Pro-active approaches to the identification of emerging risks in the food chain: Retrospective case studies

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1. Introduction and summary

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1.1 Aim of this work

In this report six case studies are carried out on food-safety and animal-health crises that have occurred in the recent past. The aim is to learn from these cases if and how the identification of emerging food-safety (and animal-health) risks can be improved by adopting a (more) pro-active approach.

In particular, in each case study it was aimed to address to the following questions:

- Was the detection/identification of the hazard timely or not?
- From which factors has the detection benefited or could the detection have benefited:
    - pro-active approaches (such as surveillance activities),
    - motivated professionals,
    - specialized expertise,
    - good coordination between actors,
    - a (more) inclusive set of indicators within and outside the food chain. By 'indicator' we mean any observable fact or pattern that may point to the emergence of a food-safety risk.

This work was carried out as a project named "Analysis of recent crises in the field of food safety and/or animal health" within the Dutch research program "Emerging risks in the Dutch food chain", a program funded by the Dutch Ministry of Agriculture, Nature and Food Quality (LNV) and coordinated by Dr. H.J.P. Marvin, RIKILT – Institute of Food Safety, Wageningen University and Research Center. The goal of the research program is to develop a system for pro-actively approaching the identification of emerging risks in the Dutch food chain.
The work described in this report serves to inform the development of such a system.

1.2 The case studies

The six cases to be studied were selected from a list of possible subjects, aiming for coverage of most "types" of emerging risks and taking into account the specialist expertise available within the six participating research institutions.
In Table 2.1 below the six crises that have been studied are listed, together with some of their characteristics and their broader relevance.

Case study *Institute responsible for the case study*	**Emergence of the risk**		**Identification or detection**			**Type of hazard**		**Broader relevance**
	New	*Re-emerging*	*Early*	*Inter-mediate*	*Late*	*Chem.*	*Biol.*	
Dioxin in pork meat 2004 *A&F*	x				x	x		Risks in packed meat; Environmental contaminants
Bovine Spongiform Encephalopathy (BSE) epidemic 1986; Variant Creutzfeldt-Jakob Disease (vCJD) 1996 *ASG*	x x		x x				x x	Epidemics of new, unknown, agents
Avian Influenza (AI) epidemic 2003 *CIDC*		x			x		x	Epidemics of notifiable animal diseases
Equine leukoencephal-omalacia (Fumanisin in feedstuff) 1989-1990 *PRI*		x			x		x	Toxicoses
Environmental contaminants in cultured salmon 2004 *RIKILT*		x		x		x		Broad range of environmental contaminants
PFCs in wild-catch fish 2001 *RIVO*	x				x	x		Man-made chemicals in the environment

Table 1.1 Overview of the case-study topics of Subproject 1.1.

The case study reports, included below, provide both relevant details on the issues at stake in the case studied as well as general insights and recommendations that can be drawn from it. In the next paragraph I summarize what the six case studies have told us about the particular issue of pro-activity in emerging-risk identification.

1.3 Summary of conclusions on pro-activity

In Table 1.2 the case-study findings with respect to pro-activity have been briefly summarized. From this summary I obtain the following overall picture. I find it useful to make a distinction between “non-holistic” pro-activity based on indicators *within* the food chain and “holistic” pro-activity based on indicators *outside* the food chain. The latter is related to the holistic approach as laid out in the PERIAPT project report [Noteborn et al. 2005], which proposes a “host environment analysis” to identify indicators outside the food chain.

Case study	**"Non-holistic" pro-activity that paid off or was lacking in the incident or crisis**	**Recommendations for "non-holistic" pro-activity**	**Recommendations for holistic pro-activity (using indicators outside the food chain)**
Dioxin in pork meat 2004	*Paid off*: Routine surveillance of dairy industry (although early detection was mere luck), specialist expertise at AID (General Inspection Department) and availability of dioxin database	- Changes in food – production process being introduced in the HACCP plan of the company - Case-specific: mapping of sources of dioxins	Monitoring changes in production processes, esp. those affecting waste streams. Indicators are changes in: - Legislation - Purchasing pattern of technical auxiliary substances - Market prices of materials
Bovine Spongiform Encephalopathy (BSE) epidemic 1986	*Paid off*: Surveillance structure and specialist expertise	Optimizing passive surveillance structure Assessment of risks when feedstuff formula changes (Though unlikely that this would have made any difference for BSE crisis)	Assessment of risks when waste-stream process changes (Though unlikely that this would have made any difference for BSE crisis)
Variant Creutzfeldt-Jakob Disease (vCJD) 1996	*Paid off*: Dedicated surveillance structure including specialist expertise. *Lacking*: Balanced risk communication	- Recognizing uncertainties - Enforcing precautionary measures taken	None
Avian Influenza (AI) epidemic 2003	*Paid off*: Specialist expertise at Animal Health Service (AHS) *Lacking*: Action taken upon occurrence of LPAI, communication between veterinary practitioners and AHS, farmer's and vet's sense of responsibility for notifying a severe clinical situation	- Specific to AI: Lowered notification thresholds when LPAI has been detected - Generic for notifiable animal diseases: stimulating better and earlier communication of on-farm clinical picture to authorities	Attention to higher risks of exposure to chemical contaminants and disease agents when introducing (or promoting introduction of) alternative production systems involving outdoor housing
Equine leukoencephal-omalacia (Fumanisin in feedstuff) 1989-1990	*Lacking:* Surveillance activities (testing of suspect batches), precautionary measures (re-routing of batches)	- Monitoring indicators for plant stress - Adjusting maize harvesting procedures and storage conditions - Testing and re-routing of suspect batches - Diversification of horse feed	Monitoring indicators for plant stress

Environmental contaminants in cultured salmon 2004	*Paid off*: Initiatives for the mitigation of the risk *per se* had been undertaken. *Lacking*: Strategic preparation to avoid crises surrounding contaminations that are not exceeding current food-safety thresholds	- Pro-active development of authorities' communication strategy, collaboratively with stakeholders - Attention to contaminants: * going or recycling into environment and/or feed chain, * with levels approaching thresholds, - Attention to products: * with strongly increasing production and consumption, * made increasingly using alternative production technology	Attention to: - Compounds for which many toxicological studies are conducted, which can cause standards setting to change; particularly for effects of combinations of substances. - Products with a strong health image, of which contaminations can become a sensitive item for the public.
PFCs in wild-catch fish 2001	*Lacking*: Risk assessment related to new classes of chemicals: the PFC problem was detected only after decades of production, during which the presence of these substances had become ubiquitous in the global environment and in humans	Risk assessment related to PFCs: current national initiatives should be integrated and further developed to enable risk assessment	Attention to industry's changes: alternative -but very similar- chemicals will be developed to replace the currently banned PFCs. The toxic en bioaccumulation potential of these alternatives should be investigated to avoid replacing the original 'problem' with a new one. Chemical industries follow the 'alternative chemical' strategy for a range of chemicals.

Table 1.2 Brief summary of the case-study results with respect to the issue of pro-activity.

Non-holistic pro-activity

As is apparent from Table 2.2, in all cases studied it was found that (more) pro-active efforts within the food chain would have been useful or desirable. So I conclude that more pro-activity can be beneficial in the first place *within* the food chain. For the elucidation of the detailed recommendations in each specific case studied I refer to the case-study reports below. One important issue in this context is the "human factor": the motives of the relevant parties in the chain as well as the incentives that these motives may produce in the face of food-safety regulations. An example of how this issue can compromise pro-activity related to re-emerging

risks is the low compliance to syndrome-reporting procedures for notifiable diseases of livestock. This example is illustrated in detail by the case study on Avian Influenza.

Holistic pro-activity

Pro-active approaches using information from outside the food chain are recommended in all six case studies, as listed in Table 2.2. In several cases these recommendations mention a specific type of indicator, such as changes in legislation, of waste streams of industries, of market volumes and prices of certain substances, trends in toxicological research, and transitions to different animal housing systems (although this latter indicator could be viewed as a "within-chain" indicator).
One important "holistic indicator" common to all three case studies of totally new risks (dioxin in pork meat, BSE, and PFCs in wild-catch fish) is "changes in the waste stream". In the cases of dioxin in pork meat and PFCs in wild-catch fish, the case studies show that when the production changes caused concurrent waste-stream changes, no assessments of risks via the waste-stream were made. E.g., for the case of dioxin in pork meat, it is concluded that production changes affecting the waste stream should be introduced into the HACCP (Hazard Analysis and Critical Control Point) plan of the food-producing company. For the case of PFCs in wild-catch fish it is concluded that current initiatives regarding risk assessment related to new classes of chemicals should be integrated and further developed. Thus it seems that a "change in the waste stream" should be viewed in the first place as a process change that necessitates a risk assessment (made compulsory by legislation and enforced by inspection) rather than as an abstract indicator for identifying and prioritizing potential emerging risks. I note however that such risk assessments are not a guarantee for identifying or preventing *new* food-safety risks arising from the change in the waste stream. E.g., in the case of BSE in cattle, if a risk assessment considering TSE risks had been made at the time when changes occurred in the rendering systems used in Great Britain, the experience with recycling of animal tissue in feed and the knowledge on TSEs available up until that time would probably not have led to TSE surveillance of cattle being recommended, but at most to scrapie prevalence in sheep being monitored.

The conclusions and recommendations of the six case studies, including the risk indicators identified, provide a starting point for the development of a "system" for pro-actively approaching the identification of emerging risks in the Dutch food chain. However, due to the limited number of six case studies, these conclusions and recommendations do not provide a fully balanced or complete overview of all the relevant pro-activity issues across the whole range of possible emerging risks in the food chain. For example, one obvious risk indicator for regional or national food-safety authorities, not yet mentioned above, is the occurrence of incidents in the food chain elsewhere in the world that have the potential to spread to their region or country. Therefore, further work is necessary at a later stage to validate the usefulness of any "prototype system" against a broad set of potential emerging risks. Furthermore, it may be worthwhile to follow up a number of further hints from the six case studies at potential risk indicators other than those mentioned above, such as:

- Recycling of animal material as input for animal production constituting a pathway for risk propagation or accumulation (BSE, dioxin in cultured fish)
- Information on the health risks from certain substances becoming available from populations exposed to high doses (dioxin emission incidents, occupational exposure to PFOs)

1.4 Reference

Noteborn, H.P.J.M, Ooms, B.W., and De Prado, M., Emerging Risks Identification in Food and Feed for Human Health, An Approach. VWA- Food and Consumer Product Safety Authority, Directorate of Research and Risk Assessment, The Hague, The Netherlands, June 2005. http://www.periapt.net/, Last accessed 5 December 2005

2. Case study: Dioxin in pork meat

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2.1 Case description

2.1.1 Introduction

The case
This case concerns the contamination of pork meat with dioxin in October – November 2004 in The Netherlands. The contaminated meat was detected through farm milk with high concentration of dioxin (contaminated via the same source as the meat). The farm milk contaminated with dioxin was discovered first and from this point other possible contaminated products were tracked down. As a result the pork meat contamination with dioxin was discovered at an early moment. The Dutch authorities activated the emerging risk action plan immediately. Therefore the pig farms suspected of having used contaminated pig feed were closed and samples were taken for testing. No pigs fed with the contaminated feed entered the packed meat distribution chain.
The dioxin entered the food chain through the use of contaminated potato peels. The contaminated peels were used for the production of animal feeds. The feed products with high concentration dioxin were then given to the animals, resulting in milk and meat with too high concentrations of dioxin.
The potato peels were contaminated through the use of marl clay with high concentration of dioxin (originating from Germany) in potato processing plants. During potato processing, potatoes are washed and sorted with clay. When using the contaminated clay to wash and sort the potatoes, particles of clay adhered to the potatoes peel resulting in high dioxin concentrations in the potato peels.
It is not clear if the contamination of clay has a natural cause or that the contamination is the result of environmental pollution (source: The Dutch ministry of agriculture, nature and food quality, LNV). However, since 1999 it is known that in some clay sediments natural dioxins are present, so it is at least remarkable that this material can be used in the food industry without carrying out test checks (source: Kennislink).

What is dioxin
Dioxin is a generic term for a group of more than 75 chlorinated organic substances, which are soluble in fats. Due to this property these substances can accumulate in animals and people. Seventeen of the existing dioxins are toxic, of which TCDD (2,3,7,8 tetrachlorodibenzodioxin) is the most toxic form.
The toxic effect of dioxin is the result of the binding to cell proteins. Furthermore, it can disturb cell growth, which affects the functioning of cells in different parts of the human body.
The toxicity of dioxin was only discovered in the seventies. Some researchers claim that these are the most toxic chemicals to which people have been exposed to so far (source: Lenntech).

Sources of dioxin
Dioxin exists in the environment due to its release during volcanic eruptions and forest fires. However, this involves fairly low concentrations compared to the human production of dioxin. There are no industrial applications for dioxins, they are by-products of other processes as the production of PCBs (poly chlorinated biphenyls), PCPs (poly chlorinated

phenols) and herbicides, metal working and the paper industry. During the combusting of substances in the presence of chlorine dioxin is also often released. This is for instance the case during the combustion of waste and leaded gas (source: Lenntech). Via gas emissions and solid residues substances
can end up in the environment as a result of which everywhere in the environment background levels are found because the substance breaks down very slowly (source: agriholland).

Dioxin can only be generated when four basic substances are present. Firstly, carbon, oxygen, hydrogen and chlorine have to react with each other. The first three substances are present in the open air. Chlorine is generally present in the form of common salt (NaCl) in for example household waste, paper and carton. Secondly, carbonhydrogens have to be present in the waste. Furthermore, metals as copper and cadmium have to be present to support formation of dioxin. Finally, the combustion technology has to be favourable, that is a sufficiently high temperature, enough time, and favourable oxygen content (source: Lenntech).
Dioxins are also formed in nature by the so-called white rot fungus which grows on dead wood and can produce dioxins from lignin.
Besides, vegetables as Brussels sprouts, broccoli, and cabbage can contain dioxin-like substances.
Dioxin is also present in tobacco smoke. In this way, an average smoker inhales a quarter of the maximum dose that can be consumed safely according to the Dutch Health Board (Gezondheidsraad) (source: agriholland).

2.1.2 Chronological description of the case

The dioxin entered the food chain through the use of contaminated potato peels. The contaminated peels were used for the production of animal feeds. The feed products with high concentration dioxin were then given to the animals, resulting in milk and meat with too high concentrations of dioxin. The farm/tank milk contaminated with dioxin was discovered first and from this point other possible contaminated products were tracked down. As a result the pork meat contamination with dioxin was discovered at an early moment and did not enter the packed meat distribution chain.
The potato peels were contaminated through the use of marl clay with high concentration of dioxin (originating from Germany) in potato processing plants.

The chronological description of the case is schematically presented in
Figure 2.1. The red box shows the starting point of the case and the black arrows represent the chronological order of the events in this case. The blue dashed boxes and blue dashed arrows show the sequence of events that would have taken place if the pig farms had not been closed on time. The green boxes and arrows show the events which led to the source of the contamination.

In a report of the Dutch animal feed board (PDV) entitled “Assessment incident dioxin contamination potato by-products 2004” a very detailed description is presented of the facts that have occurred according to the observations of PDV and the animal feed companies involved. A chronological list of the actions undertaken during the incident is included in this report (see appendix 1). Furthermore, conclusions and recommendations on this incident are provided.

