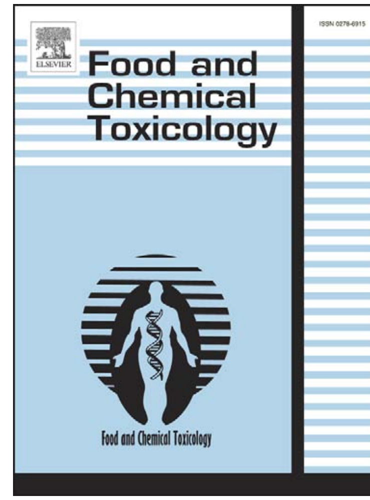

Indicators of emerging hazards and risks to food safety

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TITLE PAGE

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Paper prepared for submission for publication in the special issue of Food and Chemical Toxicology on emerging food safety issues, dedicated to SAFE FOODS Work Package 2
Revision of original submission, July 21st, 2008
* To whom correspondence shall be sent:

Abstract

There is a widely felt need to develop methods for the early identification of emerging hazards to food safety with the aim of preventing these hazards from becoming real risks and causing incidents. This paper reviews various activities and previous reports that describe methods to select indicators that can be used for the purpose of early identification of hazards. These indicators have been divided over three different environments, including i) the environment surrounding food production, ii) the food production chain from farm-to-fork, and iii) consumers. Changes in these indicators are signals that may require follow-up action. Besides indicators that are linked to specific kinds of hazards, the indicators used for vulnerability assessment can help identifying weak spots in the food production system that are sensitive to a broader range of hazards. Based on the various indicators for emerging hazards that have thus been identified in literature, a set of generic indicators is provided that can be useful for the early identification of hazards.

Keywords

Food safety, emerging hazards, indicators, early warning, food inspection

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Abbreviations

BSE, bovine spongiform encephalopathy; CDC, Centers for Disease Control and Prevention; DON, deoxynivalenol; EC, European Community; ECDC, European Center for Disease Control; EEA, European Environmental Agency; EFSA, European Food Safety Authority; EFTA, European Free Trade Association; ERS, Economic Research Service; ESA, EFTA Surveillance Agency; EU, European Union; Eurostat = Statistical Office of the European Communities; FAO, Food and Agricultural Organization; FAOSTAT = Statistical Office of the FAO; FHB, Fusarium Head Blight; FDA, Food and Drug Administration; FIVIMS, Food Insecurity and Vulnerability Information and Mapping Systems; GAP, Good Agricultural Practice; GHP, good hygienic practice; GIEWS, Global Information and Early Warning System; GM, genetically modified; GMP, good manufacturing practice; GOARN, Global Outbreak Alert and Response Network; GPHIN, Global Public Health Intelligence Network; HACCP, Hazard Analysis Critical Control Points; INFOSAN, International Food Safety Authorities Network; IPCS = International Program on Chemical Substances; ITX, isopropyl-thioxanthone; OIE, World Animal Health Organization (Office International des Epizooties); OTA, ochratoxin A; PFGE, pulsed-field gel electrophoresis; POP, persistent organic pollutant; RASFF, Rapid Alert System for Food and Feed; RFID, radio-frequency identification; SPPA, Strategic Partnership Program Agroterrorism; STEC, Shiga-like-toxin-producing *Escherichia coli* (synonymous to VTEC); UN, United Nations; US, United States; USDA, United States Department of Agriculture; VTEC, verocytotoxin-producing *Escherichia coli* (synonymous to STEC); VWA, Dutch national Food and Consumer Product Safety Authority; WHO, World Health Organization

1. Introduction

Food safety has been the topic of some recent policy changes, increased awareness among the public, and various incidents. These developments indicate that there is a need for a system that can identify food safety hazards in an early stage so that these hazards can be tackled in time, before developing into real risks. With regard to food safety hazards that are known as such, measures can be taken towards the prevention and mitigation of these hazards based on their characteristics, behavior and point of entry into the food chain. For example, good practices for agriculture and manufacturing [*e.g.*, Good Agricultural Practice (GAP)], as well as the Hazard Analysis Critical Control Points (HACCP) approach to assess risks and control them, are now commonplace in many jurisdictions. Yet it can be envisioned that for a number of risks, such measures may not be applicable given that they are yet unknown or unanticipated.

