumption of raw farmed salmon have been registered in Japan (Inoue et al., 2000) and Brazil (Cabello, 2007).

2.6 Drug residues

Veterinary treatments have always been part of the routines to prevent and treat diseases. In the farming of Atlantic salmon veterinary drugs have usually one of three purposes: as antibacterial, antiparasitic or as anaesthetics used during handling of live fish, for example during vaccination programs (Lunestad and Samuelsen, 2008). Unfortunately, a widespread and unrestricted use of large amounts of antibiotics for prophylactic purposes has been registered in aquaculture production especially in developing countries (Cabello, 2004, 2006). As a consequence, the surrounding waters have been contaminated with the antibiotics and this has resulted in the emergence of antibiotic-resistant bacteria in the aquaculture environments and in alterations of the bacterial flora both in sediments and in the water column. Antibiotic resistance has also been transmitted to pathogens of fish and of terrestrial animals including man (Cabello, 2004, 2006; Serrano, 2005): for example, quinolone-resistant clinical strains of E. coli have been identified in China (Wang et al., 2001). In addition, some of these drugs, such as malachite green, crystal violet, nitrofurans and chloramphenicol may have a direct adverse effect on humans, the first three as potential carcinogens and the latter as a cause for aplastic anemia (WHO, 2004). Additional effects, caused either by the drugs or its metabolites include allergies, and changes in the intestinal flora (Cabello, 2006; WHO, 2004). In Europe, the use of antibiotics has been markedly reduced from the 1990 and up to date: as

an example, Norway has reduced the use of amphenicols and quinolones by a 97 % from 1987 to 1996, and has thereafter remained relatively stable (NORM/NORM-VET, 2006). This reduction is mainly attributed to the introduction of effective vaccines and vaccination programs as well as improved health management. Thus, the risk of finding drug residues in salmon is a function of the frequency of using antimicrobials by the industry, and it is reduced by the implementation of restrictive legislation and successful vaccination programms (Alderman and Hastings, 1998; Cabello, 2006). In addition, both unapproved drugs (general purpose chemicals that are not labelled for drug use) and approved drugs (but administered in a manner that deviates from the labelled instructions) may be used in fish farming, particularly, in countries with more lenient legislations. The use, and responsible use, of antibiotics in aquaculture has been reviewed by Serrano (2005) and the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF; http://www.fsis.usda.gov/Codex_Alimentarius/Codex_Committee_Vet_Drugs/ index.asp) has issued a series of recommendations to governments and international organizations in order to collect information and standardize risk management and risk assessment.

Malachite green and crystal violet are triphenylmethane dyes. The former has been used as a topical fungicide and antiprotozoal agent in salmonid farming throughout the world for over 60 years. And the latter is also known to be effective in the treatment of fungal infections and it was used as a feed additive to inhibit mould and fungal growth in poultry feed before 1990. Both of them are currently banned substances and seldom, but regularly, detected in fish products. Interestingly, while the detection of malachite and leucho-malachite green is becoming increasingly sporadic, the number of cases where crystal violet is detected seems to be increasing (RASFF 2003-2008). Within the EU, each member state is required to monitor for malachite and leucho-malachite green residues with analytical methodology that meets at least the minimum required performance limit (MRPL), which in the EU is set at 2 μg (malachite and leucho-malachite green) per kg fillet (European Commission Decision of 22 December, 2003 amending Decision 2002/657/EC as regards the setting of minimum required performance limits (MRPLs) for certain residues in food of animal origin) but there is currently no MRPL set for crystal violet.