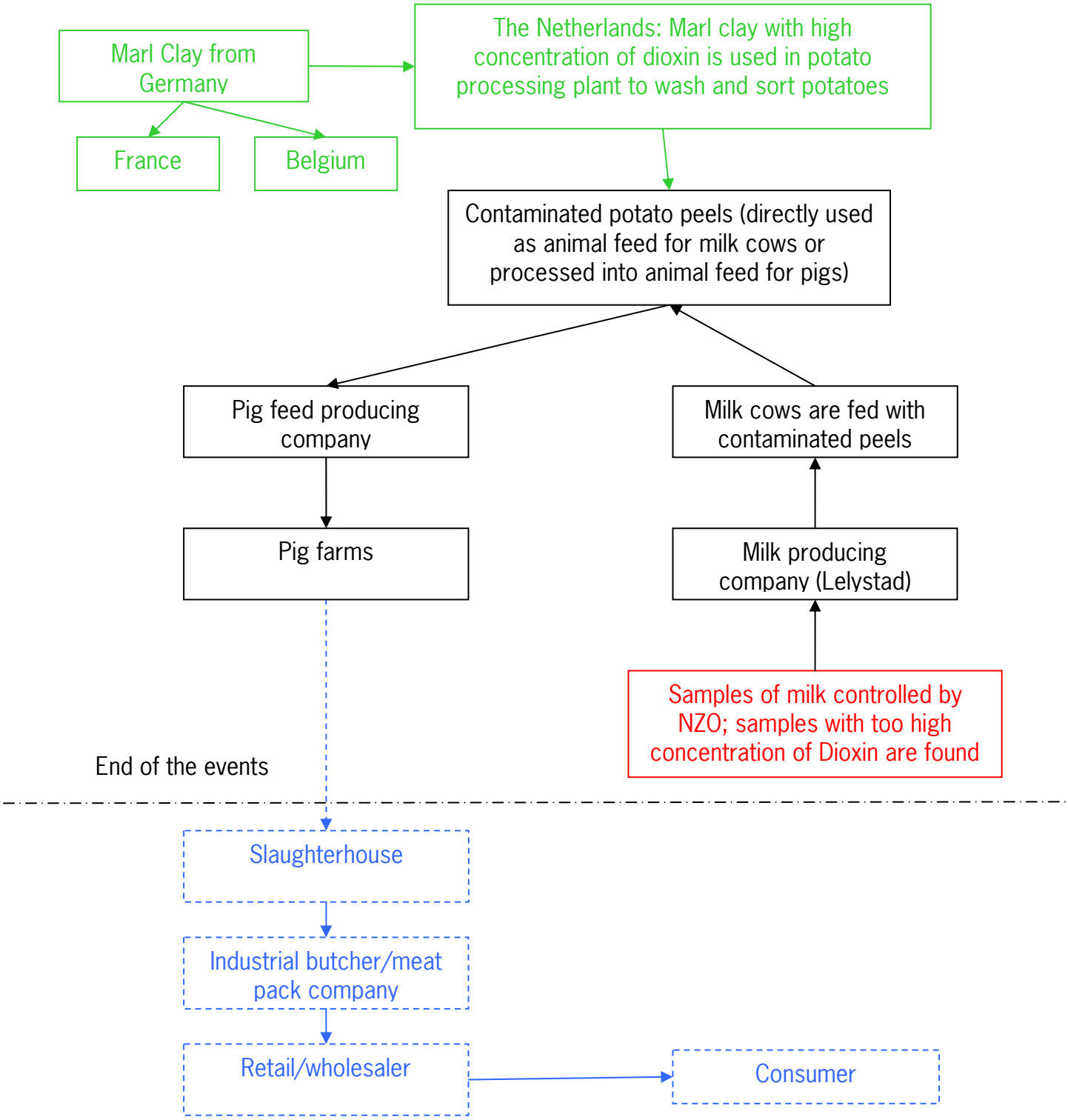

Figure 2.1: Chronological description of the case

2.1.3 Type of risk: re-emerging

Food contaminated with dioxin or exposure to dioxin is a re-emerging type of risk. Dioxin is found worldwide as a result of natural processes and can be formed as an industrial waste product in different ways as described in the introduction of this report.
Although the toxicity of dioxin has only been discovered in the seventies, there have been registrations of incidents with dioxin beyond this period. Most of the dioxin incidents in the eighties took place in areas close to waste incineration stations. An overview of dioxin incidents is provided hereafter (source: Wikipedia). The described incidents also stress the possible consequences of exposure to dioxin. In appendix 2 a more extensive list of dioxin incidents is provided.

Dioxin exposure incidents

- In 1963 a dioxin cloud escapes after an explosion in a Philips-Duphar plant (now Solvay Group) near Amsterdam. Four people die of dioxin poisoning, and 50 more suffer severe health problems. The dioxin was a by-product of herbicid production.
- In 1976 large amounts of dioxin were released in an industrial accident at Seveso, although no human fatalities or birth defects occurred.
- In 1978, dioxin was one of the contaminants that forced the evacuation of the Love Canal neighborhood of Niagara Falls, New York.
- Dioxin also caused the 1983 evacuation of Times Beach, Missouri.
- In 1997, chicken meat with high concentration in dioxins being sold in Mississippi was found. The source was naturally contaminated ball clay which was used as desiccant or drying material in the production of soybean meal used in the chicken feed.
- In the 1960s, parts of the Spolana chemical plant in Neratovice, Czechoslovakia, were heavily contaminated by dioxins, when the herbicide 2,4,5-T (also a component of Agent Orange) was produced there. Workers in this factory were exposed to high concentrations of dioxins at that time. Dozens of them fell seriously ill. A possibly large amount of dioxins was flushed from the factory into the Labe river during the 2002 European flood. No direct consequences of this incident have thus far been recorded.
- In May 1999, there was a dioxin crisis in Belgium: quantities of dioxin had entered the food chain through contaminated animal feed. 7,000,000 chickens and 60,000 pigs had to be slaughtered. The scandal that followed caused a landslide in the elections one month later.
- In a 2001 case study [1], physicians reported clinical changes in a 30 year old woman who had been exposed to a massive dosage (144,000 pg/g blood fat) of dioxin equal to 16,000 times the normal body level; the highest dose of dioxin ever recorded in a human. She suffered from chloracne, nausea, vomiting, epigastric pain, loss of appetite, leukocytosis, anemia, amenorrhoea and thrombocytopenia. However, other notable laboratory tests, such as immune function tests, were relatively normal. The same study also covered a second subject who had received a dosage equivalent to 2,900 times the normal level, who apparently suffered no notable negative effects other than chloracne. These patients were provided with olestra to accelerate dioxin elimination.
- In 2004, a notable individual case of dioxin poisoning, Ukrainian politician Viktor Yushchenko was exposed to the second-largest measured dose of dioxins, according to the reports of the physicians responsible for diagnosing him. This is the first known case of a single high dose of TCDD dioxin poisoning. Experts say that it could take two to three years for the disfigurement of his face to clear up.

[1] A Geusau, K Abraham, K Geissler, MO Sator, G Sting, and E Tschachler (2001) Severe 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) Intoxication: Clinical and Laboratory Effects. Environmental Health Perspectives Volume 109, Number 8.

Due to strict measures and rules, the exposure to dioxin nowadays has been substantially decreased. In breast milk the typical amount of dioxin is now half of what was measured 10-15 years ago. Furthermore, about 8% of people have a higher level of dioxins in their body than the maximum deemed acceptable (Source: www.varken.net).

2.1.4 Relevance to human food safety

Dioxins in the food chain
Dioxin ends up in people due to the consumption of food, because it accumulates in livestock. Fish, meat, eggs and dairy products are well-known sources of dioxin and cause 90% of the exposure. The Dutch government has determined a maximum allowed dose of dioxin in food, on which inspections are carried out. Unborn children can be exposed to dioxin as it can penetrate through the placenta and by drinking breast milk. In the industry or during application of herbicides people may be exposed to dioxins directly. Also smokers get down more dioxin than the average person (source: Lenntech).
The average contribution to the daily amount of dioxin that ends up in the body is:
- 27% by dairy products,
- 23% by meat (products),
- 16% by fish (products) and
- 4% by eggs

In **Figure 2.2**.2 it is shown from what products people's dioxin exposure arises when eating a typical North-American diet.

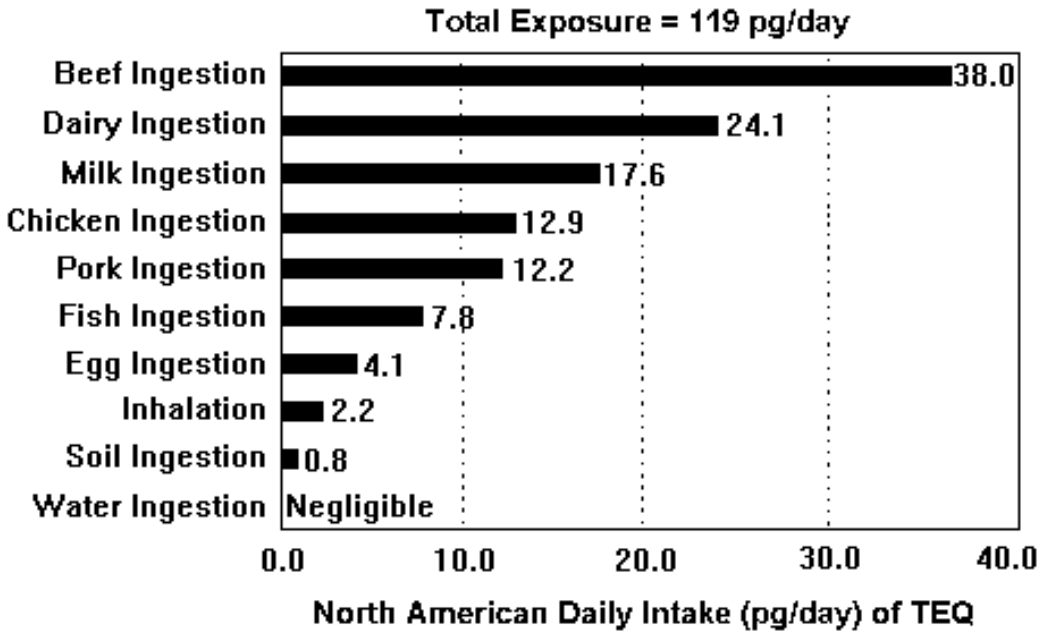

Figure 2.2: Chart from EPA Dioxin Reassessment Summary 4/94 - Vol. 1, p. 37
(Figure II-5. Background TEQ [dioxin Toxic Equivalent] exposures for North America by pathway) (source: Dioxin homepage)

Refined edible oils and fats and vegetable products contribute for 17% and 13% to the amount of dioxins and PCBs that end up in humans (Source: Voedingscentrum).
It takes a long time for the body to secrete dioxin, because it reacts with body fats and subsequently accumulates in the body. Sometimes, it may take 7 to 11 years for dioxin to leave the body via the gall-bladder (source: Lenntech).

Health aspects of dioxin
The uptake of high concentrations of dioxin causes symptoms as chlorine acne. Usually this can be cured within several months (and in worst case within several years). Furthermore, dioxin has the reputation to damage the immune system and to decrease fertility.
Children that have been exposed to dioxins before birth have symptoms like a low birth weight, a darker skin colour, eye membrane inflammation, alteration of the nails, and a delayed development.
TCDD, or the Seveso-dioxin, is a human carcinogen in the long term. Chronic exposure can cause breast cancer and liver cancer (source: Lenntech).

Control
Food stuffs and animal feed products are checked for dioxins and PCBs in different manners. Measurements in food have demonstrated that the pollution in the Netherlands (and in Europe) has decreased considerably the last years. Also the concentration of dioxins and PCBs in Dutch breast milk decreases.
In the Netherlands research institutes RIVM and RIKILT have carried out national measuring programmes in 1998 and 1999. From this it appeared that the estimated average dioxin toxic equivalent (TEQ) and dioxin-like PCBs is together about 1.2 picogram TEQ/kg body weight/day (about 0.65 picogram for dioxin only). Compared to results from the beginning of the nineties it appears that the intake of dioxin and PCBs is halved by now.
The European Committee (EC) aims to force back the concentrations in food and animal feed via regulations and seeks to establish rules to track down possible pollution at an early stage. To force back the amount of dioxins measures aimed at the sources of pollution are most successful (Source: Voedingscentrum).

In 1998, The World Health Organisation (WHO) determined the daily tolerated intake (TDI) on 1 to 4 picograms TEQ per day and per kilogram of body weight.
A recent study of the German Environmental Agency proposes that the lower end of the WHO TDI should be used for all standard settings and risk reduction measures (http://dioxin2004.abstract-management.de/pdf/p363.pdf).
From this it can be concluded that dioxin is of direct relevance for human food safety.

2.1.5 International dimension

The case has a clear international dimension. The contaminated clay, which originated the high concentrations of dioxin in food products, is imported from Germany. Next to it, the same contaminated clay is also exported from Germany to Belgium and France. Because eventually contaminated animal feed entered the market, immediate action was required. Alert notifications were sent to the European Commission by the countries involved. These alert notifications are categorised in the Rapid Alert System for Food and Feed (RASFF), which is a system that has been in used since 1979. The purpose of the RASFF is to provide the control and inspection authorities with an effective tool for exchange of information on measures taken to ensure food safety (source: European Commission).

Representatives of The Netherlands, Belgium, France and Germany were summoned to show up in Brussels. Both in Belgium and Germany several animal farms were closed because of the use of the contaminated feed (source: www.ping.be; www.omroepflevoland.nl).

Packed meat is also exported from The Netherlands to other countries. Therefore the international dimension of this case could have been larger if contaminated meat would have been exported to other countries. In this particular case that has not happened since the emerging risk is detected at an early stage.

Dioxin is found worldwide as a result of natural processes or as a result of industrial processing. Cases of food products contaminated with dioxins or exposure to high concentrations have also been registered in very different parts of the world as presented above. Also it has been found in food products which are often imported/exported. Therefore incidents with dioxin are very likely to have an international dimension.

2.1.6 Political impact factor

The political impact factor is mainly determined by the seriousness of the incident in terms of food safety. As this incident has a direct relation to human food safety, it had a high political impact factor.

Besides, the political impact factor is for a large degree determined by the way the incident is reported, because this largely influences the public opinion and other stakeholder's perception. The first reporting were the alert notifications of the involved countries to the European Union, which revealed the presence of dioxin in potato peels. As these potato peels were fed to milk cows and pigs, this implied that dioxin could be present in these animals and could end up in people after consuming milk or pork meat. The Dutch government decided to close down all milk and pork meat producing companies which had used these potato peels as animal feed (see press releases in appendix 3).

Due to the fact that the contaminated potato peels had been fed to cows (during a period of maximal 3 months) preceding the detection of dioxin in the tank milk, some milk contaminated with a (very) low level of dioxin had reached the supermarket. VWA reported that milk with a very diluted amount of dioxin had ended up in the supermarket, but that this posed no harm to human health. However, there was also a risk that the dioxin could have adhered to the potatoes used for the French Fries production. It appeared that there was no dioxin present in fries according to measurements of the French Fries producing company. Because this incident posed no actual problem to human health the public impact factor was relatively low.

Last but not least, the media has a prominent role in determining the political impact factor, as the media has a great influence on the public opinion. There has been substantial negative media coverage of this incident. However this media coverage concentrated not so much on food safety, but more on 'naming and shaming'of the organisations deemed responsible for the occurrence of the risk. Especially the most affected food company, the certifying body, the PDV[2] and the GMP+-regulation were heavily blamed. The negative media attention had partly to do with the fact that, according to the PDV, people have a misconceived image of

[2] Productschap Diervoeder (Dutch animal feed board)

the role of the PDV concerning the handing out of certifications. The fragmentary and divided reporting by the different concerned business parties also partially contributed to the negative media attention. The latter is a result from the fact that the concerned chain members (animal feed company – cattle farm – meat processor) often communicated via the media instead of directly with each other (Productschap Diervoeder 2004).

2.1.7 Risk perception of relevant stakeholders

In this incident the following relevant stakeholders can be mentioned: government, chain related associations as PDV and certifying bodies, industry, consumers, consumer organisations, environmental organisations and media.
The government, chain related associations as PDV and certifying bodies and industry have early access to actual information and facts, which implies that their perception is in better correspondence with the actual risk situation.
The information supply to consumers, consumer organisations and environmental organisations consists mainly of the reports of the media, as they have little access to specialist and factual information. As a result, the media reports determine to a large degree the perception that these stakeholders have of the risks of the incident.

2.1.8 Re-emergence in the future

Although further measures to reduce emissions of both dioxins and PCB's into the environment have been taken and the concentrations in the diet are expected to continue to decrease (source: Dioxins in food), re-emergence of the risk is most probable for the following two reasons:

1) Dioxin is present in the environment both naturally and as a waste product from industrial production (e.g. as by-product of the production of PCBs (poly chlorinated biphenyls), PCPs (poly chlorinated phenols) and of herbicides, metal working, paper industry, etc). Dioxin sources in nature already exist for centuries and they will still remain present for a long period. Therefore there are ample sources of dioxins.
2) Dioxin is taken up in fat and breaks down quite slowly. Hence it accumulates in the body fat of humans and animals where it can remain for a long time. This also contributes to increase the chance of a re-emerging dioxin contamination in the future.

2.1.9 Broader relevance of the case

Information on this case could be useful for the following type of risks:
- All contaminations with dioxin or other similar toxins in different food products;
- Contaminations through animal feed in general;
- Emerging risks in the packed meat chain.

2.2 Pro-activity paying off and lacking pro-activity

The above description of the case is in part based on interviews conducted with eight representatives of pork meat producing companies. In addition, representatives of the VWA (The Dutch Food and Consumer Product Safety Authority; responsible for the risk assessment) and Rikilt (The State Institute for Quality Control of Agricultural Products; responsible for the dioxin measurements) were also interviewed. They have participated in the crisis team which has co-ordinated the incident. Their knowledge of the case was also very useful to assess the pro-activity in this case. The answers to the following list of questions describe the pro-activity in place and the missed pro-activity in this incident.