The overall aim of the SAFE FOODS project, which is primarily sponsored by the European Commission Directorate for Research's Sixth Framework Program, is to further develop risk analysis of foods based on inputs from advanced research in both the natural and social sciences. Among other things, this is also likely to contribute to the confidence of stakeholders in the European Union's food safety governance. SAFE FOODS is composed of various Work Packages that more or less act as subprojects on different topics, including i) the use of advanced analytical methodologies to study potential effects of agricultural practices on crop composition; ii) emerging risks in food safety; iii) assessment of consumer exposure to food safety hazards by the use of advanced statistical techniques; iv) confidence of consumers and other stakeholders in risk management in food safety; and v) institutional arrangements for food safety governance. The findings of all these Work Packages are integrated into a new model on risk analysis, which will be refined with inputs solicited from stakeholders.

The early identification of emerging hazards to food safety is also a major topic of the activities of SAFE FOODS Work Package 2. Previously, Work Package 2 has made a number of accomplishments on this topic, including i) the establishment of an expert database; ii) description of a framework for timely identification of emerging hazards; iii) reports describing systems for timely identification of emerging hazards to food safety or to hazards of another nature that can be exemplary for food safety as well; iv) an analysis of conspicuous trends in European Union (EU) food safety alerts; and v) reports reviewing the background and characteristics of a selected range of hazards to food safety caused by microorganisms, mycotoxins, biochemical and chemical agents.

Besides Work Package 2, various parallel projects, such as the EMRISK project funded by the European Food Safety Authority (EFSA), have tackled the issue of early identification of emerging food safety hazards. Against the background of the previous outputs from these projects, the current publication by authors from SAFE FOODS Work Package 2 aims at describing the various types of indicators and, in particular, the methods for their selection that can be used for the early identification of emerging hazards to food safety. This information, together with the working procedures to be reviewed in a follow-up study, can then further provide a basis for the development of a system for emerging hazard identification.

2. Definitions

Various terms with specific meanings are used throughout this report, which therefore would merit from further clarification. Where appropriate, the definitions used are in line with internationally accepted definitions published by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO).

A hazard is an agent that has the potential to exert a negative effect on health. An example of a hazard in food is the presence of *Salmonella* bacteria that may cause gastroenteritis. ***The risk*** is defined as the negative effect of the hazard if it really occurs, which depends on the likelihood of the occurrence- and severity- of the negative effect (FAO, 1995; FAO, 1997).

The internationally harmonized model for ***scientific risk assessment*** is composed of four phases, namely i) hazard identification; ii) hazard characterization, that is, the characteristics specific negative health effects and the dose-response relationships between hazard and effects; iii) exposure assessment, in which the exposure of consumers ingesting the food containing the hazard is estimated; and iv) risk characterization, in which the outcomes of the three preceding phases are combined into an assessment and in which also uncertainties are taken into account (FAO, 1995). To illustrate this with an example: the hazard characterization may describe the minimum infectious dose of *Salmonella*, while subsequently the exposure assessment may help estimating the real dose to which consumers are exposed, so that the risk characterization can conclude on the likelihood of gastroenteritis caused by *Salmonella.*

Besides risk assessment, which is the scientific process assessing risks, also two other activities, that is, risk management and risk communication, are considered to be part of the internationally acknowledged risk analysis model for food safety. During ***risk management***, policy alternatives are weighed based upon the outcomes of the risk assessment process, and measures to control and mitigate the risks are subsequently defined. ***Risk communication*** is the process of exchange of information and opinion among the risk managers and risk assessors, but also between risk professionals, such as assessors, managers, and communicators, and other parties involved. Although preferably these activities are strictly separated from each other, some overlap cannot be avoided in practice. For example, risk managers have to formulate the policy for risk assessment, such as the risks to which consideration will be given and the issues that have priority (*e.g.* FAO, 1997).

With regard to emerging hazards, which are the topic of this report, the emerging characteristics of these hazards may have various causes. For instance, the hazard can be new and has not occurred before. For example, certain synthetic man-made substances may not occur in nature and are therefore new. In case such substances are hazardous and also enter the food supply, these substances would turn into emerging food safety hazards. The same may also hold true for hazards that have only occurred in the non-food area, but that also start entering the food domain. Alternatively, hazards that once have disappeared from the food domain may enter it again, for example due to changes in practice or the termination of certain risk-eliminating measures. In addition, hazards that have previously occurred in food, but that have only recently been discovered, can be regarded emerging hazards as well.

The definition of an indicator is taken from the guide on handling indicators and signals that has been published as Annex 4 to the report of the EMRISK project, which had been carried out under auspices of EFSA. This project has carried out various activities on emerging food safety risks, including retrospective case studies on food safety incidents, and has recommended a working procedure for early identification of emerging food risks (EFSA, 2006a). An ***indicator*** is considered by EMRISK as an entity that indicates the possibility that a risk may occur, due to its direct or indirect relationship with the risk. A ***signal*** is defined as a substantial change in the indicator. Signals can thus be used to flag the possible occurrence of risks. The EMRISK guide also provides a number of criteria to select appropriate indicators, which will be discussed in more details in the section on EMRISK below.