The concern of consumers about drug residues in seafoods and salmon is expected to increase (Espe et al., 2004). The EU has set some maximum residue levels (MRLs that include a safety margin) for drug residues in order to ensure that farmed fish are safe for consumption. The

EU Directive 96/23 states that for all food-producing animals, at least one sample per 100 tonnes of annual production must be examined for drug residues and other undesirable components. In addition, fish samples must be taken from a minimum of 10 % of the registered sites of production annually. It is also important to respect the withdrawal period (period of time elapsed from the last treatment until the level of residues in the tissues is lower than or equal to the MRL) prior to harvest, which is dictated by governmental regulations. The length of the period depends on the drug, it is set out in the data sheet for the medicine and it usually takes from 20 to 40 days (Fairgrieve and Rust, 2003). Farmers are required by law to record all uses of animal medicines and it is therefore straightforward to ensure that withdrawal periods are observed. The responsibility for keeping residues under the MRL lies with the veterinary surgeons and farmers who use the licensed animal medicines (Serrano, 2005).

2.7 Metals

Some inorganic chemicals essential for life at low concentrations become toxic at high concentrations (e.g. heavy metals like copper, selenium, iron and zinc). Others, such as mercury, cadmium and lead, show no function in life, are toxic even at low concentration and are requested to be monitored in salmon by law. They can enter the fish through the gills from the surrounding water or through fish meal made from contaminated raw materials, the latter being the most common route (Fairgrieve and Rust, 2003).

Methyl-mercury is the main and most toxic form of mercury (Harada, 1995; Harada et al., 1998). Fish may absorb great amounts of methyl-mercury from surface waters that can subsequently accumulate it in their tissues and in the food chains that they are part of. There are no records of farmed salmon accumulating methyl-mercury (Fairgrieve and Rust, 2003), although it has been detected in wild salmon and in other species like large predatory fish such as swordfish and tuna (Yamashita et al., 2005; FDA, 2001; RASFF, 2008). Methyl-mercury can pose harm to human health, particularly neurobehavioral development and the EU regulation 466/2001 allows a maximum content of 0.5 mg mercury per kg fillet in most species, while the measured levels vary in the interval 0.02-0.06 mg/kg.

The toxicity of arsenic depends on its chemical species and in contrast to mercury whose most toxic form was the organic, the inorganic forms of arsenic are the most toxic ones (Amlund et al., 2006). The non-toxic arsenobetaine (Amlund et al., 2006) is the predominant form in

marine fish (Francesconi and Edmunds, 1997), while lipid soluble forms of arsenic, called arsenolipids, may be present in fish oil and contribute significantly to the total level of arsenic in complete feedingstuffs. Little is known about their carry over from feed to flesh and potential toxicity to humans (Sloth et al., 2005) and while complete feedingstuffs have a maximum limit of 4 mg/kg arsenic (European Commision Directive 2003/100/EC; Tab. 3), there is no EU maximum level for arsenic in foods, although some member countries have established their own limits.

Cadmium is also a contaminant of interest and although its uptake from food is low, once taken up it accumulates in liver and kidneys. The maximum permitted level of cadmium in fish in the EU is 0.05 mg/kg wet weight (European Commision Regulation 2001/466).

Toxic elements like fluorine (which generally occurs in nature as fluoride) may be found in certain raw materials used in the manufacture of salmon feed, such as marine crustacean, since fluorine is one of the most abundant elements in the environment. Fluorine is beneficial to human health in trace amounts, but can be toxic in excess. Complete feeding stuffs has a limit of maximum content of 150 mg/kg (European Commission Directive 2003/100/EC; Tab. 3) and raw materials used in the manufacture of salmon feed are required to be screened for fluorine contamination.

2.8 Organic Compounds

2.8.1 Antioxidants

Antioxidants like ethoxyquin, butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are synthetic additives widely used to preserve feed stuffs and fish feed from spontaneous oxidation. Antioxidants stabilize critical oxidation-susceptible nutrients that are naturally present in a fish feed composed of several feedstuffs so that losses are minimal from mixing and storing (FAO, 1980).

2.8.2 Melamine and cyanuric acid

Worldwide contamination of a large variety of foods and feeds with melamine has received a significant amount of attention during 2007 and 2008. Melamine, whose molecular formula is $C_3H_6N_6$, contains 66% nitrogen by mass, and it was fraudulently added to increase the nitrogen content in foods and feeds to falsify their protein content. This was possible because the protein content in foods and feeds is usually indirectly estimated by the Kjeldahl method.