1) *How is the emerging risk detected? Can the detection moment be considered early, late or in-between?*

The emerging risk was accidentally detected. The high concentrations of dioxin in the farm/tank milk (start point of the incident) were detected in a routine analysis within the national milk monitoring programme of the dairy industry.

The sampling set up of the national milk monitoring programme is the following:
- milk of 3 to 7 milk farms are collected by a milk collection truck/route;
- per month there are 9000 milk collection trucks/routes (each with milk originating from 3 to 7 milk farms depending on the size of the farm);
- 20 milk collection trucks/route are analysed per month;
- 10 times per year a pooled milk sample of 4 milk collection truck/routes is analysed.

Next to it, in the frame of a monitoring programme of the agricultural sector financed by the Ministery of Agriculture an extra set of 40 individual milk farms are analysed per year.

Regarding the time span between detecting the risk and carrying out actions, some time delay occurred. This is due to the fact that dioxin analyses had to be carried out, which takes about three days.

From the point of view of public health, the risk was detected early since the milk did not reach the consumers and was not even in the distribution chain. However from the perspective of someone expecting an early warning of an emerging risk, the detection was late because there were already some indicators/changes in the normal pattern. If these would have been picked up on time, the potential risk would have been detected much earlier (see question 6).

2) *Which pro-active actions did play a role in the detection of the emerging risk?*

The detection occurred due to a routine analysis within the monitoring programme of the dairy industry itself; no further pro-active approaches existed. However from the moment that dioxin was found in milk till the closing of the pig farms a number of actions were taken to track down the source of the contamination and search for other potentially contaminated products. In this search process two actions have played an important role:
- Identification of the type of dioxin by comparing the structure of the dioxin founded in the milk with other dioxins analysed before (data base). This made it possible to define that the dioxin should be originating from clay (the pattern was similar to the dioxin found in an incident with clay from Germany in 1998). The presence of this specific knowledge/expert analysis was important.

- Well trained and motivated personnel (inspectors) were able to find the link between the clay and the potato peels.

3) *Would a holistic approach (i.e. attend to indicators from outside the respective chain) benefit the detection of the emerging risk? Were any specific indicators from outside the chain missed?*

Yes, indicators from outside the chain could have anticipated the emergence of the risk and indeed they were missed. These indicators are presented in the answer to question 6.

4) *In case of an early detection of the emerging risk, what would the consequences be if the emerging risk would have been detected later (i.e. the early detection would have been missed)?*

In case the high concentration dioxin in the milk had not been detected it would have entered the distribution chain and would have been consumed. The amount of dioxin was not high enough to be considered a public health risk. However, if the risk was not detected, the use of contaminated clay and respective contaminated potato peels could have led to a systematic source of dioxin entering the human food chain.

5) *In case of a late detection of the emerging risk, which pro-active approaches could have increased the chance of detecting the emerging risk earlier?*

A better coordination of processes could have resulted in an even earlier detection of the risk, i.e. it could even have resulted in the anticipation of the risk. What kind of processes would be important is explained in detail here below.

6) *Would the detection of the emerging risk benefit from a better use of the indicators from outside the respective chain (holistic view)?*

The answer to this question is: yes.

Complementary information on the background of the case
The washing and sorting of potatoes in the potato processing industry used to be done with salt. However the use of salt is environment unfriendly and therefore the Dutch government issued a new law to forbid the use of salt. As a consequence of the new law the potato industry seeked for alternatives, and so is the use of clay to wash and sort potatoes was introduced in the process. These events occurred in the beginning of 2004. The potato industry started buying clay and so the contaminated clay ended up in the process.

The following indicators from outside the chain can be used for an early detection of the emerging risk:

- changes in processes in the food industry, in particular those that affect the waste streams of the process (these changes should also be introduced the HACCP plan of the respective company);
- changes in legislation; in this case it is important to analyse and anticipate what the consequences of the new law will be for the different actors directly or indirectly affected by the new law;
- monitor the changes in the amount of clay and other materials being traded; changes in the purchasing pattern of technical auxiliary substances;

- changes in market prices of materials, ingredients and technical auxiliary substances (because prices are often directly correlated with supply and demand of the respective material or substance).

2.3 Conclusions and recommendations

One of the most important conclusions of this emerging risk case is that the contamination with dioxin could have been expected and anticipated. Although the high concentrations dioxin were detected early enough in terms of public health, the possibility of a contamination could have been expected if the responsible authorities would have picked up the signals (indicators) arising from a change in legislation and subsequent change in production process. From these changes the incident ultimately originated.

Furthermore, this emerging risk case is specifically a good example on how a holistic view, i.e. monitoring indicators from outside the respective chain can play an important rol in the early detection of possible risks. These indicators would be of high value in an early warning system:

- changes in legislation;
- changes in production process (due to new laws, but also due to technological developments, new more cost effective solutions, development and production of new products, etc);
- changes in trade volumes and prices of materials, ingredients, etc deployed in the food industry.

In the case of dioxin incidents, an early warning system would very much benefit from a worldwide overview of dioxin sources. The mapping of sources of dioxins is feasible because these sources remain intact for a long period of time.

A general conclusion on the kind of indicators is that they are related to changes. Changes *to the existing situations and patterns* are important leads to possible risks.

Considering the facts, actions and decisions taken in the course of the incident (crisis management) the following can be concluded and recommended:

- The relevant potato processing companies involved did not recognise the risk of dioxin in marl clay in their risk assessment and have not introduced it in their HACCP plan. When the process was changed (the use of salt replaced with clay) this should have been introduced in the HACCP plan.
- Communication between the different parties involved and the communication towards the media was not always optimal giving rise to wrong interpretations of the situation, inefficiency and misconceptions of the actual risk. Therefore a better communication strategy, based on providing transparent communication, is recommended. In particular towards the media, a spokesman should be appointed who is responsible for all communication to the media.
- Not all available data was used, resulting for instance in closing more pig farms than what would have been necessary. On the other hand, the UBN database (registration number of animal farms in The Netherlands) was not updated and therefore the information was not complete or correct.

- After some complications regarding the data and intervention processing options were resolved, the recall of contaminated shipments was well organised and adequately managed.

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A word of gratitude should be addressed to Dr. Marcel Mengelers of The Dutch Food and Consumer Product Safety Authority (VWA) and Wim Traag of The State Institute for Quality Control of Agricultural Products (Rikilt) for providing me with valuable information, answering questions and discussing the case in detail with me.

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3. The BSE crisis in Great Britain

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3.1 Case description

In this case report I study in some detail the identification of the emerging BSE risks to cattle (1986) and to humans (1996) in Great Britain. The aim is to identify, with the benefit of hindsight, the scope for success that had existed for a more pro-active approach to lead to earlier identification of the risk and/or to better risk management. In this first section I briefly describe some basic aspects of the case.

Detection of the risk to cattle in 1986

In December 1986 pathologists at the Central Veterinary Laboratory (CVL) in Great Britain identified the possibility that cattle had developed a spongiform encephalopathy transmissible in the same way as scrapie in sheep. The head of the pathology department in a minute to colleagues wrote: “If the disease turned out to be bovine scrapie it would have severe repercussions to the export trade and possibly also for humans if for example it was discovered that humans with spongiform encephalopathies had close association with the cattle.” (BSE Inquiry, Vol. 3, 1.37). In December 1987 John Wilesmith (CVL) identified the use of Meat and Bone Meal (MBM) containing ruminant-derived tissue in feed for ruminants as the likely source of infection with the disease, by then named Bovine Spongiform Encephalopathy (BSE).

Detection of the risk to humans in 1996

On 16 March 1996 Dr Robert Will of the Creutzfeldt-Jacob Disease Surveillance Unit (CJDSU) in Great Britain reported the identification of a new variant of Creutzfeldt-Jakob Disease in an emergency meeting of the British Spongiform Encephalopathy Advisory Committee (SEAC). SEAC concluded that same day that the possibility that BSE constituted the risk factor for this new disease “should be taken very seriously”.

BSE and pro-active decision making

The events taking place from the mid-1980s until early 1996 have been described and commented in detail in the report of the “BSE Inquiry” [1], conducted in the period 1998-2000. Due to this detail and as a result of the impact of the BSE crisis, the subject of this case study forms essential material for the historical study of the possibilities of and requirements for pro-active management of emerging risks. Some of the lessons that can be learned from this crisis (discussed below) should apply to a broad spectrum of possible emerging risks.

In 1986/1987 it became clear that a completely new hazard to cattle had emerged in the form of BSE. From that moment it was also clear that BSE presented a *possible* risk to humans. In

the Executive Summary of the Report of the Inquiry, chapter 4, the following conclusions are formulated on MAFF's assessment of the risk posed by BSE to humans:

"One of the most significant features of BSE and other TSEs is the fact that they are diseases with very long incubation periods. Thus the question whether BSE was transmissible to humans was unlikely to be answered with any certainty for many years, and scientific experiments were bound to take a long time. The Government had to deal with BSE against this background of uncertainty as to the transmissibility of the disease."

As a result of the belief, stimulated by the first risk assessment by the Southwood Working Party, that this possible risk to humans was 'remote', precautionary measures against human exposure were not introduced very swiftly, and initially often without good enforcement. The detection in 1996 by the CJDSU of the reality of human BSE risk was as timely as reasonably possible, and proved the wisdom of the pro-active measure in 1989 to start a targeted CJD surveillance programme. However, because the demonstration of the human BSE risk took place only in 1996 due to the long incubation period of new variant CJD (vCJD), it could not prevent the preceding many years of human exposure. That exposure could have only been reduced by a better management of the (at that time still) 'possible' risk.

International dimension and political impact

The international dimension of the BSE crisis in GB has been very important. The economic interests of the British cattle sector, partly depending on exports, were one of the reasons why there was a need to avoid disproportionate fears and risk-management demands by the public for a human risk that had been described as "remote" in an assessment by authoritative scientists. To this end, the agriculture ministry MAFF adopted and stuck to a reassuring risk communication strategy in which uncertainties were underplayed and in which changes in the likelihood, as perceived by experts, that BSE might be transmissible to humans were ignored [1,2]. In the report of the BSE inquiry it is suggested that this communication strategy has contributed to the shortcomings of the risk management by the British authorities in period of 1987-1996, as this message was undermining the implementation and enforcement of precautionary measures. Furthermore, in [2] it is suggested that some useful options for precautionary measures were ignored because of a fear of undermining the official reassuring message of there being "no risk to humans". In addition, the reassuring risk communication contributed strongly to the loss, in 1996, of public confidence in the ability of the British government to protect food safety, which lends the BSE crisis a very big political impact factor.

Risk perception of the consumer

BSE is an example of a 'dread risk': the consumer feels he cannot control his own exposure to the hazard, whilst the consequences of exposure may be horrific and fatal. Also, the risk is new and thus the consumer is unfamiliar with it. As a result, the BSE risk is likely to be perceived by the consumer as more important than one would expect on the basis of simply comparing the risk probability to that of other deadly risks. [Here I must note however that in the early years of the vCJD epidemic there was no scientific basis yet for objectively calculating a useful risk probability, as at that time it was not yet possible to estimate the level of human susceptibility ("species barrier") with any useful precision [3]]. Loss of trust in the authorities responsible for risk management after these have had to retract a reassuring stance

in their risk communication ("No risk to humans", "There is no BSE in German cattle", "I don't have any reason to think that this (3rd Dutch BSE case) is more than an incident" [4]) may further add to a 'disproportionality' of consumer's worries about the BSE/vCJD risk.

Re-emergence

In ever more new countries BSE is being detected for the first time. In many cases such a detection follows a period of time in which the relevant national policy makers have argued that their country does not have or can not have a BSE problem, and in which sometimes the risk has been insufficiently managed. This once again proves that 'learning from the past' often is difficult.

3.2 Pro-activity paying off and lacking pro-activity

3.2.1 The discovery of the emerging risk in 1986 (cattle)

Early to intermediate detection

The emerging risk to cattle was detected in 1986/1987 in two steps, as described in de paragraph 2.3.1: first the new disease was found, and subsequently the likely risk factor (feeding of MBM) was identified. Was the detection of the new disease in cattle a timely detection? For answering this question the following passages from the report of the BSE Inquiry are relevant:

- "Individual cattle were probably first infected by BSE in the 1970s. If some lived long enough to develop signs of disease, these were not reported to or subject to investigation by the Central Veterinary Laboratory (CVL) of the State Veterinary Service (SVS).
- The Pathology Department of the CVL first investigated the death of a cow that had succumbed to BSE in September 1985, but the nature of the disease that had caused its death was masked by other factors and was not recognised at the time. This is not a matter for criticism.
- The Pathology Department considered two further cases of BSE at the end of 1986 and identified these as being likely to be a Transmissible Spongiform Encephalopathy (TSE) in cattle. This identification was commendable.
- This part of the story demonstrates both the benefits and the limitations of the passive surveillance system operated by the SVS."

  [From the "Executive Summary of the Report of the Inquiry, 2. The identification of the emergence of BSE"]

As the new disease was spreading in the cattle population in a self-propagating fashion, such that there was an exponential increase in the prevalence of infection, detection of the disease was bound to happen at some point in time. Based on the judgement from the BSE Inquiry report, I may conclude that there has been no unnecessary delay in the detection. The passive surveillance system in place served its purpose, but certainly had its limitations, which made a very early detection of the new disease unlikely. The passive surveillance system in place was designed in the following way. Veterinary practitioners could call in help from a regional Veterinary Investigation Center (VIC). The VICs were part of the State Veterinary Service

(SVS, part of the agriculture ministry MAFF) and were closely linked to the pathology department of the Central Veterinary Laboratory (CVL), itself also part of the SVS. This system is a form of passive surveillance as it is not actively looking for possibly new diseases, but only awaiting the notifications, questions and/or materials for diagnosis that arrive at the VICs. The timeliness with which a new disease is detected in such a system is limited by the following factors (BSE Inquiry report, paragraph 1.45):

- The level of vigilance and inquisitiveness will differ between individual farmers
- The level of vigilance and inquisitiveness will differ between individual vets
- Submission of cases and samples by the veterinary practitioner is on a voluntary basis, and is partly a commercial decision
- Not all veterinary practices use the services offered by the VIC; alternatives exist in the form of private labs and in-house facilities

Analysis of the relevant samples collected in the years before BSE was detected produced only one BSE-positive case. This shows that on the basis of the material gathered in the passive surveillance system, earlier detection of the new disease in cattle could hardly have been possible. Therefore, the only real potential for improving on the timeliness of detection is in an improved design of the passive surveillance system, such that its ability of early detection would suffer less from the factors mentioned above.

Was the identification of the cause of BSE in cattle (hazard or risk factor identification) a timely identification? The BSE Inquiry report concludes the following:

- "Gathering of data about the extent of the spread of BSE was impeded in the first half of 1987 by an embargo within the SVS on making information about the new disease public. This should not have occurred.
- By the end of 1987 Mr John Wilesmith, the Head of the CVL Epidemiology Department, had concluded that the cause of the reported cases of BSE was the consumption of meat and bone meal (MBM), which was made from animal carcasses and incorporated in cattle feed. This conclusion was correct. It had been reached with commendable speed.
- The following provisional conclusions of Mr Wilesmith, which were generally accepted at the time as a basis for action, were reasonable but fallacious:
    - the cases identified between 1986 and 1988 were index (ie, first generation) cases of BSE;
    - the source of infection in the MBM was tissues derived from sheep infected with conventional scrapie;
    - the MBM had become infectious because rendering methods which had previously inactivated the conventional scrapie agent had been changed.
- The cases of BSE identified between 1986 and 1988 were not index cases, nor were they the result of the transmission of scrapie. They were the consequences of recycling of cattle infected with BSE itself. The BSE agent was spread in MBM.
- BSE probably originated from a novel source early in the 1970s, possibly a cow or other animal that developed disease as a consequence of a gene mutation. The origin of the disease will probably never be known with certainty.
- The theory that BSE resulted from changes in rendering methods has no validity. Rendering methods have never been capable of completely inactivating TSEs."

[From the "Executive Summary of the Report of the Inquiry, 3. The cause of BSE"]

I note that the Report's conclusion that BSE could not have resulted from changes in rendering methods is flawed, as will be explained in paragraph 2.3.3 below. I do agree with the conclusion that the identification of the consumption of MBM as the transmission route of BSE was a commendably speedy identification. Therefore, with hindsight, only the presence of a surveillance system suffering less from the limitations mentioned above could have shortened the time spanned by the overall process of risk detection and identification of BSE.

Surveillance approach and potential for earlier identification of the actual hazard

In paragraph 1.46 of the BSE Inquiry report we read:

"While we have not found any shortcoming on the part of MAFF in identifying the emergence of BSE, we accept the evidence of Mr Sibley of the BCVA as to the natural limitations of the passive surveillance system."