3. Categorization of methods for the early identification of emerging hazards

For the purpose of oversight, we propose a categorization of early identification methods based on their points of application within the food production chain (Figure 1). Various methods aim to identify factors outside the food production chain that contribute to the development of food safety hazards within the food chain. The consideration of such external factors corresponds to the larger box in Figure 1. These external factors may already exist and thus be used for measurement, such as in the approach recommended by EMRISK (see below), or may occur in future, such as in futures research exploring different plausible scenarios for the future.

<< Insert Figure 1 around here >>

Other identification methods focus on hazards as they occur, during food production from farm to fork, which corresponds to the inserted left hand box of Figure 1. Food control agencies measure known hazards and report positive detects through systems such as the EU Rapid Alert System for Food and Feed (RASFF), which can provide useful inputs for research at this stage of the food chain. In addition, food-producing companies have to carry out their own risk assessments, which can be both business-management- and legal- requirements. Within company settings, identified hazards are often measured at critical points in the production process according to the HACCP approach. Other relevant methods pertaining to this stage of the food chain are the methods of “vulnerability assessment,” which helps identifying weak spots in the production process, and “situational awareness,” which comprises the real-time measurement of many entities in food production and the appropriate processing of all these measurement data into signals that flag potential hazards (see below).

After consumption, identification methods aid the early recognition of risks as they occur. Please note that the term “risk” is used here because the hazard has already exerted adverse effects and therefore is not hypothetical anymore. In this stage, it is desirable to contain the risk, for which early recognition will be useful. Early identification of risks is supported, for example, by food-borne disease outbreak reporting systems, including public health surveillance and other epidemiological tools. Recent advances have been made for example in molecular epidemiology, in which the use of molecular detection techniques facilitate the discernment of food poisonings that are related, thus facilitating the early tracing back to the source of the adverse reaction. In addition, voluntary reporting by consumers, such as through telephone call centers, can be useful in this respect.

Interestingly, identification of emerging hazards in the surrounding environment depicted in Figure 1 includes the use of “predictive early warning” systems described by Marvin and co-workers in their review on systems for identification of emerging hazards (2008). The identification of emerging hazards in the food production chain relies upon “reactive hazard-focused” systems, while hazards during or after consumption do so upon “reactive endpoint-focused” systems mentioned by the same review (Marvin et al., 2008).

4. Identification of hazards during food production from farm to fork

This section highlights various examples of initiatives and approaches towards early identification of emerging hazards in the food chain ranging from agricultural production via retail and the consumer to the public health system. These approaches take various factors into account, each to a varying degree, such as the system, the local facility and process, and the hazard itself.

4.1. Food system vulnerability assessment

4.1.1. United States (US) Government approach

Since the terrorist attacks of September 11th, 2001, various measures have been put into place by the US government, including those that aim to protect the food system against becoming a vehicle for acts of "agroterrorism." The activities against potential agroterrorism are designated "food defense" and carried out by the Strategic Partnership Program Agroterrorism (SPPA) in cooperation between various departments, including, the Department of Homeland Security, Food and Drug Administration (FDA), US Department of Agriculture (USDA), Department of Health and Human Services, Federal Bureau of Investigation, and the private sector. It was realized that part of the hazards potentially introduced into food by agroterrorism might be new or at least different from the ones that had already been known to occur accidentally. Interestingly, this situation is highly similar to the emerging hazards that are the topic of this review, although the latter ones are considered to be accidental rather than intentional. The methods and indicators that the US authorities use to identify hazards and the "weak spots" in the food manufacturing system are therefore also of interest to the topical study (FDA, 2006).

As regards potential hazards, the FDA has made a classification of potential threats by using a list compiled by the Centers for Disease Control and further narrowing it down based on a variety of factors, such as the stability of the hazardous agent in food, the ability to distinguish the agent on the basis of color or taste, the toxicity of the agent, the availability, and the public health impact. In addition, chemical and microbiological agents are classified according to characteristics that are important in this regards, such the heat stability of microorganisms and the toxins they produce, or the heat stability and acute toxicity of chemical toxins.

One of the food defense methods employed by the US authorities is identification of the parts of the food production system that appear most vulnerable to acts of agroterrorism and which are therefore designated "critical nodes." Therefore a possible point of entry of a hazard into the system, the critical node, is predicted, while the exact nature of the hazards may not have to be predicted.