This method measures the amount of nitrogen in the sample and then the nitrogen value is multiplied by a factor depending on the type of protein expected to be estimated one. Contaminated products had therefore much lower protein amount that the ones declared. Apparently, however, melamine contamination became a safety issue when the added melamine was itself contaminated with cyanuric acid, a related chemical that can be produced during the manufacture of melamine. The first cases of contamination were detected in pet feeds and caused a particularly high mortality in cats. Puschner et al., (2007) showed no effect on renal function in cats fed with melamine or cyanuric acid alone, but they detected the formation of crystals in the kidneys of cats fed a combination of melamine and cyanuric acid that were responsible for the acute renal failure that ailed these animals. It has later been shown by Reimschuessel et al., (2008) that several species of fish and pigs fed a combination of melamine and cyanuric acid also developed renal crystals similar to those detected in the cat and that melamine and cyanuric acid residues could be identified in edible tissues of fish. The European Commission decided that composite products, including feed, that contain milk products originating in or consigned from China shall be checked, including laboratory analysis (European Commission Decision 2008/798/EC) and products containing more than 2.5 mg melamine per kg are to be immediately destroyed.

2.8.3 Organochlorinated and -brominated compounds

There are 210 different congeners of dioxins and dioxin-like compounds (PCDD/Fs) and 17 of them, with chlorine substitution in positions 2, 3, 7 and 8 are the most toxic. These 17 congeners and 12 dioxin-like PCBs, have the same mode of action, namely by binding to the aryl hydrocarbon receptor, however, they display different potencies and usually they appear as mixtures. To express the overall toxicity of such a mixture as a single number, the concept of "International Toxic Equivalents" (TEQ) was developed. The "Toxic Equivalent" (TEQ) is used to estimate the toxicity of the less toxic compounds as fractiona of the toxicity of the most toxic one, called 2,3,7,8-TCDD. Each compound is attributed a specific "Toxic Equivalency Factor" (TEF). This factor indicates the degree of toxicity compared to 2,3,7,8-TCDD, which is given a reference value of 1. To calculate the total TCDD toxic equivalent (TEQ) of a dioxin mixture, the amounts of each toxic compound is multiplied by their Toxic Equivalency Factor (TEF) and then all of them are added together. Long-term exposure leads to increased dioxin levels in fatty tissues and may result in developmental problems in children, and may affect liver, thyroid, reproduction, behaviour and immune functions and induce cancer. The EU Scientific Committee for Food and The Joint FAO/WHO Expert

Committee on Food Additives (JECFA) established tolerable intake levels for 'dioxins' in 2001 (EC, 2001; WHO, 2001). A threshold approach was used to estimate a tolerable daily intake (TDI) of 2 picograms (pg) TCDDs per kg of body weight. This was extended to include other PCDDs, PCDFs and dioxin-like PCB. Because of the long half-lives of these compounds in the human body, the TDI was expressed over a longer time period (a week or month). The EU Scientific Committee for Food established provisional tolerable weekly intakes (PTWI) of 14 pg WHO-TEQ per kg of body weight and the JECFA established a provisional tolerable monthly intake of 70 pg WHO-TEQ per kg of body weight. There are some differences in the approaches used by other authorities to assess the risks of dioxins and dioxin-like compounds to human health.