The BSE Inquiry report gives the following general recommendations for surveillance policies (BSE Inquiry report, paragraph 1.48):

"If surveillance is to be effective, it is vital that:

- any new disease in animals should be identified as soon as possible;
- once identified, that the potential implications for human health of the disease, having regard to all potential routes of transmission, are considered by scientists with appropriate qualifications; and where potential risk is identified, appropriate measures are taken to address that risk."

Regarding the identification of BSE, the Inquiry report comments on the lessons to be learned as follows [Vol. 1, Chapter 14, commentary 1267]:

- "An effective system of animal disease surveillance is a prerequisite to the effective control of animal diseases.
- An effective system of passive surveillance will depend upon farmers and their veterinarians having the incentive and the facility for drawing instances of animal disease to the attention of the SVS.
- Research into methods of diagnosis should form an integral part of an animal disease surveillance system.
- The proximity of the nearest veterinary centre of investigation to the farm where the disease occurs will be an important factor in determining whether or not a casualty is referred for pathological examination.
- The identification of BSE demonstrated the importance of the animal disease surveillance system of the SVS and of the close links that existed between the Veterinary Investigation Centres (VICs) and the Central Veterinary Laboratory (CVL).
- It is important that details of a new disease which may have implications for human and animal health should be disseminated within the State and private veterinary systems in order to encourage the reporting of similar cases."

In 2003 the 10-year UK Veterinary Surveillance Strategy [5] was launched, describing how the Department for Environment, Food and Rural Affairs (Defra) plans to work in partnership with others to provide earlier warning and more rapid detection of disease threats facing the UK.
We note that the Inquiry's recommendations for surveillance policies cited above do not touch upon the issue of cost-effectiveness. Clearly, the most effective potential surveillance strategy might also be the most expensive, and decision makers will need to take the limitations of financial resources into account. Another issue of importance is quality control. Evaluation of the quality of a surveillance strategy should be carried out on a regular basis. In this context, the number of reported suspect cases (say in a certain region) can serve as a readily available performance indicator.

3.2.2 The possibilities for pro-active identification of a possible risk to cattle

Could a more pro-active approach to food safety, e.g. using indicators outside the chain, have made it possible to identify a possible TSE risk to cattle much before 1986?

In the early seventies of the last century, the hypothetical possibility that feeding animal tissue infected with a TSE to animals (of the same or of a different species) could transmit the TSE was widely known in the scientific community. Carlton Gajdusek received the Nobel prize for his work on kuru (a human TSE transmitted through cannibalistic rites in the Fore tribe in Papua New Guinea) and in his Nobel lecture [6] he remarks: "(…) the virus of natural mink encephalopathy, which, presumably, had its origin in the feeding of scrapie sheep carcasses to mink on commercial mink farms." From this it does not immediately follow that the feeding of MBM would constitute a theoretical risk of transmitting a scrapie-like TSE, as for reaching that conclusion one would have to assume a very strong heat resistance of the agent.
On the one hand, MBM had been used for many years in cattle feed throughout the world apparently without causing any TSE problem in cattle. On the other hand, in Iceland the feeding of meat and bone meal to ruminants was reportedly subject to a voluntary ban coming into force in 1978, reportedly [7] to avoid the risk of cannibalism suggested by the possible link between scrapie en transmissible mink encephalopathy. From an EU assessment of BSE risks in Iceland [8] I cite: "According to Iceland, there is a "verbal agreement" not to use MBM in ruminant feed since 1978. However, no regulation was issued and no compliance data were provided."
The conclusion in the BSE Inquiry report that "the theory that BSE resulted from changes in rendering methods has no validity as rendering methods have never been capable of completely inactivating TSEs" ([1], Executive Summary, Chapter 3) is flawed, because a reduction in *the degree* of inactivation can make the difference between a "stable system" in which each case of BSE infection on average produces less than one offspring case and an "instable system" in which the infection will propagate epidemically [9]. A change in the British rendering process in the late seventies (a phasing out of the use of solvents to extract fat from greaves) was followed by a transition in 1982 to a nutritionally improved formula for cattle feedstuffs enhancing the inclusion of MBM concentrations ([1], Volume 13, Chapter 7, paragraph 28-30). At least the second change is likely to have contributed to the instability of the animal protein recycling system for spread of BSE.
Had a more pro-active approach to food safety, using changes in production processes as indicators of a potential for newly emerging risks, been in place in Great Britain say from 1975 onwards, would it have triggered precautionary action after the change in the rendering

process in the late seventies or in the feedstuff formula in 1982? Yes, it may be speculated that, given the results of studies in the late 1970s on the decontamination of scrapie strains by rendering at different temperatures, such a pro-active approach would have led to recommendations for monitoring scrapie prevalence in sheep. It is highly unlikely however that this would have led to a recommendation for the surveillance of *cattle* for a new TSE. Furthermore, a monitoring of sheep for changes in scrapie prevalence, as no clear changes would have occurred, would have not been of any help for earlier detection of BSE in cattle. Some scope for more pro-activity is present in the passive surveillance system in place in GB in the 1980s. A system with more positive incentives for veterinarians to submit material of diseased animals and with fewer negative incentives (financial and time costs), in which private-lab results are shared with the SVS, could have made the surveillance system more powerful in picking up new diseases. More information and materials reaching the SVS would have perhaps made it possible to identify BSE in cattle about 1 year earlier. Whether the potential gains of a more powerful surveillance system justify the extra costs is an important issue, such that a costs-effectiveness analysis needs to inform decision making.

3.2.3 The discovery of the emerging risk in 1996 (humans)

Early detection

In the "Executive Summary of the Report of the Inquiry" one of the main conclusions reads: "Cases of a new variant of CJD (vCJD) were identified by the CJD Surveillance Unit and the conclusion that they were probably linked to BSE was reached as early as was reasonably possible", and I agree with this conclusion. The early detection of vCJD had been made possible by the pro-active recommendation in 1989 of the *Southwood Working Party*, the scientific committee advising the British government on the management of BSE risk, to set up surveillance for CJD (The subsequent *Tyrrell Committee* Report recommended the setup of a specialized unit).
In [1] (Executive Summary, Chapter 13) this is described as follows:

"The Southwood Working Party noted that if BSE were to be transmitted to humans it would be likely to resemble CJD and suggested that surveillance be put in place to identify atypical cases or changing patterns of the disease.

- The task of detecting any variation in the characteristics of cases of CJD which might indicate infection with BSE was entrusted to the CJD Surveillance Unit (CJDSU), a research team of dedicated medical scientists headed by Dr Robert Will, a neurologist with extensive experience of CJD.
- No role in this was given to the Public Health Laboratory Service (PHLS), an established service for the surveillance of new and existing disease, among other things.
- The decision to establish a new team specifically for this purpose was vindicated by the prompt detection of the emergence of vCJD by the CJDSU."

On 16 March 1996 the conclusion was reached by the Spongiform Encephalopathy Advisory Committee (SEAC) that the most likely explanation for the cases of a new variant of CJD in young people was exposure to BSE. The arguments behind the conclusion that the CJDSU had been prompt in its detection of vCJD are given in Volume 8, Section 5 of the Inquiry report:
"5.160 The worst fears of officials and advisors were realised when, on 8 March 1996, the

CJDSU reported to SEAC that they were of the opinion that cases in ten young people could be a new form of CJD. The circumstantial evidence of a link with BSE led to the public announcement on 20 March 1996."

"5.169 We believe that the presentation to SEAC on 8 March 1996 could not have been made sooner. It was necessary to establish the clinical and pathological characteristics of the condition in a sufficient number of patients to justify the conclusion that a new variant of CJD had been identified. The findings had to be checked by independent scientists and clinicians, and it had to be shown that what appeared to be a new variant was not in fact a type of CJD previously reported in young people, either in the UK or abroad, before the BSE epidemic. Furthermore, the DNA of each patient had to be analysed to exclude a disease-producing mutation of the prion gene. These were all prerequisites to the conclusion that there was a new variant of CJD which was probably linked with BSE. The time taken to establish a link with BSE does not warrant criticism. A wrong conclusion, hastily drawn, could have created unwarranted public anxiety and could have been very damaging to public confidence."

Contingency planning and the potential for managing the detected risk more promptly

In contrast to the pro-active mindset of the Southwood Working Party apparent in recommending CJD surveillance, the approach of the responsible civil servants in MAFF in 1996 lacked pro-active thinking:

- "It should have been apparent to both MAFF and DH by early February 1996 at the latest that there was a serious possibility that the scientists would conclude that it was likely that BSE had been transmitted to humans. The two Departments should have worked together, in consultation with SEAC, to explore the possible policy options that would be available should this occur.
- There was no interdepartmental discussion or consideration of policy options within either Department until the middle of March 1996. The views of SEAC were awaited, both as to whether the cases of vCJD were linked with BSE, and as to what action should be taken if they were. This was an inadequate response." [1] (Executive Summary, Chapter 13).

This leads the Inquiry committee to formulate the following "lessons from the final months" in Volume 1, Chapter 14, Commentary 1279:

"The Government was taken by surprise and wrong-footed by the announcement by SEAC that a new variant of CJD had been identified which was probably linked to BSE. It should not have been. The growing apprehension that this might be the case had been expressed by Dr Will and other members of SEAC at its meetings on 5 January 1996 and, more forcibly, 1 February. Representatives of MAFF and DH present at those meetings did not put their colleagues on the alert that SEAC might be moving towards this conclusion. The possibility of this should nonetheless have been appreciated by those who received the reports of the SEAC meetings. They did not, however, consider any contingency plans. There were no interdepartmental discussions about the gathering storm. Everyone waited to see what SEAC had to say."

3.2.4 Successes and failures in the pro-active identification and management of a possible risk to humans

Although it is in part due to pro-active BSE policy making that the *reality* of the risk to humans was detected as early as reasonably possible, there were clearly important shortcomings in pro-active policy making after the identification, in the late 1980s, of a *possible* risk to humans.
Also in view of the many years of human exposure that necessarily (due to the long incubation time of vCJD) occurred before the possible risk became a proven one, the following two issues seem of equal importance to the early detection of vCJD:

- Early identification of the possible human risk.
- Adequate precautionary policy making in the face of this possible risk.

As far as the first point is concerned, I note that within MAFF the hypothetical issue of a risk to humans was identified immediately after the discovery of BSE, as is apparent from paragraph 2.3.1 above. I.e., from a point of view of pro-active signalling of possible risks to humans, no unnecessary delay occurred beyond any delay in detecting the risk to cattle. However, the management of the possible human risk was compromised by three main things:

- Serious shortcomings of the initial risk assessment report produced by the Southwood Working Party, leading MAFF officials to believe that the risk to humans was ‘remote’.
- MAFF’s subsequent decision to focus on reassurance in their risk communication to the public.
- The absence of a coordinated or comprehensive consideration given to the various routes by which BSE might infect human beings or other animals.

In the Executive Summary of the Report of the Inquiry, Chapter 4, the following conclusions are formulated on MAFF’s assessment of the risk posed by BSE to humans:

- “MAFF officials appreciated from the outset the possibility that BSE might have implications for human health.
- By the end of 1987 MAFF officials had become concerned as to whether it was acceptable for cattle showing signs of BSE to be slaughtered for human consumption. However, the Department of Health (DH) was not asked to collaborate with MAFF in considering the implications that BSE had for human health. It should have been.
- Only in March 1988, by which time MAFF officials had advised their Minister that animals showing signs of BSE should be destroyed and compensation paid, did MAFF advise the Chief Medical Officer (CMO) Sir Donald Acheson of the emergence of BSE and ask him for his view of the possible human health implications.
- On Sir Donald's advice, an expert working party, chaired by Sir Richard Southwood, was set up to advise on the implications of BSE. After their first meeting in June 1988, the Southwood Working Party advised that cattle showing signs of BSE should be slaughtered and destroyed. This advice was of crucial importance in safeguarding human health. The Working Party had concerns about some occupational health risks in relation to BSE and some risks posed by medicinal products. They notified the responsible authorities of these concerns. On 9 February 1989 they submitted a Report to the Government in the knowledge that it would be published. The report concluded that the risk of transmission of BSE to humans appeared remote and that 'it was most unlikely that BSE would have any implications for human health'.
- This assessment of risk was made on the following basis:

- BSE was probably derived from scrapie and could be expected to behave like scrapie. Scrapie had not been transmitted to humans in over 200 years and so BSE was not likely to transmit either.
- So far as occupational and medicinal risks were concerned, the authorities which had been notified about these could be relied upon to take appropriate measures to address them.

- The Report did not, as it should have done, make clear the basis for its assessment of risk. It did comment that if the assessment was incorrect the implications would be extremely serious. This warning was lost from sight. The *Southwood Report* was, in years to come, repeatedly cited as constituting a scientific appraisal that the risks posed by BSE to humans were remote and that no precautionary measures were needed other than those recommended by the Working Party.
- Precautionary measures were nonetheless put in place that went beyond those recommended by the Working Party. The wisdom of those measures was demonstrated as the years went by and facts were learned about BSE which threw doubt on the theory both that it was derived from scrapie and that it would behave like scrapie.
- In May 1990 a domestic cat was diagnosed as suffering from a 'scrapie-like' spongiform encephalopathy. This generated widespread public and media concern that BSE had been transmitted to the cat and might also be transmissible to humans. Subsequently, more domestic cats were similarly diagnosed. These events shifted the perception of some scientists of the likelihood that BSE might be transmissible to humans. By 1994 the Spongiform Encephalopathy Advisory Committee (SEAC) evaluated the risk of transmissibility to humans as remote only because precautionary measures had been put in place."

With respect to the measures to address the food risks posed by BSE to humans, chapter 7 of the Executive Summary of the Report of the Inquiry makes the following remarks:

- "The Southwood Working Party considered that all reasonably practicable precautions should be taken to reduce the risks that would exist should BSE prove to be transmissible to humans. However, they did not make this plain in their Report and did not recommend that the possible risks from eating animals incubating BSE but not yet showing signs of the disease ('subclinical cases') called for any precautions, other than a recommendation that manufacturers should not include ruminant offal and thymus in baby food. This was a shortcoming in their Report.
- Because of a failure to subject the *Southwood Report* to an adequate review, MAFF and DH failed to identify this shortcoming. Concern about the food risks posed by subclinical cases was, however, expressed by some scientists, by the media and by the public. With the agreement of DH, MAFF reacted by announcing in June 1989 that those categories of offal of cattle most likely to be infectious (SBO) were to be banned from use in human food. The introduction of this vital precautionary measure was commendable. However, this ban was presented to the public in terms that underplayed its importance as a public health measure.
- Careful consideration was given by MAFF and DH in 1989 to the terms of the human SBO ban, with one important exception. During the consultation process, concerns were raised about the practicality of ensuring the removal of all of the spinal cord during abattoir processes, and about the practice of mechanical recovery of scraps left attached to

the vertebral column for use in human food ('mechanically recovered meat' or MRM). However, MAFF officials discounted these concerns without subjecting them to rigorous consideration - in particular no advice was sought as to the minimum quantity of spinal cord that might transmit the disease in food.

- MAFF gave detailed consideration to spinal cord and MRM in 1990. A lengthy paper was submitted to SEAC, the Government's new expert advisory committee on TSEs. Unhappily, as a result of a breakdown of communications, MAFF officials understood that the members of SEAC were not concerned about the inclusion in human food of an occasional scrap of spinal cord, so that no action was called for. In fact the advice of some, at least, of the members of SEAC was premised on the false assumption that spinal cord could readily be removed from the carcass in its entirety, and would be so removed.
- This was one of a number of occasions that has given rise to lessons for the future about the proper use of expert committees by the Government."

With respect to risks to humans posed by other pathways of BSE infection, Chapter 11 of the Executive Summary of the Report of the Inquiry makes the following remark:

"There was a need to establish all the pathways by which bovine products or by-products might come into contact with humans or other animals. This need was recognised by MAFF officials at an early stage and also by the Government's expert advisers on BSE. However, the exercise was never carried out prior to March 1996. As a result, no coordinated or comprehensive consideration was given to the various routes by which BSE might infect human beings or other animals."

Volume 1, Chapter 14 of Report of the Inquiry lists the lessons to be learned from the emergence of vCJD:

- "Although likelihood of a risk to human life may appear remote, where there is uncertainty all reasonably practicable precautions should be taken.
- Precautionary measures should be strictly enforced even if the risk that they address appears to be remote.
- All pathways by which vCJD may be transmitted between humans must be identified and all reasonably practicable measures taken to block them."