The method initially used for vulnerability assessments was a six-step procedure that is part of "Operational Risk Management." The six steps consisted of I) hazard identification; II) risk assessment; III) analysis of risk control measures; IV) making control decisions; V) implementation of risk controls; and VI) supervision and review. This procedure had previously been used in the aerospace and nuclear energy sectors. For each scenario involving a certain hazardous agent or activity, the risks were classified based on a matrix in which the severity and likelihood of occurrence are offset against each other. The outcomes could be "high," "medium," or "low" risks. Factors that were considered included the accessibility to attackers, impact on health, toxicity or pathogenicity of the hazardous agent, and compatibility of the agent with characteristics of the food and its processing.

The tool currently employed for the vulnerability assessment is "CARVER + Shock." The acronym CARVER stands for "Criticality, Accessibility, Recuperability, Vulnerability, Effect, and Recognizability," and each of these terms can be considered an indicator in the sense of our definition. The term "Shock" pertains to the anticipated psychological impact of an attack in the short- and long- term. For each of the terms of CARVER, a score is assigned to specific phases in a flow diagram representing the food facility or sub-system for a specific product, ranging from 1-10, with 10 being the highest risk score. In addition, a profile of the potential attacker is developed, which will be further considered throughout the assessment. SPPA carries out CARVER+Shock analyses out involving teams of 20-30 experts from a wide range of backgrounds. After a time period of preparations and instructions, the team will work together for several days to work out the scenarios. The outcomes are general for a given food production sector and do not identify weaknesses in a specific company. It is expected that the information developed - and experience gained - with these analyses by SPPA will allow companies to carry out their own internal CARVER+Shock analyses.

Criticality means the magnitude of the impact on consumers' health and the economy, and is ranked based on the estimated casualties and economic damage. The highest score of 10 corresponds to over 10,000 lives lost and more than 100 million US dollar economic damage. Accessibility stands for the ease by which food-producing or –handling facilities can be accessed by individuals who have not been authorized to access the point of potential contamination. The classification is based on physical barriers, restricted access for non-staff, observation of the facility, and availability of information on the facility. Recuperability means the ability of a system to recover from damage, with a score of 10 corresponding to more than a year needed for recovery. Vulnerability is characterized by the ease by which sufficient quantities of a hazardous component can be brought into contact with the food as determined both by the characteristics of the food and agent and by the structure of environment, such as the capability to work unobserved. Effect relates to the impact on the production capacity, in other words the part of the system that will be damaged, with a score of 10 designating more than 50% of the system being affected. Recognizability relates to the ease by which the target can be recognized by the attacker, with the highest score signifying a clear recognizability with little training being required to recognize the target.

"Shock" brings together the data from the CARVER evaluation and assesses the impact that an attack, if it would occur, might have on the health, psychological, and economic status of the nation. Besides the number of casualties and economic impact, also factors like religious or symbolic importance of the target and the sensitivity of subpopulations are considered. Again, a score ranging between 1 and 10 is assigned.

Once the vulnerability assessment has been completed, countermeasures that can be formulated include the restriction of access to critical nodes, modification of processing characteristics in order to warrant destruction of certain hazardous agents, adjustment of equipment design, and development of rapid detection methods (FDA, 2006).

4.1.2. Other approaches

Many recent developments may impact on the agricultural food production and trading system, including the trend towards globalization, climate change, and increased agricultural productivity. In the face of this complexity of the food supply, Fraser and co-workers (2005) proposed to assess adaptability of food-consuming communities rather than predicting food security in order to map out those communities or segments of communities that are most vulnerable to threats.

The model that Fraser and co-workers propose is based on experience with a similar model, the Panarchy framework, which is used for landscape-ecology. This model discerns three important factors that define a community's vulnerability towards threats, that is, the wealth of a system, its diversity, and connectivity. Wealth correlates with biomass in landscape ecology and is also considered to correlate with loss of diversity accumulated in the initial phases of biomass accumulation. Examples of defining the wealth for food supply purposes can be found in development economics and food security studies. On one hand, wealth of the food-consuming community can be regarded to contribute to vulnerability because the damage that can be inflicted to a system will be bigger, that is, the capital losses will be higher. On the other hand, from a social perspective, wealth also implies that resources are available that can be invested in order to avert risks. Fraser and co-workers propose to apply "entitlements" to food as known from food security studies. Entitlements may be direct, by self-production of food, or indirect, by purchase of food from the market. In addition, transfer entitlements pertain to food provided as aid or welfare. A higher number of entitlements correspond to increased wealth and less vulnerability.

Connectivity is supposed to contribute to the rapid spread of a hazard. In ecological modeling, the connectivity can be assessed by considering the pathways that can be taken. For environmental chemicals, this has taken the shape of "fugacity" representing the partition and transport of the chemical between different environmental compartments, such as the atmosphere. In the food system, this can be translated to the dislocation of hazards through transport media. As an example, these authors mention the contamination of milk with dioxins produced during waste incineration through uptake by cows in the vicinity of the waste incinerator, and subsequent collecting, processing, and sales of the cows' milk in urban centers.