There are theoretically 209 different congeners of polychlorinated biphenyls (PCBs) (Hjeltnes et al., 2006). As the dioxins, these compounds are all lipophilic, highly persistent, accumulate within food chains and their lipophilicity increases with the increasing degree of chlorination. The type and potency of the toxicity of the congeners vary with the number of chlorines substituted and the placement of the chlorine on the phenyl rings. Restrictions were introduced in their use since the 70's, and today PCBs are banned in most countries. PCBs are also complex mixtures of compounds and they are divided in two groups of PCBs: dioxin-like PCBs, which are included in the tolerable intake levels established for PCDDs and PCDFs, and non-dioxin-like PCBs, which constitute a major part of the PCB congeners found in human tissues and food. The latter PCBs do not bind to the aryl hydrocarbon receptor and affect mainly the developing nervous system and neurotransmitter functions, while dioxin-like PCBs have toxicological effects similar to TCDD/Fs. The main exposure of man to PCBs is considered to arise from the food and fatty fish is regarded as an important source (Hites et al., 2007). The toxicological profiles of polybrominated biphenyls (PBBs) are expected to resemble those of the PCBs but TEFs have not been allocated and nor have relevant toxicological evaluations been conducted (Håstein et al., 2006).

The brominated flame retardants (BFRs) include brominated bisphenols, diphenyl ethers, cyclododecanes, phenols and phthalic acid derivatives; and some of these substances are environmental POPs, with the potential to contaminate the food chain long after production has ceased. There are theoretically 209 different congenes of polybrominated diphenyl ethers (PBDEs) (see Håstein et al., 2006). As the PCBs, they are lipophilic and in this case the lipophilicity increases with the degree of bromination. Tri- to hexa-BDEs are easily absorbed,

persistent they accumulate in the trophic chain, and they are more bioactive than deca-BDE, which may be transformed to lower brominated BDEs. In general, the toxicological databases for these compounds are poor. The liver is the target organ for PBDEs: penta-BDE is the most toxic congener and deca-BDE the least.

2.9 Physical contaminants

Physical hazards and foreign bodies that may be potentially harmful, such as glass, metal, wood, bones, stones, hard plastic etc, must not be found in food. They may cause injury to the gastrointestinal tract including cuts and perforations in the mouth, damage to the teeth, gums, tongue, throat, stomach and intestine. Natural hard components of seafood, such as bones, are usually not cause of injury because the consumer is aware of their presence, but in products sold as bone-free injury may indeed occur (FDA, 2005). Foreign bodies may also be introduced in the food during manufacturing or distribution and control measures for physical hazards can include periodically checking all equipment for damage or missing parts, passing the product through metal detectors and the use of X-ray detectors (Huss et al., 2004).

Although physical hazards/foreign bodies rarely cause serious injury, generally they are among the most commonly reported consumer complaints. Because the injury occurs immediately or soon after eating, the source of the hazard is often easily identified. In the weekly alert and information notification system for RASFF (2008), during a period when 435,500 metric tons of Norwegian farmed salmon were imported by the EU-countries (EFF, 2008), only 4 physical contaminants were reported and none of them in salmon products.

2.10 Radionuclides

Technetium-99 (Tc-99) is a silver-grey, radioactive metal. It occurs naturally in minute amounts in the earth's crust, but is primarily man-made as a by-product from the operation of nuclear reactors. The Tc-99 produced in the reactor may become a part of its airborne, liquid, or solid wastes and may be found at very low concentrations in air, sea water, soils, plants and animals. Higher amounts may be found close to contaminated facilities such as weapons facilities and nuclear plants. Tc-99 is very mobile in the environment, especially under aerobic conditions. Tc-99 enters the chain when fish eat contaminated feed or drink contaminated sea water. In Europe, a survey of 14 fish farms revealed traces of Technetium-99 discharged from Sellafield, and although the levels were very low and presented no threat to public health, the salmon industry has since supported the Government's proposed nine-

month moratorium on Tc-99 discharges (N-Base, 2003). Tc-99, being a beta-emitter, is a health hazard only if it is taken into the body where it concentrates in the thyroid gland and the gastrointestinal tract. The body, however, excretes half of the ingested Tc-99 within 60 hours and half of the remaining Tc-99 in the next 60 hours. As with any radioactive material, there is an increased chance that cancer or other adverse health effects can result from exposure to radioactivity (Food Standards Agency, 2003).