With regard to the second lesson above, the BSE Inquiry Report suggests (Vol. 1, Chapter 6) that the quality of implementation and enforcement of the human SBO ban of 1989 must have been negatively influenced by MAFF's reassuring risk communication that accompanied it. The ban was presented as a practical means to provide even more reassurance to the public in making sure that the Southwood Report's recommendation on baby food, currently fulfilled, would remain fulfilled in the future. The baby food recommendation in itself was described by Southwood to MAFF representatives as a matter of "extreme prudence" ([1], Vol. 6, 3.30; and [2]). The government's risk communication was embodied in the following part of a joint news release on 13 June 1989 by MAFF and the Department of Health announced the intention to introduce an SBO ban to cover all human food, which quoted the answer of the Minister of Agriculture, Fisheries and Food to a written Parliamentary Question by Mr Tim Boswell, MP ([1], Vol. 6, 3.256):

"The Government has already taken wide ranging action to deal with this new disease problem and has acted on all the recommendations made by the Southwood Working Party

which was set up to look at all aspects of the disease, including any human health implications.
Although the Southwood Working Party regarded the risk to humans as remote, the Government acted on their recommendation that, as a precautionary measure, all cattle suspected as having BSE should be slaughtered and destroyed to take them out of the food chain.
As a matter of extreme prudence, the Southwood Working Party also suggested that certain offals should not be used in the manufacture of baby foods. We established in February that these offals are not in fact currently used by baby food manufacturers. In order to provide even more reassurance to the public, I indicated then that we would bring forward regulations to ensure that there is no possibility of their use in the future.
In working out the details, I have concluded that a better way of dealing with this would be to ensure that the relevant types of bovine offals should be rejected at slaughterhouses for all cattle so that they cannot be used for human consumption in any way. (…) This approach also deals with a separate problem, namely ensuring that if there is any risk that there are cattle incubating the disease but not showing clinical symptoms which are not being slaughtered and destroyed, their offals do not enter the food chain either."

Thus MAFF underplayed the public health relevance of taking out the offals from subclinically infected animals and gave the impression that the ban was not really a necessary precautionary measure. In the Inquiry Report, Vol. 1, Chapter 6, the presentation is commented as follows:

"568 This at least referred to the subclinical animals, but in terms that suggested that there was no more than a risk that some of these might go for slaughter. In fact this was inevitably happening on a substantial scale."

"569 How far the presentation, which played down the importance of the human SBO ban, influenced people's attitudes we shall never know. We had evidence from many sources, however, of a perception that the ban was not really necessary as a public health measure."

In part this misrepresentation might have been caused by the wish not to endanger the authority of the Southwood Working Party, in part it might have been caused by the fear that when admitting the true rationale of the policy, public opinion might 'overreact' and pressure would rise to take further, but truly unnecessary, precautionary measures.

3.3 Conclusions and recommendations

The main conclusions of this case study and their implications for pro-active approaches to the identification of emerging risks are as follows.

- Surveillance structures in place in Great Britain have been successful in achieving an early (human risk in 1996 and risk to cattle in 1986) detection of emerging BSE risks.
- With regard to the BSE risk to cattle I conclude:
    - A more pro-active approach to risk identification could perhaps have yielded a benefit. The passive surveillance structure could have been (even) more powerful if farmers and veterinarians had been given more positive incentives to submit animal material to Veterinary Investigation Centers for diagnosis and/or a common database had been present, supplied by both the State Veterinary Service and veterinary practitioners.

  - It may be speculated that in a pro-active approach in which changes in production processes are used as indicators of a potential for newly emerging risks, the identification of a possibly enhanced scrapie risk in sheep would have been triggered in the late 1970s or early 1980s by the changes in rendering processes and the subsequent enhancement in the amount of MBM included in ruminant feedstuffs. Subsequent monitoring of scrapie in sheep would however not have been useful for detecting BSE in cattle, and it seems unlikely that monitoring of cattle themselves would have been recommended.
- With regard to the BSE risk to humans I conclude:
  - Precautionary actions against the human risk were compromised by several issues, including the shortcomings of a first risk assessment.

I would like to make the following recommendations on pro-active policy making:

- Assessments are needed of the likelihood of introducing new risks when changes are made in production processes (including feeding and housing of animals)
- Proper investments in surveillance structures and specialist expertise are vital
- Pro-actively signalling potentially emerging risks is only a first step. Swiftly introducing adequate precautionary risk management and appropriate risk communication may be as difficult or even more difficult, especially when the risk is not yet a proven risk or its magnitude and/or properties are subject to large uncertainty.

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3.4 References

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4. Case study: the high-pathogenicity Avian Influenza epidemic in the Netherlands in 2003

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4.1 Case description

Avian Influenza

Avian Influenza is a viral disease of birds and is caused by influenza A viruses. Influenza A viruses that infect poultry can be subdivided into two groups: low pathogenicity (LPAI) and high pathogenicity avian influenza (HPAI) viruses on the basis of severity of disease after experimental infection (Alexander, 2002). HPAI outbreaks in domestic poultry are limited to the subtypes H5 and H7 (Swayne and Suarez, 2000), although not all viruses of these subtypes will cause HPAI. On several other occasions in the past, e.g. in the USA (Bean et al., 1985), Mexico (Garcia et al. 1996), Italy (Capua and Marangon, 2000), Chile (Rojas et al., 2002), the Netherlands (Elbers et al., 2004) and Canada (Bowes et al., 2004) it has been shown that HPAI-virus strains developed from a LPAI-virus strain by means of mutations mostly involving insertions near to the cleavage site. Mutation of influenza viruses are assumed to occur randomly and are attributed to mistakes made by the polymerase needed for virus genome replication. Mutants will survive and emerge whenever they have a selective growth advantage over the majority of the virus population. A positive selective pressure only seems to exist in poultry. Therefore, the longer the presence and the larger the spread of LPAI H5 and H7 viruses in poultry the more likely HPAI virus will emerge (Alexander, 2003). Thus mutation being a stochastic event, combined with mutant selection, explains the variability in time before the emergence of HPAI from a LPAI virus.

It is well known that waterfowl and shorebirds (wild and domesticated) are the major natural reservoir and source of all known influenza A viruses (Swayne and Halvorson, 2003). Wild bird surveillance studies performed in North America showed that in particular Anseriformes (like ducks and geese) and shorebirds are frequently carriers of influenza A viruses. Recently, surveillance studies in Europe confirmed the higher prevalence in ducks compared to other waterfowl but no viruses were isolated from shorebirds indicating regional differences (De Marco et al., 2003; Fouchier et al., 2003). Nearly all viruses isolated from wild birds are low pathogenic, and the few that were highly pathogenic could be associated with major outbreaks in domestic poultry. Only after low pathogenicity viruses of H5 and H7 subtype are introduced in poultry, in particular chickens and turkeys, high pathogenicity mutants come up after variable length of time (Alexander, 2003). In 19 of 24 outbreaks that were reported during the past 46 years evidence showed that the virus was introduced from wild fowl and then mutated either in a short period (15 cases) or after several months (4 cases) into a HPAI variant.

HPAI outbreaks in the Netherlands
HPAI outbreaks were first described in the Netherlands in poultry in 1924 in the municipalities Achterveld, Scherpenzeel and Woudenberg (situated in the same area that was struck during the 2003 epidemic). The last time HPAI was observed in the Netherlands was in 1927 in the same area as in 1924 (van Heelsbergen, 1927). HPAI was never reported before

by the Netherlands to the Office International des Epizooties (OIE) in Paris. However, after an absence from the Netherlands for more than 75 years, a serious suspicion of an infection with HPAI virus on several poultry farms in the "Gelderse Vallei" was reported on 28 February 2003 (Elbers et al., 2004). The "Gelderse Vallei" is an area in the central-eastern part of the Netherlands with a very high density of poultry and poultry farms. Consequently, the governmental authorities were informed. It was the start of a large HPAI epidemic with the H7N7 strain, in which especially the high-density poultry areas were severely hit.

Re-emerging risk
Strictly speaking the epidemic was due to a re-emerging risk, as it had happened before in the Netherlands. However, because of the time period of almost 75 years between disease events, it was felt by the poultry industry as if it was a new risk. There is a lot to say about this view, and this is discussed in section 2.4.2.

Human health risk
In the first days of the eradication campaign, a number of veterinary practitioners showed a conjunctivitis (an infection of the mucosal membrane of the eye) after having visited infected poultry farms (Koopmans et al., 2004). Conjunctivitis can be the result of virus replication in the mucosal membrane of the eye. Historically, at that time there was one publication known of a possible human infection by birds with the avian influenza H7N7-strain. In 1996 a H7N7 virus was isolated in England from the eye of a 43-year-old woman with mild one-sided conjunctivitis who kept ducks (Kurtz et al., 1996). In 1979, several marine researchers developed conjunctivitis when examining stranded and dead harbor seals on Cape Cod in the USA. The disease in the seals was associated with an influenza virus that was antigenically similar to A/Fowl Plague/Dutch/27 (H7N7) (Webster et al., 1981). Furthermore, in Hong Kong a total of 18 people got infected and 6 people died after exposure to H5N1-infected poultry on live bird markets (Shortridge et al., 1998). During the second half of the 1990s outbreaks in poultry, due to H9N2 subtype, have been reported from several countries around the world. In March 1999 two independent isolations of AI virus of subtype H9N2 were made from girls aged one to four who recovered from flu-like illnesses in Hong Kong (Peiris et al., 1999). Subsequently, 5 isolations of H9N2 virus from humans on mainland China in August 1998 were reported. During the H7N1-epidemic in poultry in Italy in 1999-2000, no clinical signs were observed in people in close contact with infected poultry during the eradication campaign (Capua and Marangon, 2000).
The risk assessment in the first days of the epidemic in the Netherlands therefore was that the human risk was small, but not zero. After more influenza-like symptoms were seen in veterinary practitioners and other people in close contact with infected poultry in the days after, and in addition a veterinarian was diagnosed with a human influenza H3N2-infection while working with infected poultry, an active case-finding operation was started and a stringent protocol was implemented (Koopmans et al., 2004). The protocol consisted of vaccination (against the human influenza H3N2 strain) of people working with infected poultry, prophylactic administration of antivirals and use of protective devices (glasses, clothing etc.). Retrospectively, one has to conclude that transmission of H7N7-virus occurred to a considerable number of people in direct contact with infected poultry, and there are indications for transmission from person-to-person in a few cases. Due to a very unfortunate course of events, a 57-year-old veterinary practitioner died on April 17th as the result of pneumonia followed by acute respiratory distress syndrome and related complications after infection with the HPAI subtype H7N7-virus (Fouchier et al., 2004). He visited a poultry flock with a possible suspicion of HPAI-infection on April 2nd in an area outside the protection and surveillance zones of the primary outbreak area, wearing protective devices,

but without receiving prophylactic treatment with antivirals. The stringent protocol was indicated for people working inside the protection and surveillance zones, because they were likely to be exposed for longer time periods to HPAI-virus. The clinical symptoms of the veterinary practitioner (fever and headache, but no conjunctivitis or respiratory disease) on April 4th were not associated with an HPAI-infection (Fouchier et al., 2004). Because of his farm visit on April 2nd, a throat and eye swabs were collected on April 9th, but RT-PCR tests performed in 2 laboratories were negative. After admission into a hospital, his clinical situation deteriorated and he died a few days later. Afterwards, the results of a bronchoalveolar lavage indicated that he died of an infection with AI virus (subtype H7N7). Because AI virus can be found in products from infected poultry like table eggs and meat products, the export of poultry products from the Netherlands was prohibited.

Transmission to other countries
After the international announcement of HPAI-outbreaks in the Netherlands, our neighbouring countries Belgium and Germany, took stringent precautions in order to prevent introduction into their country and measures were taken to detect a possible introduction into poultry as soon as possible:
a) Crisis unit was put in state of high alert; b) Nation-wide ban on gathering of poultry and other birds; c) Nation wide transport ban of live poultry and hatching eggs; d) Stringent and nation-wide biosecurity measures on poultry holdings; e) Limited access to poultry holdings, especially for any person in contact with poultry in Netherlands; f) Increased vigilance with regard to poultry and egg transports at the Dutch-Belgian border; g) Notification of any disease or increased mortality for which HPAI could not be excluded; h) Prohibition of medical treatment of poultry unless samples have been sent to regional Animal Health Service; i) Tracing of all Belgian high-risk contact holdings (import of live birds or hatching eggs / indirect contact with infected Dutch premises); j) Establishment of protection and surveillance zones as a result of outbreaks in the Netherlands near the Belgian border.

There was a first suspicion of an HPAI outbreak in Belgium on March 11th in a 12,000 broiler flock in the municipality of Ravels near Poppel (less than 0.5 km from the border with the Dutch province of Noord-Brabant). Suspicion was raised after 2,000 birds died on one single day. The poultry flock in Ravels was depopulated within 24 hours of the suspicion as a precautionary measure. Backyard poultry in an area within a one-kilometer radius of the suspect flock was depopulated and destroyed. On March 24th, the definite diagnostic test result for the suspicion in Ravels was negative.
A second clinical suspicion of an AI-outbreak was raised on April 15th in a 10,500 parent poultry stock in the municipality of Meeuwen-Gruitrode (less than 14 km from the border with the Dutch province of Limburg). Lab confirmation of infection came on April 18th: positive for HPAI subtype H7.
Within a period of 2 weeks a total of 8 HPAI outbreaks occurred:
- four more outbreaks in the area around first outbreak (in Bree and Kinrooi);
- three other outbreaks 60 km west of the primary outbreak area (in Meer and Westmalle).
In the period of April 16th to May 15th 2003, a total of 129 poultry flocks were depopulated, comprising a total of 3.2 million birds. It can be concluded that probably due to the high level of alertness in response to the AI-outbreaks in the Netherlands and a quick response (depopulation of infected flock and pre-emptive slaughter of neighborhood flocks), only a limited number of outbreaks occurred in Belgium.

In Germany, there was a first suspicion of an AI outbreak on April 9th in a 32,000 broiler flock in Viersen (± 16 km from the Dutch Border, between Venlo and Mönchen-Gladbach). A

few days later, the lab confirmatory test indicated a negative result. A second suspicion of an AI-outbreak was raised in the evening on May 8th in a 30,000 broiler flock in Swalmtal (± 10 km from Dutch Border, same area as the first suspicion). The flock was culled the next day as a precautionary measure, as were a few contact flocks (total 80,000 birds). Within a radius of 3 km around the suspect flock, all poultry flocks were pre-emptively culled within 48 hours. On May 13th, the laboratory confirmation was positive for HPAI subtype H7. No further cases were reported since May 13th and restriction measures were lifted as of June 24th 2003. As in the case of Belgium, it can be concluded that probably due to the high level of alertness in response to the AI-outbreaks in the Netherlands and a quick response only one outbreak occurred in Germany.

Political impact factor

The recent CSF-, FMD and AI epidemics in the Netherlands, in which large numbers of animals were killed on infected premises, were covered intensively by the media. The general public was confronted with the killing of thousands of healthy (in the case of FMD: vaccinated) animals in the framework of pre-emptive culling to stop the epidemic. It was very difficult to convince the general public that these animals were killed because of trade circumstances and regulations. Furthermore, hobby farmers and children with one or two sheep, goats or chicken, lost there animals to pre-emptive culling, which resulted in a social outcry. With respect to AI there is even a much higher political impact due to the zoonotic aspects of AI. The human pandemic viruses of 1957 and 1968 appeared to have arisen by reassortment between viruses present in the human population and avian influenza viruses. Until 1996 there were only a very limited number of reported infections in humans exposed to AI. However, in recent years, a series of isolations from people having contact with poultry have been reported. The impact these subsequent human infections on public health issues was greatly enhanced by the high death rate in those shown to be infected. The main danger appears from the possibility that people infected with the AI viruses are simultaneously infected with a “human” influenza virus, in which case reassortment can occur with the potential emergence of a new virus fully capable of spread in the human population, resulting in a true influenza pandemic. The prospect of possibly ten thousands (and maybe millions) of human deaths during a future influenza pandemic is a huge fear factor, with tremendous political impact.

Risk perception of relevant stakeholders

The government and the commercial poultry industry are well aware of the risk of re-emergence of AI. The 2003 epidemic in the Netherlands was a very costly event, both for industry and government. Almost 80% of the poultry production in the Netherlands is exported, implicating a heavy dependence on trade. After the epidemic the Dutch poultry industry indicated that it would not survive a future AI epidemic of a comparable size. There is a broad scientific consensus that wild waterfowl acts as the natural reservoir for LPAI viruses. Although not completely proven, there is also scientific consensus on the idea that AI is most probably introduced into commercial poultry by exposure to infected wild waterfowl and their excreta (EFSA, 2005). However, risk perception seems to be different for hobby farmers and farmers using alternative production systems. This is emphasized in the discussion around the temporary obligation of free-range poultry farmers to keep their poultry inside, due to the threat of introduction of HPAI virus of subtype H5N1 from East Asia. The Society for Biological Poultry Farmers states that there is no evidence that migratory birds transmit (LP)AI viruses to commercial poultry (Borren, 2005). So, in their view there is no reason why their animals could not continue to use outdoor facilities without adjustments to their outdoor housing facilities preventing contact with wild waterfowl. Furthermore, they

state that not the outdoor-ranging but international transportation of poultry and the high number of contacts occurring between large commercial poultry farms are the factors causing a high risk for introduction of AI. This view is shared by the biological consumer organization "Stichting Wakker Dier" (Thieme, 2005).