Whilst diversity is considered to contribute to the ability to withstand shocks in an ecological system, Fraser and co-workers propose to use a model that financial investors use to spread risks of investments, the Modern Portfolio Theory. In this theory, it is realized that risks exists, but the components of a portfolio containing multiple investments are so diverse that they are not equally affected by economic developments. Although systemic risks that pertain to a whole system, such as a drop of the share market, cannot be eliminated, the impact of unsystemic risks, which do not affect all components, can be reduced. The diversity in a portfolio can be assessed by considering the covariance between components' response to changes, with a high covariance representing similar behavior and therefore little diversity. For example, the yield of wheat fields in a large monoculture are may show high co-variance. A low covariance therefore would signify reduced risk.

Fraser and co-workers conclude that modern agriculture is wealthy, non-diverse, and narrowly connected. Therefore, policies should strive towards increasing diversity without causing prices to rise much. Urban agriculture might help increasing diversity in this respect (*e.g.* as a complement to rural agriculture, see Mougeot, 2000, and references therein). In addition, instead of taking measures on a national scale, trade links should be maintained if they are not connected to hazards occurring in the food system, such as in geographically separated areas (Fraser et al., 2005). Similar to the models used by the US authorities, the model proposed by Fraser and co-workers is not predictive of specific hazards but aims to facilitate the identification of areas of the food production and trading system that warrant closer examination.

4.2. Situational awareness

Another track followed by the US authorities within their food defense activities is the development of "situational awareness." This awareness is a combination of measurements of objective values representing the situation and the interpretation of the outcomes of these measurements, as well as the conclusion with regards to the future implications.

Lindberg and co-workers (2005) proposed to translate this concept of "situational awareness" to the domain of food production. Information about the situation can be collected in real time within and outside the food production chain. Within food production chains, this includes data generated by implementation of quality management systems, such as the HACCP approach and Line Inspection Management. Such data also can include the tracing of movements of ingredients and food products throughout the chain, from farm to table, as well as waste streams inside food-producing facilities.

Developments in analytical technologies, such as cost-efficient detection devices at the nano-scale for detection of hazardous chemicals and micro-organisms, can further add to the real-time data collected for this purpose. Modern radio-frequency identification (RFID) devices that are invisible to the eye and added to consignments of food products, which is currently already being demanded by a big retail company, could be helpful in this respect, allowing for detection of movements of goods at the doorgate. Data from outside the food chain can include public health reports and warnings against tampering with foods (Lindberg et al., 2005).

The data collected should then be processed and interpreted, based on insights into the attributes of the specific parameters that are measured as well as insights into the relations between these parameters. This can be done automatically using ontologies and inference machines, similar to the search machines used for Internet queries. Therefore the combination of real-time data with the ontologies would match this paper's definition of an indicator.

Food defense is part of the situational awareness activities of the US Homeland Security Operations Center, which serves as national point for sharing of information and also as national coordination center for incident management. This center also hosts the inter-agency National Bio-Surveillance Integration Center, which aims to assist decision makers by providing data on naturally occurring and artificial threats to agriculture and food, among others. In addition, the US Department of Health and Human Services has modernized its BioSense disease surveillance program through which hospitals can report findings in real-time, which contributes to situational awareness.

4.3. Good practices and HACCP

As mentioned above, risk assessments are part of the HACCP approach and have to be carried out after the food production process in a given link of the food production chain, such as the factory, has been mapped. Following the risk assessment, critical points have to be defined at which hazards will be analyzed, of which the results will trigger risk-mitigating actions, if necessary. The progress of the HACCP has to be reviewed periodically, and the outcomes of the measurements and actions undertaken will serve as basis for modifications and adjustments of the system.

Brown and McClure (2006) note that emerging pathogens may not be included in the microbiological risk assessments for good practices and HACCP-based food production systems in an industrial setting. Yet any known potential pathogen that may occur should be considered, also if the information is fraught with uncertainties. Risk assessments of emerging pathogens should include the four stages defined above (section 2). Uncertainties and variability should be considered, and in certain cases, data on other hazards similar to the one under consideration may be useful as well.

The possible effects that any changes in the food chain have on the occurrence of risks should be considered, for example in case of changing nature either of raw materials or of their geographic origins. The same also applies to changes in processing and storage conditions. Also the effects of processing *per se* on the pathogen of interest should be considered. If processing eliminates or reduces the hazards associated with an identified pathogen, the risk assessment should consider the possible effects of deviations from these processing conditions. These authors also recommend that in case of emergence of pathogens, the effectiveness of measures against this pathogen during food production should be assessed as soon as possible, if need be on the basis of assumptions about the characteristics of the pathogen (Brown and McClure, 2006).