3 Best manufacturing practices and control measures

According to the EU Regulation 178/2002, food and feed business operators at all stages of production, processing and distribution within the businesses under their control shall ensure that foods, and feeds, satisfy the requirements of food law which are relevant to their activities and shall verify that such requirements are met. In the aquaculture industry, best manufacturing practices (BMPs) and control measures allow producers, processors, buyers and importers to respond to consumer pressure and ensure that their farmed seafood comes from environmentally and socially sustainable methods of production; in addition to ensuring the use of processes that maximize food safety. These practices are laid down by national and international legislation, industry guidelines and Codes of practices, quality standards (Global GAP Standards, SQF 2000 Code etc.), internal company trials and experience. The fundamentals of best practices start with a good HACCP plan. HACCP is an obligatory, systematic and preventive approach to food safety that addresses the prevention of physical, chemical and biological hazards during production rather than focus on the inspection of finished products. HACCP is used in the food industry to identify potential food safety hazards, so that key actions at Critical Control Points (CCP's) can be taken to reduce or eliminate the risk of the hazards (FAO, 1998). BMP should be used at all stages of food production from receipt of raw products to manufacturing processes, including packaging and distribution.

Fish producers must have written procedures for dealing with deviations from the critical limits established at the control points, and this includes an immediate investigation to identify the sources of contamination. Production must stop upon detection of a deviation and the food produced during, immediately after and immediately before the deviation took place must be recalled. Depending on the type of product and the stringency of the food business

operator, those products may be released to the market only after suitable analyses proves that they conform to the requirements or, applying the precautionary principle, be rejected anyway. The products must never be released if there is any suspicion that they may be contaminated. Where a product has been withdrawn because of an immediate health hazard, other products which are produced under similar conditions, and which may present a similar hazard to public health, should also be evaluated for safety and may need to be withdrawn. The need for public recall should be considered when it is suspected that affected products may have left the manufacturing premises (Codex Alimentarius, 1997).

4 Risk analysis and Emerging risks

The end product of the European aquaculture industry is often destined to be sold in a European retail chain. Therefore, the requirements of the retail chains need to be implemented in addition to the regulatory and industry requirements. The retail chains usually require all production stages of the supply chain to have an externally audited quality management system in place. The quality system would be required to be based on a HACCP system that is in turn based on a risk assessment of the food safety hazards. The process of deciding which food safety hazards will be controlled explicitly within the HACCP system is known as risk analysis. There are three steps of this process: risk assessment, risk management and risk communication. Risk assessment is the evaluation part of the process that identifies the relevant food safety hazards and then assesses those risks using a combination of the severity of the hazards and the likelihood of that hazard actually occurring within a particular step of the supply chain process. In a more complex methodology, the likelihood of the consumer exposure is also undertaken. After the risk assessment process is completed, the risk management process of identifying and implementing the relevant control measures is undertaken (Huss et al., 2004).

Under the EU-financed integrated research project "Promoting Food Safety through a new integrated Risk Analysis Approach for Foods" (SAFE FOODS, FP6-506446), one of the key objectives was the establishment of a working procedure for the identification of emerging food safety risks (Kuiper and Kleter, 2009): HACCP process only identifies hazards that have already been known to occur in the specific food supply chain step under study, not unexpected hazards that have not yet been known to occur within that product and process.

Thus, emerging risks, newly identified hazards, or hazards from unexpected sources need to be identified by different approaches which are often referred to as "predictive early warning systems" (Marvin et al., 2009). The databases used in these systems are usually Government owned, such as the Pan European Rapid Alert System for Foodstuffs (RASFF). Despite the vast amount of data being collected and collated by the 115 Government and 61 non-Government institutes involved this task, new or unknown hazards may still remain unidentified (Kleter et al., 2009).