Is re-emergence of this risk likely to happen in the future?
In the last 40 years of the 20th century, reports on severe HPAI outbreaks have, fortunately, been infrequent (Table 1). In the last 5 years, however, increased occurrence of HPAI is noticed, especially in South-East Asia, where it seems that the disease has become endemic and eradication has not be achieved so far.

	Country	Year	Subtype		Country	Year	Subtype
1	Scotland	1959	H5N1	15	Australia	1997	H7N4
2	England	1963	H7N3	16	HongKong	1997	H5N1
3	Canada	1966	H7N3	17	Italy	1997	H5N2
4	Australia	1966	H7N7	18	Italy	1999-2000	H7N1
5	Germany	1979	H7N7	19	Chile	2002	H7N3
6	England	1979	H7N7	20	Netherlands/Belgium/ Germany	2003	H7N7
7	USA	1983	H5N2	21	South East Asia[2]	2004-2005	H5N1
8	Ireland	1983	H5N8	22	Canada	2004	H7N3
9	Australia	1985	H7N7	23	USA[3]	2004	H5N2
10	England	1991	H5N1	24	South Africa	2004	H5N2
11	Australia	1992	H7N3	25	Peoples Republic of North Korea	2005	H7N?
12	Australia	1994	H7N3	26	Kazakhstan	2005	H5N1
13	Mexico	1994	H5N2	27	Russian Federation	2005	H5N1
14	Pakistan	1994	H7N3				

Table 4.1 High pathogenicity avian influenza outbreaks in domestic poultry[1] worldwide since 1959.

[1] Where outbreak is wide spread and effecting more than 1 species, the isolate from the first outbreak identified is listed

[2] Cambodia, China, Indonesia, Japan, Lao PDR, Malaysia, Republic of South Korea, Thailand and Vietnam reported disease in this period; the relationship of these viruses to A/Hong Kong/97 (H5N1) remains unclear at present.

[3] This virus did not kill chickens infected experimentally, but had multiple basic amino acids at the HA0 cleavage site.

The recent CSF- and FMD epidemics in the Netherlands, in which large number of animals were killed on infected premises and on pre-emptively culled farms, was covered intensively by the media and there was societal commotion in the lay public on the conventional production methods in the Dutch livestock industry. Besides, there was a social outcry on the killing of thousands of healthy (vaccinated) animals in the framework of pre-emptive culling to stop the epidemic.
After these events, due to societal pressure, development of alternative production methods in the agricultural industry was promoted by the Dutch Ministry of Agriculture, Nature Management and Food Safety. Over the last 6 years, the number of free-range layer chickens and layer chickens produced in a biological production system in the Netherlands has increased two and three-fold, respectively (figure 1).
According to the recent EFSA-report on Animal Health and welfare aspects of Avian Influenza (EFSA, 2005), the disease has escalated in the last years (in contrast to the 40 years before that), resulting in a global crisis with 50 million birds culled or dead in the EU alone between 2000 and 2003. Poultry holdings located under migratory flyways or in close proximity with wild bird breeding or resting sites are considered to have a greater risk of exposure to AI. This risk is thought to be enhanced in case of establishments with outdoor access and areas that have a high poultry density. Considering the future trend of more outdoor-production due to public demand and the observed higher rate of occurrence of AI in the EU and the rest of the world, it can be concluded that re-emergence of this risk is likely to happen in the future. The rate at which re-emergence may happen will, among others, depend on preventive measures (biosecurity, design of housing systems) taken in the Dutch poultry industry in the coming years.

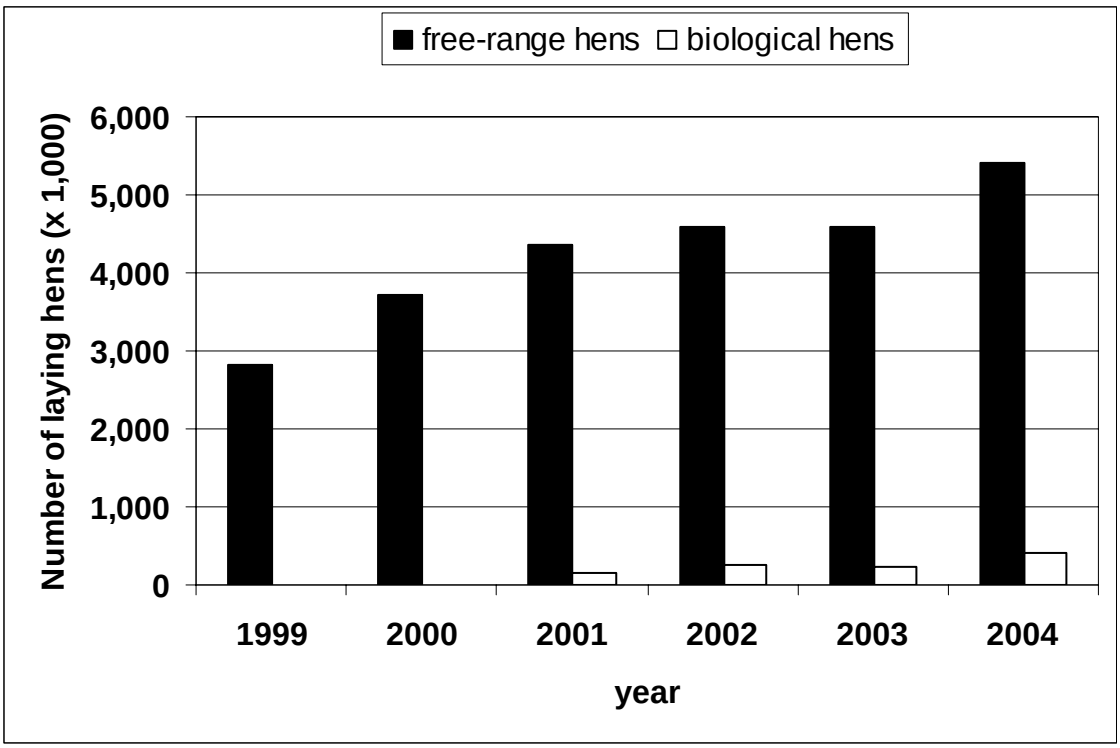

Figure 4.1. Development of the number of laying hens in free-range facilities and in biological production in the Netherlands 1999-2004 (source: Biologica/EKOmonitor and Product Board for Livestock, Meat and Eggs).

Detailed description of the detection of the emerging risk

A detailed description of the detection of the first HPAI-infected poultry flocks was published by Elbers et al. (2004). Briefly, the first five cases were located in the "Gelderse Vallei", an area in the central-eastern part of the Netherlands with a high density of poultry and poultry farms (± 4 poultry farms/km^2). The premises of Case 1 (free-range layers) and Case 5 (parent-stock broilers) were situated opposite to each other at the same road (± 500 meters distance) in the same municipality. The premises of Case 3 (free-range layers) were located at the same road as Case 1 and Case 5. Case 2 (caged layers) was situated in the same municipality as Case 3, the premises of Case 2 and Case 4 (free-range layers) were situated close to each other (± 600 meters distance).

On Saturday 22 February, a decrease in feed and water intake in poultry of case 1 was seen. The day after (Sunday 23 February), there was continued decrease in feed and water intake, and start of increased mortality (1.5%). During the rest of the week 4 other flocks experienced severe clinical problems, expressed as high and extremely fast progressive mortality (see figure 2 and 3) and severe diarrhea.

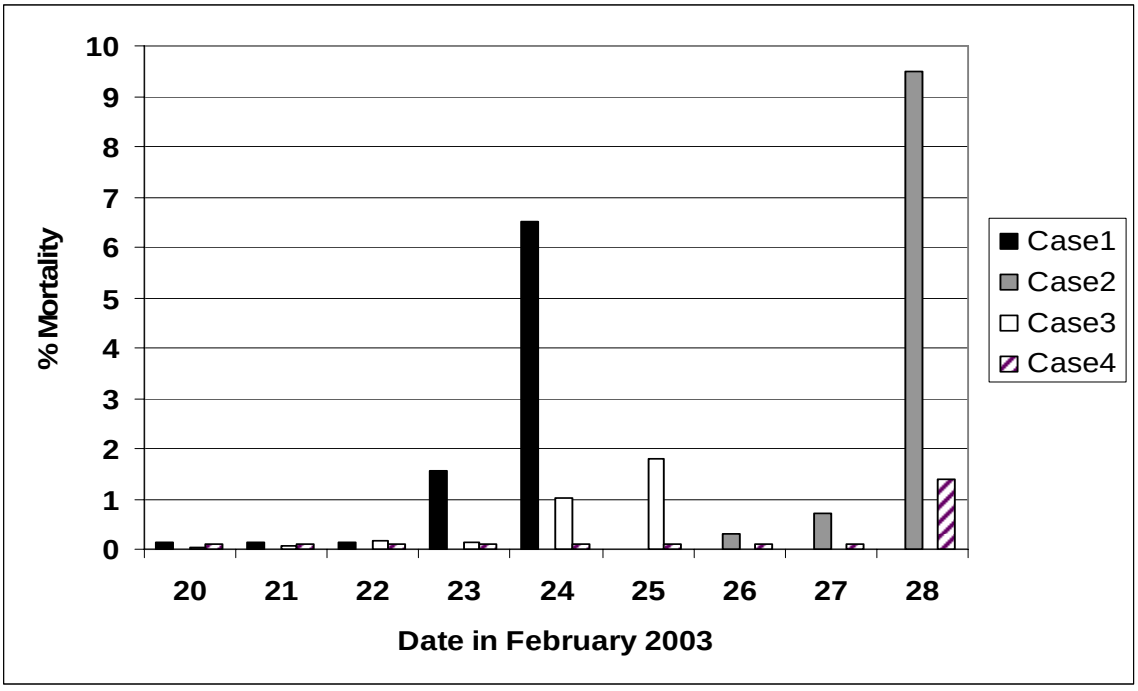

Figure 4.2. Development of mortality over time in the first four poultry flocks during the HPAI (subtype H7N7) epidemic in the Netherlands in 2003.

None of the poultry farmers or veterinary practitioners notified the official veterinary authorities of a dramatic clinical situation. A few dead birds per flock were sent for post-mortem examination (PME) to the Dutch Animal Health Service (AHS), a private veterinary laboratory. During PME, the majority of submitted birds showed peritonitis, in a few cases swollen liver, swollen spleen, slight tracheitis. Anamnesis (history taking) sent together with birds were in some cases of poor quality, there was no specific mention on extent of mortality

(reason for submission was often indicated as “increased mortality”). PME resulted in preliminary diagnosis: *E. Coli* or *Salmonella gallinarum*. During the week, supplementary laboratory investigations indicated: a) negative results trying to culture *Salmonella* or *E.Coli*; b) a test to exclude Newcastle Disease (ND) as cause of the slight tracheitis seen during PME was negative. On Friday 28 February, supplementary laboratory investigations of tissues from poultry submitted from case 1 and case 4 on *S.gallinarum* is still negative. In order to exclude other possible causes, the laboratory of the AHS started diagnostic tests on ND and AI in tissue samples from poultry submitted from case 1 and case 2. In addition, a veterinary poultry expert from the AHS was sent to both poultry flocks for clinical inspection. Report in the afternoon by telephone of the veterinary poultry expert describing a dramatic clinical situation in case 1 and case 2, coincided with a positive test result for AI on tissue samples from case 1 and case 2. This resulted in a notification of a serious suspicion of AI to the veterinary authorities.

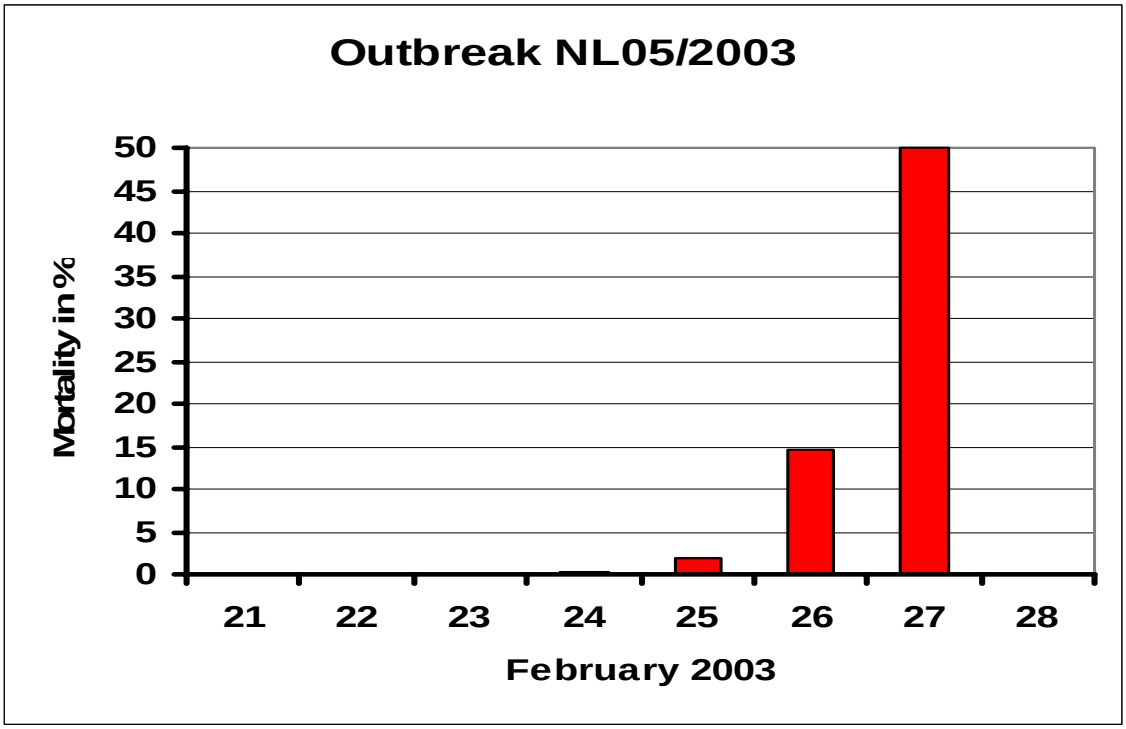

Figure 4.3. Development of mortality over time in poultry flock nr. 5 during the HPAI (subtype H7N7) epidemic in the Netherlands in 2003.

4.2 Pro-activity paying off and lacking pro-activity

Which pro-active approaches contributed to detection of the AI-outbreak?

The introduction of HPAI in commercial poultry flocks in the Netherlands was perceived by the industry as a new emerging risk (in contrast to a re-emerging risk for which one could have prepared oneself). In the end, final detection of the first AI-cases, several days after the start of an exponential increased mortality, benefited from the presence of veterinary specialists at the Animal Health Service. These specialists started a differential-diagnostic laboratory test to exclude or confirm AI after subsequent laboratory examination of samples from birds with disease problems in several poultry flocks in the “Gelderse Vallei” for several days failed to support a conclusive diagnosis.

However, detection could have been much earlier if veterinary practitioners and poultry farmers in the field had taken their responsibility by notifying the veterinary authorities of a very severe clinical situation. There was every reason to do that because the direct signs of a developing emergency were loud and clear by means of an exponentially increasing mortality in the poultry flocks that could not be denied.

Did detection benefit from a holistic approach?
There are no indications at all that detection of the first AI-outbreaks in the Netherlands in 2003 benefited from a holistic approach by signals from indicators outside the chain.

Could detection have profited from a more holistic approach?
One could say indirectly, and on a more general level. It is clear that alternative production methods have been promoted by government, and as a result there has been a considerable increase in the number free-range poultry. The increase in outdoor production could have been used as a signal in a holistic approach to warn for an emerging risk, but it was not used. Retrospectively, as a response to the increase in free-range and biological poultry production, specific monitoring programs could have been created for these poultry flocks with a higher risk of AI-introduction. Although there have been many warnings from the scientific community in the past years that these alternative production methods constitute a higher risk of exposure to e.g. chemical contaminants and disease agents (parasites, bacteria and viruses) through contact with wild fauna and their excretion products, there was a primary focus on creating a market for biological products and getting retailers interested in selling these products to consumers. One can conclude that in the past years (and more or less even now) it was “politically incorrect” to ask attention for the risks involved with these production methods.