Besides the changes in the food chain itself, the authors also realize that other changes may lead to emergence of food pathogens, such as changes in the characteristics and prevalence of the pathogen itself, in the particular human population consuming or in contact with food, and in the environment (Brown and McClure, 2006).

During hazard identification, indicator microbes that are measured to indicate the presence of other microbes should be representative for the latter, reflecting the same distributions and sensitivities to processing conditions. Indicator organisms are less available for viruses and protozoa than for bacteria. Brown and McClure nevertheless note that there is a need for direct monitoring of pathogens.

As regards the characterization of the hazard, the data available for emerging pathogens will frequently be incomplete. As a basis for estimates on dose-response relationships, surveillance and clinical data can be used in combination with data on the intake levels of the implicated foods (Brown and McClure, 2006).

The exposure assessment of an emerging pathogen should consider the chain and route of exposure as well as the course of a contamination. The effect of differences in various factors within and outside the food chain, such as agricultural practices, on the exposure should be considered (Brown and McClure, 2006).

The risk characterization, which brings together all the information from the hazard identification, hazard characterization and exposure assessment, should be able to indicate uncertainties and knowledge gaps. Modeling studies can be done based on analogies with other microorganisms that can act as surrogate, including non-harmful species or pathogens with a long record of knowledge. These modeling studies enable the timely delivery to risk managers of an initial quantitative risk assessment that cannot await longer-lasting data collection with the specific emerging pathogen. These authors also stress that a comparatively large amount of information is available on bacterial pathogens than on other groups of pathogens, such as insight into the mechanisms of horizontal transfer of virulence factors. In addition, they note that the high share of viruses in the contingent of emerging pathogens is associated with their ability to mutate relatively rapidly (Brown and McClure, 2006).

4.4. Prediction of the occurrence of mycotoxin-related hazards

Mould growth on crops, particularly cereals, has received a lot of interest from the food safety viewpoint because some plant-pathogenic moulds are known to produce compounds named mycotoxins that are also harmful to the human and animal consumers of these crops. Various factors favor mould growth, which can differ among the mould species involved, such as the optimal temperature and humidity. Several predictive models have been developed that aim to predict the growth of moulds on crops and the formation of mycotoxins by these moulds, particularly on the plant parts that have to be harvested. Such models may help making decisions on whether fungicides should be used on the crop or not, or identifying possible contaminations further downstream. Although the current review focuses on generic indicators, it is felt that these predictive models for mycotoxin formation provide an interesting example of how environmental data, in this case meteorological, can give indirect indications of a food safety hazard.

Prandini and co-workers (2008) provide an overview of current initiatives in the field of predictive. models for the growth of *Fusarium* moulds on wheat, causing a plant disease known as "Fusarium Head Blight (FHB)." These models use meteorological variables, such as temperature, precipitation, and humidity. In addition, several models also predict formation of mycotoxins, such as deoxynivalenol (DON) and zearalenone (ZEA; Prandini et al., 2008).

A model used in Italy considers mould behavior and its invasion of wheat, based on temperature, rainfall, crop water content, mould species, and growth stage of the crop. Based on the risk of FHB thus predicted, the risk of production of DON and ZEA can also be predicted. In other nations, including US, Canada, Argentina, and Belgium, other predictive models based on meteorological data are used for FHB and mycotoxin in wheat (Prandini et al., 2008).

4.5. Factors influencing the occurrence of chemical and biochemical hazards in food and feed

Recent developments have occurred involving the presence of chemical and biochemical hazards in food besides the mycotoxins already mentioned above. A recent study highlights various developments including toxic contaminations of botanical products, non-authorized antibiotic residues in imported shrimps, natural toxins present in pesticides of natural origin, and non-authorized genetically modified (GM) crops in crop commodities. The aim of this study has been to formulate common indicators for the hazards considered in these cases that can help identifying similar hazards in an early stage of their development, and thereby achieving the prevention of incidents (Kleter et al., 2008a).

The case study on non-authorized GM crops includes i) the past incidents in the US surrounding Starlink™ maize, which has been authorized for feed use only but nevertheless has been found to occur in food; and ii) experimental pharmaceutical crops, for which the containment during field trials has been insufficient, raising the possibility of potential commingling with conventional crop harvests. In both cases, regulations have already been in place but their enforcement could not prevent commingling from occurring. The incidents have led to stricter regulations and segregation measures that may help preventing such events from recurring (Kleter et al, 2008a). Recent incidents with rice containing traces of experimental GM varieties that have previously been field-tested indicate that such contaminations cannot be completely ruled out yet.