Specific hazards associated with illegal activities, in particular if intentional and clearly fraudulent, such as the recent case of melamine from Chinese origin, are very difficult to predict by any of the current risk assessment methods in use within the European Aquaculture industry (Kleter and Marvin, 2009). To identify these hazards a method needs to detect the weak points or vulnerability within a production system that may, at a later stage, enable a newly emerging or deliberately inserted hazard, to occur or multiply (Kleter and Marvin, 2009). Within the SAFE FOODS project, 17 indicators of the early identification of emerging hazards were identified, but loss of traceability was not one of them (Kleter and Marvin, 2009).

5 Identification of vulnerabilities in the production of farmed salmon

One of the aims of the project Σ-Chain was to develop methodologies to optimize traceability with respect to chain vulnerability to contamination. The work that follows here relates to one of the activities of the project, namely the identification of the vulnerability within the production chain of farmed Atlantic salmon. The term vulnerability included the lack of traceability in the chain and the term traceability referred to documentation flow, analytical techniques, physical and electronic tracking and tracing technology. It must be noticed that vulnerable steps may not always result in contamination but they should be given extra attention to improve product security and chain control.

The identification of vulnerabilities needs the mapping of the whole production chain and the identification of all possible relevant contaminants, including their potential entry points and spreading routes, the control measures and corrective actions. All the available product documentation needs to be attached to the flow chart and information on physical or

electronic data tracking and tracing technologies must added to the relevant steps in the chain. The Σ-Chain project identified as critical steps change of ownership and packaging removal: about 40% of the salmon processors evaluated in one European country failed product trace checks due to missing documentation at these steps. In addition, paper gill tags were lost at the heading and filleting steps and paper labels from external packaging as well as the data contained on them could be lost with the packaging removal.

Assessment of the flow charts of the production chain in combination with the relevant contaminants was carried out according to a modified version of the Failure Mode and Effects Analysis methodology (FMEA). FMEA is a method of reliability analysis that improves the operational performance of production cycles to reduce risk levels. The method was developed and implemented initially in 1949 by the US Army and is now used mainly in the manufacturing and engineering industries (Scipioni et al., 2002) FMEA, together with HACCP, has been applied by a few large corporate food manufacturers to minimise the risk from food safety and product quality hazards. In addition to the standard HACCP assessment criteria, namely the severity and likelihood of the hazard, the FMEA method uses a third criterion: the detectability of the hazard within the process being assessed. Each of these three criteria is given a score and the scores are multiplied to get the Risk Priority Number (RPN) (Barendsz, 1998).

In the Σ-Chain project, the loss of traceability was considered and assessed as a hazard, along with the previously reviewed biological, chemical and physical ones. In addition to the RPN, we wished to obtain a Vulnerability Priority Number (VPN) which was estimated as follows. First, it was necessary to estimate the severity, which is the factor indicating the impact that an event of vulnerability has on the consumer. Severity is not restricted to a rating of the food safety hazards only but also includes the assessment of process failure, although food safety hazards rank highest in severity. Secondly, the likelihood of occurrence needed to be estimated, which indicates the frequency of a vulnerability event happening. The last parameter to be calculated was the detectability: a measure of the combination of the presence or absence of reliable methods or procedures applied to identify the event happening, and with what frequency. A scale for severity from 1 to 10, for likelihood from 1 to 5 and for detectability from 1 to 3 was used (see Table 2). In the 10-points scale for severity there is space between individual ratings to allow for subjective or qualitative rating. The difference between light (3) and medium (5) can be the substance-specific (some chemicals arouse more

suspicion than others). All the vulnerabilities rating 8 or higher in severity must be further investigated. After rating all three factors (severity, likelihood and detectability), they are multiplied to get the Vulnerability Priority Number (VPN) as illustrated in Table 3 for a few vulnerabilities. The higher the VPN, the higher the priority for addressing the vulnerability.

Table 2. Vulnerability Priority Number (VPN) = Severity x Likelihood x Detectability. The higher the VPN, the higher the priority for addressing the vulnerability.