If detection was late, which pro-active actions could have increased the probability of detection?
As stated in section 2.4.1, the emergence of the AI-outbreaks in the Netherlands were felt by the poultry industry as if it was a new risk, coming out of the blue. However, there is much to say about this view.
In 2002 and the beginning of 2003, AI outbreaks in domestic poultry were reported from the USA (low pathogenicity AI (LPAI) subtype H7N2) (Nolen, 2002), Chile (LPAI and HPAI subtype H7N3) (Rojas et al., 2002), and Italy (LPAI subtype H7N3) (Capua et al., 2002). So, in different areas around the world, and even close by in Europe, LPAI outbreaks occurred in the months preceding the outbreak in the Netherlands, but this did not lead to a higher level of preparedness or precautionary measures in the Netherlands. In a sense, one did not learn from the past because on several other occasions before the start of the epidemic in the Netherlands in 2003, e.g. in the USA (Bean et al., 1985), Mexico (Garcia et al. 1996), Italy (Capua and Marangon, 2000), Chile (Rojas et al., 2002), it has been shown that a HPAI-virus strains developed from a LPAI-virus strain by means of mutations mostly involving insertions near to the cleavage site.
At that time, LPAI outbreaks were not considered as notifiable by the international community. However, due to the large epidemics in the Netherlands in 2003 and in Canada in 2004, which started as an introduction of LPAI, the international community has changed its views and the new OIE-guidelines for the control and eradication of AI has also incorporated measures to fight LPAI infections of subtype H5 and H7.

In the year 2000, precautionary measures were indeed taken in the Netherlands due to the thread of a large HPAI-epidemic occurring in Italy in 1999-2000 (Capua and Marangon, 2000). Stringent measures were established by the veterinary authorities in the Netherlands embodied by the Directive Flock Control Avian Diseases 2000, (DFCAD-2000). These measures were introduced to detect a possible AI-outbreak (including LPAI infections) as quickly as possible (Heijmans, 2000; Heijmans and Komijn, 2000). According to DFCAD-2000, every poultry farmer was obliged to counsel his veterinary practitioner when a flock was treated due to a possible infectious disease or mortality of a flock was 0.5 % or more per 24 hours. Call-in of the veterinary practitioner was also obliged when in reproduction flocks or layers the mean egg-production was decreased by 5% or more in a period of one week. The veterinary practitioner clinically inspected the flock and took 20 blood samples per poultry house for detection of antibodies against AI virus. The results of the clinical inspection were collected into a central database. Over 2000 examinations were performed on the basis of clinical signs exceeding the threshold-levels in a period of 5-6 months. At the end of 2000, when the HPAI epidemic in Italy was under control, the DFCAD-2000 in the Netherlands was dismantled. If the DFCAD-200 still would have been in operation in 2003, and poultry farmers would have adhered strictly to the notification thresholds, it can be speculated that detection of the first outbreaks could have happened much earlier.

4.3 Conclusions and recommendations

a) increased and progressive mortality should always be a signal to exclude AI in the differential diagnosis as cause of disease problems on poultry farms;

b) intensive contact between the veterinary practitioner in the field and the veterinarian executing PME is much needed to have all relevant data and developments at ones disposal in order to come to a conclusive diagnosis;

c) if clinical findings like high mortality suggest the possibility of HPAI, the pathologist should decide to submit clinical samples to the reference laboratory, even if PME gives no specific indications for HPAI;

d) the best way for early detection of a HPAI outbreak is to have poultry farmer and/or veterinary practitioner report occurrence of high mortality or a large decrease in feed or water intake or a considerable drop in egg production immediately to the syndrome reporting system currently in operation;

e) after the epidemic the syndrome reporting system continued to be in operation, but there is a small basis for it in practice: most farmers still ignore to notify a critical disease situation (Agrarisch Dagblad, 17 November 2004; Agrarisch Dagblad, 28 May 2005.). In many cases this is done with the argument that a notification will harm them economically (isolation of farm). Therefore, there is a definite need to facilitate the notification process. Part of the solution is that the isolation period of a poultry farm can be shortened due to the use of a PCR-test to exclude AI in a suspect situation (within 24 hours test result).

g) it is recommended to sent tissue samples from poultry submitted for post-mortem examination at the Animal Health Service to the National Reference laboratory in case of an inconclusive diagnosis but with increased mortality as a reason for submission, in the case of a specific anamnesis (respiratory and/or digestive problems), or in the case of a diagnosis indicating respiratory problems.

h) in order to detect low pathogenic avian influenza (LPAI) infections of subtype H5 or H7 that could possibly change to HPAI, a continuous monitoring system has to be up, in which

high risk commercial poultry flocks (e.g. free-range and biological in the neighborhood of large ponds and lakes) are screened for antibodies against AI virus. Such a system has been set up in the Netherlands a year ago. In this system, serum samples are investigated for antibodies against AI-virus at the following sampling frequency:

- broiler / quail / guinea-fowl / layer flocks once every year (30 samples);
- duck / geese flocks once every year (40 samples);
- turkey flocks every production round (30 samples);
- breeding animals once every year (30 samples);
- poultry with free-range facilities : once every 3 months (30 samples).

It should be clear that the operational sampling frequency is not at all adequate to detect as early as possible AI introduction in these flocks. For the high risk flocks a frequency of sampling of probably at least once a week is necessary to detect as early as possible AI introduction in these flocks. In that case there is a need to investigate whether other sample media (e.g. eggs) should be used in the monitoring system, in order to make the monitoring economically feasible.

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5. Case study: Equine leukoencephalomalacia in 1989/1990

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5.1 Case description

The case

Fumonisin are a recently described group of secondary metabolites produced by a specific group of *Fusarium spp.*, particularly *F. verticillioides* and *F. proliferatum*. Human consumption of fumonisin contaminated maize and maize based products is associated with high levels of esophageal cancer in certain areas of the globe. The first reports of moldy maize, *F. verticillioides* and the causal role of fumonisin occurred late 1989/1990 when several cases of mortalities among horses and pigs were reported (for general reading see [1] and [2]). A more detailed description of those cases follows below.

Large numbers of horses and pigs in the US died in the fall and winter of 1989-1990 after having been fed feedstuffs containing maize contaminated with fumonisin (see Table 5.1).

Pathology	Region	# cases	Reference
Equine encephalomacalia, ELEM	Arizona	66	8
Porcine pulmonary edema, PPE	Georgia	34	2
ELEM	East & Midwest	87	7
PPE	Iowa	43	5
ELEM	Iowa	55	6

Table 5.1. Cases of equine encephalomacalia (ELEM) and porcine pulmonary edema (PPE) in the United States in 1989/1990

This mortality occurred on a number of farms, including a breeding and training farm in Arizona where 18 out of 66 purebred Arabian horses were affected [8]. Of these 18 horses 14 (=68%) died within 1 to 2 days, whilst the remaining 4 partially recovered [8]. These latter animals were mildly affected with impaired vision and devaited lips and noses [8]. Most animal 61/66 had been fed maize from two different batches. These batches consisted of cob parts, damaged kernels as well as undamaged kernels. 10 out the 14 animals that died were autopsied Gross pathological findings included liquefactive necrosis in parts of the cerebral white matter and hemorrhagic foci of various sizes in the brain stem. Portions of the cerebrum in some animals disintegrated when removed from the cranial vault [8].
The contaminated feed lots were removed from the diet at the onset of disease and animals that were fed only the uncontaminated lots did not become ill.

Type of hazard

Equine leukoencephalomalacia (ELEM) has been already known since 1891 as “circling disease” or “moldy corn poisoning”. Horsemen have known that moldy corn can cause severe neurological disorders and kill horses. Moldy corn is not uncommon, particularly

when corn is stressed by drought and/or insects. This is exacerbated by wet harvest conditions and when poor storage occurs.
In conclusion, this is a re-emerging risk, but the causal relation between the mycotoxin fumonisin and the most prominent producer *Fusarium verticillioides* (syn. *F. moniliforme*) as *F. proliferatum*, as a second producer [4] is new. In 1970 *F. verticillioides* was identified as the most frequently occurring fungus in corn associated with ELEM but it took until 1988 before the chemical structure and the biological activity of fumonisin were elucidated. These included experiments where ELEM could be experimentally induced after intravenous or oral administration of pure fumonisin [3].

Causes of plant stress

Damage to the kernel by insects leads to an increased risk of reaching critical levels of the fungus and associated with that increased concentrations of the mycotoxin. Drought stress may lead to physical damage of the kernels thereby allowing the fungus to penetrate the tissue without having to cross any biological barriers.
Strong variations in relative humidity impose stress to the fungus as it has been shown that growth and toxin production occur at different water potentials. E.g. growth occurs at relatively higher humidity whereas FB1 production still occurs at humidity levels where the fungus is unable to grow. *F. verticillioides* is commonly found in most seeds and the fungus is therefore regarded as an endophyte. This implies that the fungus is always there and the condition of the plant is decisive for the outcome of the balance between both. When conditions are such that the plant is weakened, the fungus will have an opportunity to disturb this equilibrium.

Relevance to food safety

High concentrations of fumonisin together with high densities of *F. verticillioides* are observed in two regions of the world (the Eastern Cape of South Africa and a region in North-East China). In both areas there is a high incidence of oesophageal cancer [3] This predominantly affects the local population that for food is largely dependent on the consumption of maize products. The consumption of beer brewed from (moldy) maize is common practice in the Eastern Cape. This strongly enhances the health risk as it seems that alcohol facilitates easier absorption of fumonisin by body tissues, especially the oesophagus.

International dimension

EU policies measures have led to a preliminary tolerance limit of 1000 ppb fumonisin in various maize products. As a result, several maize-producing countries are unable to sell their products on the EU market at present. In the United Kingdom in 2003, all tested maize products originating from biological production were found to contain more fumonisin than allowed. Great Britain has recalled all these six tested brands of organic corn meal from its food stores after they were found to contain dangerous levels of fumonisin, a cancer-causing natural toxin produced by a fungus. The organic cornmeals were found to average as much 9,000 parts per billion (ppb) fumonisin whereas the European Union's action limit range from 2000 ppb in unprocessed maize to 200 ppb in processed maize-based foods for infants and young children and baby food (to become effective as of 01 October 2007). Ironically 5 out of 6 products originated grown maize grown in the UK or Denmark [9]. In contrast, the fumonisin concentration in maize products from conventional producers did not exceed the tolerance limit.

Political impact

Secretary general Kofi Annan of the UN challenged the European regulation:

> "A World Bank study has calculated that the European Union regulation on aflatoxin costs Africa $670 million each year in exports of cereals, dried fruit and nuts. And what does it achieve? It may possibly save the life of one citizen of the European Union every two years..... Surely a more reasonable balance can be found"

Stakeholder perceptions

Relevant stakeholders have not been properly identified and data therefore are not available, but in view of the survey in the UK and the impact on trade from Africa this ought to be a factor of utmost importance

Possible re-emergence of the risk

Drought stress and stress caused by insects are very difficult to prevent, which also holds for many other forms of stress. Evidently the condition of the plant is of vital importance for the outcome of the interaction between plant and fungus. The re-emergence of ELEM, PPE and other pathologies in consumers of FB-contaminated corn and corn products is likely. GMO maize expressing the crystal protein gene from *Bacillus thuringiensis* showed good results in several field experiments. Breeding for resistance to drought stress seems to have good perspectives as well.

Broader relevance

Some of the conclusions from this case study should apply to a range of possible toxicoses, such as a general appreciation of the indicators rainfall, and different kinds of plant stress.

5.2 Conclusions and recommendations

Any indicator for plant stress could be helpful in early warning. Subsequently the procedures used during harvest and storage are vital for the final FB level in the commodity. These include fast and sufficient drying not only beyond the point where growth ceases, but beyond the humidity level where FB is no longer produced.
Chemical analyses of batches suspect for the mycotoxin based on the above indicators could have eliminated the risk by re-routing these batches to other, less sensitive, animal species, since horses are particularly sensitive to fumonisins. Diversification of horse feeds and/or switching to other batches of maize/silage can avoid new cases of ELEM, as was shown in the Arizona case [8].

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6. Case study: residues of PCBs, dioxins, and organochlorine pesticides in cultured fish

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6.1 Case description

6.1.1 Introduction

This case study pertains to the development of the response to a study on the occurrence of environmental contaminants, including PCBs and dioxins, in cultured salmon. The global production and consumption of cultured salmon has gone through a rapid growth in the past twenty years. The possible impact of negative reactions of consumers on the production of- and trade in- salmon can therefore be substantial.

The study on the occurrence of contaminants in cultured salmon was published in the scientific journal Science in January 2004. In this study, the occurrence of a group of organochlorine contaminants, which are PCBs, dioxins, and two pesticides, was investigated in farmed and wild salmon from different regions. Based on these results, the authors quantitatively estimated the likelihood of cancer to occur, based upon which they issued a consumption advice. This pertained in particular to cultured salmon because the levels herein were higher than in wild salmon.

This study and the advice by the authors received a lot of attention in the media and led to reactions from the public, among others in Northern America. There were also reactions from the authorities and the fish industry. From these reactions, it became evident that the subject had sensitivity among the public. Authorities in general responded by indicating that the study confirmed the results of monitoring previously carried out by them and that the reported values were below the legal thresholds. Some authorities also pointed at the positive health effects of salmon consumption. The industry responded, among others by pointing at its efforts towards reducing contamination of fish feed as much as possible. Also the contribution of other foodstuffs to the intake of dioxins and PCBs was mentioned with the purpose of putting the contribution by consumption of salmon into a broader perspective.

The risk of cancer by exposure to organochlorine compounds was known at the start of the study. Also studies on the occurrence of organochlorine compounds in cultured and wild salmon had previously been performed, albeit at a smaller scale. New elements in this study were the scale at which the tests had been carried out in different regions; the calculation method that the authors had employed for estimation of risk; and the consumption advice that had been issued by the authors. In addition, the results had previously been published in more specialized scientific journals than Science, and therefore had been available to a smaller target audience.

In summary, the case pertained to a risk that had already been known and that acquired a greater dimension by a new interpretation by scientists and perception among citizens that previously might not have been informed about the contamination of fish. Practice has shown that “re-emergence” of the problem is possible. Actually, the same authors as those of the Science article have published another article on the contamination of salmon with flame retardants (PDBEs; Hites et al., 2004b). This study did not arouse as many reactions as did

the article on organochlorine compounds. The organochlorine compounds can serve as model for a series of similar environmental contaminants that are transferred from fish feed to fish destined for consumption.

6.1.2 Scientific background

Hites and co-workers (2004a) studied the concentrations of various contaminants, which are 12 organochlorine pesticides, PCBs and dioxins, in salmon fillets. A distinction needs being made between cultured salmon and salmon fillets that were obtained from retailers. The salmon's origins were Europe, North- and South-America. In total, 246 composite samples (3 fish or fillets per sample) were analyzed.

Overall, the levels of 13 out of 14 contaminants were significantly higher in cultured fish with respect to wild fish. Four representative contaminants were subsequently studied in more detail, *i.e.* PCBs, dioxins, toxaphene, and dieldrin. The levels of these contaminants were the highest in cultured salmon from Europe, that is, from Scotland and the Far Øer islands, whereas cultured salmon from the US state of Washington and from Chile showed lower levels. In fish bought from super markets, a similar difference was observed between Europe and North- and South-America. The samples with the lowest levels of contamination predominantly originated from wild salmon. These trends showed parallels with salmon feed from various regions, which is considered as the most probable source of the differences. This type of feed contains, among others, fish meal and fish oil, in which the previously mentioned contaminants can accumulate themselves through the biological feed chain.

Although the threshold values of the American Food and Drug Administration for PCBs and dieldrin had not been exceeded, the authors carried out a risk estimation for the observed residue values. This was because the FDA has not imposed threshold values for toxaphene and dioxins. The authors also stated that the threshold values of the FDA for the other contaminants have not been solely based on health aspects. For the estimation of risk, the researchers employed a model that is used by the American Environmental Protection Agency for consumption of fish and the associated risk on cancer by PCBs, dieldrin, and toxaphene. This model was focused, among others, on the risks of consumption of fish caught in the environment, such as sport fishers and aboriginal inhabitants of nature reserves. The authors employed this model in order to calculate the number of fish-containing meals that could be consumer "safely". For cultured salmon in general and most of the salmon purchased from the super markets, this amounted to one meal per month, while for European cultured salmon in particular, this amounted to half a meal per month (once per two months). The recommended frequency of consumption of wild salmon was higher, ranging from one to eight meals per month (Hites et al., 2004a). Later re-calculations showed that even more stringent advice should be given, also for wild salmon, if a cancer risk of only $1*10^{-5}$ is considered acceptable (Foran et al., 2005). The method of calculation for the risk of cancer differs between the EPA and many other international organizations.