The case on botanicals considers Chinese Herb Nephropathy occurring in patients on a herbal slimming preparation containing toxic herbs that have been misidentified as the common herb ingredient. In addition, the case of intoxications following the consumption of star anise tea has been studied, in which also a misidentification of a toxic relative of star anise has occurred. General risks associated with herbal medicines include i) misidentification, which can be prevented by unequivocal designations, such as in Latin, and which may arise from weeds contaminating cultivated herbs or noxious plants resembling wild-growing herbs; ii) contamination with harmful contaminants; iii) interaction with other medications; iv) adulteration; and v) presence of herb-intrinsic natural toxins (Kleter et al, 2008a).

The case on pesticides of natural origin considered the reported property of the natural pesticide rotenone that caused Parkinson's disease-like symptoms in experimental animals at high doses, and the possible occurrence of toxic components in neem tree extract due to novel processing procedures. The potentially new hazards identified in this case included new extraction methods for the production of natural pesticides, as well as the ability of biological pesticides containing living micro-organisms to multiply after their application (Kleter et al, 2008a).

The case on antibiotic residues in imported shrimp pertains to several incidents of traces of chloramphenicol and nitrofurans occurring in shrimp produced in Asian countries. Because Codex alimentarius has been unable to define maximum residue limits (MRLs) for these antibiotics based on inconclusive toxicology data, the EU follows a "zero tolerance" policy against these antibiotics. Due to intensification of aquaculture of shrimp in third countries, disease pressure may also rise, in response to which producers may be prone to use antibiotics, depending also on the availability of antibiotics, the local regulatory conditions, and education and awareness among producers. Factors have been identified that have contributed to the incidents, including the lack of international harmonization and quality assurance; zero tolerance policy towards certain residues with concurrent improvement in analytical sensitivity of their detection; illegal use or easy availability of antibiotics; and increased production and trade of aquaculture products, indicative of intensification that may possibly lead to increased disease pressure conducive to antibiotic use (Kleter et al, 2008a).

Based upon these and various other cases considered by these authors, general recommendations of potential relevance to occurrence of similar hazards in future have been formulated. First, it is recommended to develop databases with data on contaminants that potentially occur in food and feed products, particularly contaminants or products for which importing and exporting nations have different production methods and regulations. Secondly, pro-active searches should be conducted for the potential presence of contaminants, among others with the aid of the aforementioned database. Thirdly, in international trade, incidents may be prevented by imposing rigorous requirements for quality systems, regulations, and controls by the exporting nation (Kleter et al., 2008a).

4.6. Trend analysis based on data from food law enforcement activities

National and regional authorities have regulations and law-enforcing food control activities in place in order to detect hazards in food and to ensure that the food supply is safe. Besides the controls that food inspection agencies have to carry out on a statutory basis, also monitoring activities for certain hazards in certain products can take place on a selected number of samples in order to gain insight in the situation surrounding these specific hazards. The data generated by these activities, such as published in annual reports of some authorities, could provide inputs for trend analysis for the identification of potentially emerging hazards. However, it is obvious that the hazards measured by the food inspectors must have previously been identified and investigated. Previously unknown emerging hazard and known or re-merging hazards that are for some reason not considered at the moment may therefore be overlooked.

An open source of data coming from food inspection activities in the EU is the RASFF system, which contains notifications of hazards in food and feed that are filed by RASFF members, including national food safety authorities of the EU and the European Free Trade Association (EFTA), as well as the European Commission. The RASFF publishes weekly overviews of the notifications received from members, as well as annual reviews highlighting conspicuous trends, on its website. The notifications fall into the two categories of i) alert notifications pertaining to hazards that are of relevance to other members, possibly requiring also additional measures from their site, and ii) information notifications pertaining to hazards that can be contained, for the information of other members only.

An analysis of the hazards notified through RASFF during the four-year period from July 2003 till June 2007, including 11,403 notifications, has been carried out by Kleter and co-workers (2008b). The notifications were categorized according to date, product, hazard, specific agent, nation and region of origin, nation filing the notification. Hazard categories included microbiological, chemical, biological, mycotoxins, physical, quality, nutrition, fraud, labeling, hygiene, defective packaging, and transport. The developments in the numbers of notifications over time have been considered within these categories in order to verify if trends in the occurrence of hazards can be observed.