Severity[1)]	Likelihood[1)]	Detectability
1 = Of no consequence. No impact expected	1 = Improbable event, i.e. once every five years	1 = Will be detected, ie detection procedure is applied frequently and is reliable
3 = Customer complaints will occur. Light hazard or threat, possibly to quality issues	2 = Remote possibility, i.e. once per year	2 = Detection procedure is applied. Possibly detected (reliability and frequency not appropriate or not known)
5 = Medium hazard or threat	3 = Occasional event, i.e. once per month	3 = No detection procedure is applied. Unlikely to be detected (not procedurally covered vulnerability)
8 = Severe hazard or threat (incl. prohibited substances / fraud). Consumer sickness including long term chemical effects i.e.cancer	4 = Probable event, i.e. once per week	
10 = Immediate hazard or threat (incl. precautionary principle application) Consumer death including acute chemical effects i.e. melamine poisoning	5 = Frequent event, i.e. once per day	

[1)] The procedure is based on the "Failure Mode and Effects Analysis (FMEA) Methodology" (Scipioni *et al.*, 2002).

The modified FMEA methodology was used to assess the effectiveness of control and corrective measures in food production chains by applying the modified FMEA method a second time, after assessing the current and potential control measures in place to control the potential contaminants comparing vulnerability priority numbers before and after the application of the control measures. The additional control measures usually affected the detectability score of that process step. Potentially vulnerable steps were thus identified in the process flow chart and assessed for ranking. As already mentioned, the following information was required: the list of identified priority contaminants, their entry points into the production chain, potential multiplication, spreading and accumulation, existing control points, whether analytical methods testing are available and whether the contaminant is currently tested for, the testing step number and details of the testing.

It must be kept in mind that the vulnerable steps and their ranking must be identified and estimated respectively for each individual food business operator and product in a given time; and the ranking must be revised and updated regularly. It is not possible to produce a generic ranking of vulnerabilities for the production of farmed salmon for example, since different producers do have different routines, chain maps, suppliers and they may also run different sets of controls and analyses, so the results obtained from one particular company and product are strictly speaking applicable only to that company and product at that time. Table 3 illustrates the calculation for a few steps selected and have been selected for illustration purposes only.

Table 3. Example of ranking of a selection of steps in the production of farmed salmon according to their vulnerability. In bold the highest ranking vulnerable steps.

Preliminary Vulnerable steps (Hazard entry step)	Potential hazard	VPN before the application of control	VPN after the application of control	Ranking of the step
Disinfection	Crystal violet	**72**	**48**	**1**
Feeding	Melamine	**72**	**32**	**3**
Feeding	Mercury	30	10	6
Feeding	Cadmium	30	10	6
Feeding	PCB	24	8	7
Medicated feed	Chloramphenicol	32	16	5
Evisceration	*Clostridium botulinium*	30	20	4
Heading	Loss of tags	5	5	8
MAP or tray packing	*Clostridium botulinium*	24	16	5
MAP or tray packing	Documentation failure	**60**	**40**	**2**
Change of ownership	Documentation failure	30	20	4

6 Conclusions and future trends

The progress made in understanding and combating food poisoning risks associated with seafood in recent years has had a positive impact on the number of incidences of illness associated with seafood consumption in Europe (Dorè, 2008). According to RASFF, the number of incidents regarding the detection of contaminants in farmed Atlantic salmon is very low at the moment. Attention has been paid to the risks of emerging contaminants in fish but it seems that the benefits of fish intake exceed the potential risks of its consumption (Mozzafarian and Rimms, 2006). Still, continued research and development into safe, nutritious and documented feed materials, together with the implementation of stringent quality and safety assurance procedures and appropriate screening and sampling protocols throughout the production and distribution chain, will provide the basis to ensure the

production of high quality European Atlantic salmon. Despite this, there are new challenges for risk managers in Europe, which include globalisation of trade and an increasing reliance on imported seafood into the European Union as well as global warming, all of which have potential implication for the incidence of food poisoning in general (Dorè, 2008). These threats to public health require careful consideration and developing a robust understanding of the processes involved in seafood-borne illnesses and developing tools to monitor for pathogens and toxins.

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