Prior to the study by Hites and co-workers (2004a), several studies into the levels of contamination of cultured salmon with organochlorine compounds had already been conducted. These studies had been conducted at a smaller scale with less samples, among others in Canada (Easton et al., 2002) and Scotland (Jacobs et al., 2002). One of the most important conclusions of these earlier studies was that the levels of contaminants in cultured salmon correlated with those in salmon feed, into which contaminated fish had been processed, among others.

6.1.3 Reactions after publication of the study

The publication of the study by Hites and co-workers in Science led to a response from various sources.

Consumers
After reports had appeared in the media about the study published in Science, sales of cultured salmon to consumers declined in some nations, such as France and Canada (Fisheries and Oceans Canada, 2005; Hénard, 2004). This decline was in the order of magnitude of tens of percents. In other nations, such as England and Netherlands, the sales of cultured salmon would not have experienced any backlashes according to media reports (BBC, 2004; Marine Harvest, 2004).

Environmental movements
Interest groups that are focused on the environment responded negatively, such as the American "Environmental Working Group" that called upon the FDA to impose more rigorous health standards for salmon, demanded labeling of cultured salmon, and advised consumers to eat wild salmon instead of cultured salmon (EWG, 2004).

Authorities
The American authorities, such as FDA and EPA, have been cited in the media; however, official responses could not be traced on the websites of these institutions. The employed model was withdrawn by the EPA from its website. In general, the FDA stated that there was no reason for concern and the observed levels were below the limits imposed by the FDA. On the other hand, the EPA regarded this study as an opportunity to make choices about which kind of fish the consumer would prefer to eat (for example, Stokstad, 2004). The response of the Canadian ministry of health had a similar content as that of the FDA (Health Canada, 2004).

The reactions of European authorities in general pointed in the same direction. The British Food Standards Agency (FSA) pointed at the fact that the measured levels corresponded with those that previously had been measured during surveillance programs in Great Britain, and that they fell within internationally defined limits. In these results, Scottish salmon would not show differences between wild and cultured variants. The FSA also pointed out that the calculation method for the cancer risk, as employed by Hites and co-workers (2004a), has not yet been recognized internationally, and that also health-beneficial effects are associated with the consumption of fat fish. Moreover, a decreasing trend in contamination of fish has become noticeable in the past years. The FSA did not deviate from its previous advice to consume fish twice a week, including fat fish once a week (less for mothers; FSA, 2004).

Of more or less similar meaning was the advice of the French national food authority ("Agence Française de Sécurité Sanitaire des Aliments"; AFSSA, 2004). Also the Dutch national food authority ("Voedsel en Waren Autoriteit") concluded that the contamination levels in fish are followed by monitoring programs and that the consumption of fish offers more health benefits than disadvantages (VWA, 2004).

The European Food Safety Authority (EFSA) published a risk assessment in 2005, instigated by the study in Science. While the assessment mentioned the issues that had also been treated by the national authorities, it also went into the contamination with methylmercury, the

comparatively high levels in fish from the Baltic Sea, and the fact that the study in Science had not taken season-dependent variability into account (EFSA, 2005).

Industry
Industrial interest organizations, such as "Salmon of the Americas" (SOTA, 2004), called the study results misleading. It was pointed to the fact that, among others, other foodstuffs, such as meat and milk, contribute more to the intake of organochlorine compounds by consumers than salmon. Also, reference was made to the health benefits of the consumption of salmon. In addition, the efforts of the industry towards decreasing the fraction of fish meal and fish oil in fish feed, as well as the level of environmental contaminants, were mentioned.

6.1.4 Developments

After the publication of the article in Science, the same group of authors has published results of analyses of other contaminants in salmon, which are heavy metals and brominated flame retardants. For metals, it was concluded that no consistent difference was observed between wild and cultured salmon (Foran et al., 2004).

The study on brominated biphenyl ethers (PDBEs), a widely used group of flame retardants, yielded in essence the same pattern as for the organochlorine compounds: levels in European culture fish were higher than in those from North- and South-America, while cultured fish as a whole had higher levels than wild salmon. An exception to this was one type of wild salmon, the "chinook" salmon, which also contained high levels of PDBEs. According to the authors, the cause of this deviation lies in the fact that this salmon primarily feeds upon other fish and reaches a higher size. The levels in fish feed corresponded with the trend in PBDE levels in salmon itself (Foran et al., 2004).

The study on PDBEs shows that the results for organochlorine compounds can be extrapolated to compounds with similar properties, such as PCBs and PDBEs.

In addition, the same author group has conducted a recalculation of the risk estimation, in which the effect of the intake of fish on the exposure to organochlorine compounds was considered. For this, the "Tolerable Daily Intake" established by the WHO [1 pg 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin equivalents (TEQ)/kg body weight/day] and the background of intake from other foodstuffs were taken into account (Foran et al., 2005).

These studies were, however, published in specialized scientific journals with predominantly scientists as the target audience.

6.2 Pro-activity paying off and lacking pro-activity

As can be inferred from the data summarized above, authorities already had in place monitoring and surveillance programs for various contaminants for a long period before the publication of the study in Science. In addition, it was known from scientific literature that organochlorine compounds could accumulate through the biological feed chain and through fish feed into fatty tissue of fish. Also the toxicity of these compounds had been described and legal measures had been taken, in particular in the European Union, in order to protect the citizens against negative health effects.

The problem appears to have arisen from the combination of the following factors:

- Focus. According to criticisms, the study focused on a single foodstuff that might on one hand contain a comparatively high level of organochlorine compounds, but that on the other hand is consumed to a limited extent as compared to other foodstuffs containing the same contaminants. Authorities and industry also referred to the benefits of fish consumption for health. In this regard, there would have been a need for a "holistic view."
- Interpretation of results of measurements: The model that was employed by the authors of the article in Science yielded other results than would have been considered acceptable based upon, for example, the TDI. Furthermore, the results were presented in this case as consumption advice, which is also transparent for non-insiders and which directly affect the behavior of consumers.
- Scope: the target audience of the journal Science is probably bigger than that of specialist scientific journals and reports on surveillance. Possibly, this medium reaches a wider audience, which has not been previously informed on this matter. Moreover, the high-ranking status of the journal can play a role in this. The reputation of the journal also has caused the regular newspapers to take on this topic.
- Other incidents and "issues" that played on the background, like the association of cannibalism among animals with danger for food safety (among others, BSE, "fish eats fish"), environmental aspects of fish culture and the like.
- Market trends. The culture and consumption of salmon has firmly increased over the last few years.

6.3 Conclusions and recommendations

Possible actions by policy makers with regard to food safety should perhaps pertain more to risk communication than to the mitigation of the risk *per se*, given that for the latter, initiatives are already being undertaken.

For the communication, the factors mentioned above can be taken into account. This should be done in a pro-active manner. A communication strategy can be developed in advance in collaboration with "stakeholders". Communication and education on a regular basis, for example by the "Voedingscentrum," probably will aid preventing a "crisis" situation surrounding similar problems.

The opinion of food safety experts about possible future problems can also be solicited. The Dutch national food authority ("Voedings en Waren Autoriteit"), for example, recently applied the "expert choice" method to risks in cultured salmon. Experts of the Dutch national food authority's inspectorate for food and consumer products (VWA/KvW), the institute of fisheries research (RIVO), RIKILT-Institute of Food Safety, the national institute of public health and environment (RIVM), and Nutreco indicated how big they estimated the likelihood and impact for chemical, microbiological and physical hazards. Of the 33 items, organochlorine compounds had the highest score based on the formula "risk = likelihood * impact," followed by *Listeria monocytogenes*, noxious metals, and antibiotics, respectively (VWA, 2005).

In addition, contaminants in food, for which similar problems can occur as for organochlorine compounds, can be pro-actively identified. Indicators that, in combination with each other, can facilitate the early identification of similar problems include the following items:

- Contaminants for which accumulation may occur through environment, biological feed chain, or recycling ("fish eats fish")
- Contaminants of which the levels in products lie comparatively little below the internationally established thresholds and that can exceed these thresholds by adaptations of the thresholds (for example, if the threshold for dioxins is lowered from 4 to 2 pg TEQ/kg bw/day). In other words, compounds for which an increased likelihood exists that the interpretations of risks can differ among different experts.
- Compounds for which many toxicological studies are conducted, which can cause standards setting to change quickly based on progress in insight. This holds particularly true for, among others, effects of combinations of substances.
- Products with a strong health image, of which contaminations can become a sensitive item for the public.
- Products of which the production and consumption are strongly increasing.
- Products for which an alternative production technology is increasingly applied, by which also the risk on contamination with specific contaminants is increased.

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7. Case study: Perfluorinated contaminants, a new group of contaminants that accumulate in fish

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7.1 Case description

The first papers on perfluorinated compounds (PFCs) as emerging chemical contaminants have been published in 2001 [1, 2]. PFCs find a wide variety of applications as surface active compounds (PFOS: perfluoroctanesulfonate) in e.g. fire fighting foams, paints, skiwax and as polymerisation aid (PFOA: perfluooctanoic acid) in the production of PTFE (Teflon). Teflon has widespread applications in e.g. industries and households (e.g. anticaking layer in frying pans). PFCs enter the environment during production of the compounds and during and after the use of products in which they have been applied. Besides, volatile PFC precursors are transported in air over large distances. Through biological and chemical processes in the environment PFCs may be generated, resulting in another source of these compounds. Production of PFOS has been stopped on a voluntary basis by USA based industries since 2000. However, currently alternative compounds are being produced and applied that strongly resemble the above compounds. As a result, the group of PFCs produced by industries and being reported in literature consists of >10 compounds and is growing [3].
Since the discovery in 2001, mainly groups in North America have been publishing on the levels and distribution of these compounds in the (aquatic) environment [1, 2, 4, 5]. However, publications on human toxicity of these compounds are scarce. Available reports of producers (e.g. 3M) and independent research laboratories show that exposure to PFCs is found to be carcinogenic in rats, inducing tumors of the liver, and of the thyroid and mammary glands [6]. There is limited information available on the presence of PFCs in the Dutch and European environment. Concerning food, there is no data on the presence of these compounds in food items (except for some fish samples), which hampers the evaluation of human intake and therefore human risk assessment.
The case of PFCs has developed similarly as those from other commercially produced chemicals such as polychlorinated biphenyls (PCBs) and brominated flame retardants (BFRs).During several decades, these chemicals are being produced and applied in consumer and industrial products. After several years (see Diagram 7.1), independent research results show that these chemicals have adverse effects. Following these findings, (international) governmental bodies can decide to ban the production and use of the chemical by legislative measures. In parallel to above process, industries have already started to develop alternative products with similar properties, often based on similar chemistry (as this requires only slight modifications of production processes). In the case of PFCs, PFOS has been used in the past as surfactant. 3M has banned the production of PFOS since some years, but now produces a very similar compound: PFBS (perfluorobutanesulfonate).

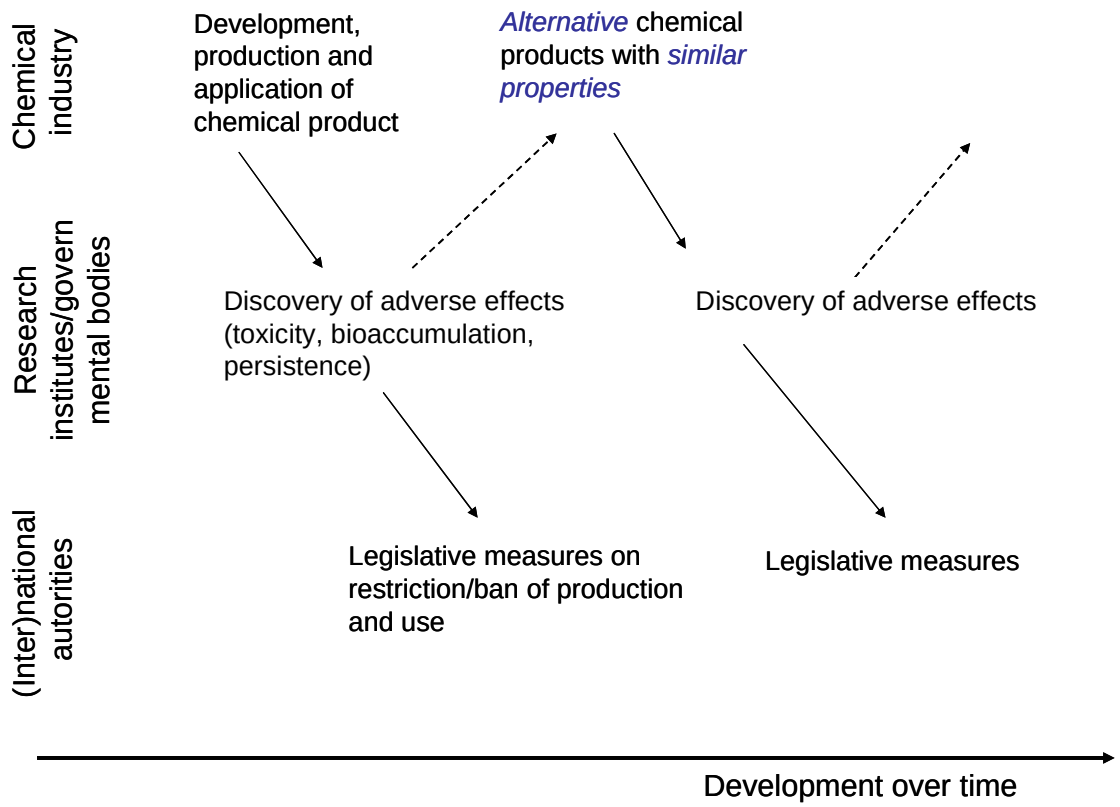

Diagram 7.1 Pattern of emergence of new chemical contaminants.

7.2 Pro-activity paying off and lacking pro-activity

The presence and accumulation of PFCs in occupationally exposed workers at production facilities is regarded an early indicator of a potential human exposure risk. The problem of PFCs was initially detected by accumulation of PFOS in occupationally exposed workers in a PFOS production plant. PFOS was found at 100-1000fold higher levels in blood compared to non-occupationally exposed people [7]. In the case of PFOA, the occupational exposure was only detected after decades of production. Industry (Dupont) was fined by the EPA recently for mischievously withholding test information that showed transfer of PFOA to the human foetus and PFOA exposure of people living in the vicinity of a manufacturing site [8]. In conclusion, industries do not necessarily show pro-activity with unwelcome information on exposure and toxicity of their chemicals. Research by independent institutes and pressure of (inter)national authorities is required to accurately respond to these potential new chemical risks. The sooner new chemicals are captured in legislation, the lower are the chances that they can become ubiquitous in global environment through extensive production and use.
RIVO participates in the EU research project PERFORCE (www.science.uva.nl/perforce). This project targets at an inventory of distribution of PFCs in the European aquatic environment, including food chain analysis, point source research and the development of analytical quality control tools. Research has shown that PFCs are widespread in the European environment, including the Dutch aquatic system [9].
PFCs are also found in Dutch commercial fish, partly due to a PFC production facility at the Scheldt river in Antwerp, Belgium. Within the PERFORCE project, no attention will be paid to human risk assessment. No research will be carried out to levels of PFCs in food items (other than fish). It is therefore necessary to make an inventory of levels of PFCs in foods of various origins in order to determine possible risks for human consumption. The research gap

on PFCs has been recognised by EFSA, who has started a working group on evaluation of PFOS and its salts (http://www.efsa.eu.int/science/contam/contam_meetings/977/contam_12th_plenmeet_minutes1.pdf and also http://www.efsa.eu.int/register/qr_panels_11_en.html).
Concerning future (PFC) chemicals a range of patents provide industries with possibilities to produce 'new' or very alike alternative chemicals for those that have been banned [10]. A pro-active approach will facilitate the determination of the adverse effects of these chemicals in an early stage. This approach should consist of (1st) making a desk study of publicly available data (yearly production volume, patents, fields of application) on manufacturers of high production volume chemicals (HPVCs). A list of possible (PFC) substances will result from this study, which will be judged for their toxicological relevance. Secondly, biological and chemical screening methods can be employed to identify prioritised chemical substances and to determine the levels in the environment and food. This proactive approach would determine risks in an early stage and prevent that risks are discovered 'by accident'. Such an integrated system is currently not in place, although several elements are covered by (inter)national institutes and governmental bodies. Therefore, it is required to integrate activities. Also, the development of powerful analytical chemical and biological screening techniques is required.

7.3 Conclusions

To conclude, PFCs are a new class of compounds that require a human risk assessment consisting of:

- Evaluation of toxicity of the individual PFCs
- Assessment of the food contamination path-ways and the determination of t6heir levels in important food groups
- Human intake assessment

Furthermore, a pro-active approach towards new classes of (PFC) chemicals will prevent the accidental discovery of toxic high production chemicals. Several elements are currently in place at (inter)national bodies but should be integrated and further developed.

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