A number of conspicuous trends are noted, including an increase in the notifications pertaining to migration of substances from utensils that may come into contact with food and to fraud-related issues. Also several temporary highs are observed, such as in the occurrence of food contact substances, including the ink component isopropyl-thioxanthone (ITX); the illegal dye Para Red in spices & condiments and Sudan dyes in red-colored palm oil; unauthorized GM crops in imported rice and maize products; the unauthorized insecticide isophenfos-methyl in bell peppers; and the fish parasite *Anisakis* in fish products. For most of these cases, notifications have been followed up by measures taken by the national authorities and conspicuous events with a given year have been noted also by RASFF in its annual reports. The authors conclude that it could be useful to combine the RASFF data with complementary data, including safety assessments of the particular hazard, risk management measures (*e.g.* food control inspections) that have been taken before and after the notification, and background information on the particular hazard (Kleter et al., 2008b).

5. Epidemiology and surveillance supporting early response to emerging food safety risks

If the occurrence of an emerging hazard has led to food poisonings and other adverse health effects due to consumption of foods or feed containing the hazard, it may be more appropriate to speak of “emerging risks,” with a less hypothetical connotation than “emerging hazards.” Early detection of emerging risks in this stage will still be beneficial, such as to prevent diseases from spreading widely. International organization, national and regional authorities, and the food sector have put various mechanisms in place in order to carry out monitoring and surveillance of adverse events following consumption. Progress has been made in this area, particularly in a number of fields, of which some examples will be further highlighted below. It should be noted that monitoring of animal disease may be considered an approach applying to farm to fork as well because a disease in food-producing animals may constitute a hazard in its own right to health of consumers of edible products produced from the affected animals.

5.1. Zoonotic disease

As previously mentioned above in the summary of the EMRISK project, the World Animal Health Organization OIE (French: "Office International des Epizooties") has set up an electronic notification system for animal diseases. The veterinary authorities of member states have to notify the OIE of the occurrence of animal diseases from a list of notifiable diseases in the frame of the Terrestrial Animal Health Code and the Aquatic Animal Health Code. This list also contains various diseases that are of relevance for human food safety, such as bovine spongiform encephalopathy (BSE) in cattle. In addition, emerging diseases that have not been listed, but that are expected to have major impact on livestock health, should be reported to OIE.

Currently, the OIE, in cooperation with FAO and WHO, is preparing the Global Framework for the Progressive Control of Transboundary Animal Diseases (GF-TAD). The impetus for this initiative has been the strive for a coordinated approach towards interventions following the recent experiences with the international avian influenza epidemics. It is realized that the majority of animal disease epidemics take place in developing countries and that appropriate resources and measures can thwart these epidemics before spreading to other areas. The GF-TAD is to facilitate exchange of information between the three organizations (FAO, WHO, OIE) and national and regional authorities. This will enable early warnings and additional measures to mitigate the threat at its source, such as the use of appropriate vaccines and healthcare (Lubroth, 2006).

Also national and regional trend analyses of reports of zoonotic disease incidences can provide useful information on the possible emergence of such diseases. For example, EFSA publishes regular overviews of the developments in zoonotic diseases within the EU as one of the European Community's regulatory tasks as defined under directive 2003/99/EC. This directive stipulates that the data on zoonoses collected by national authorities of the EU should be brought together as part of a coordinated monitoring effort. The data to be collected include the prevalence of certain zoonotic pathogens in animals; antimicrobial resistance in some pathogens; frequencies and details of food-borne outbreaks; and human disease data. Additional human data, including data from Enter-net (see below), are provided for this purpose by the European Center for Disease Control (ECDC). The specific zoonoses and the causative pathogens on which data have to be provided are listed in an annex to directive 2003/99/EC. These notifiable zoonoses and pathogens include the bacterial diseases of brucellosis (caused by *Brucella*), campylobacteriosis (*Campylobacter*), listeriosis (*Listeria*), salmonellosis (*Salmonella*), tuberculosis due to *Mycobacterium bovis*, and verotoxigenic *E. coli*. In addition, parasitic diseases that have to be reported include the worm diseases of echinococcosis (*Echinococcus*) and trichinellosis (*Trichinella*). A number of other viral, bacterial, parasitic, and other zoonoses and pathogens have to be reported, depending on the situation. Antimicrobial resistance monitoring data minimally includes the resistance measured in specific pathogens, including *Salmonella* and *Campylobacter*, in livestock and derived food products. In addition, resistance is also measured in intestinal bacteria that serve as indicators for other, less prevalent bacteria. These indicator bacteria are *E.coli* as a gram-negative bacterium and *Enterococcus faecalis* as a gram-positive one.

EFSA has recently published its first annual report with an overview of zoonotic diseases in the EU and associated non-member states. Interestingly, the report highlights several links between the various types of data. For example, *Campylobacter* occurs frequently in live poultry, pig, and cattle. Meat of cattle and pigs, however, shows lower prevalence of *Campylobacter*, which is considered to relate to prevention of contamination of meat with intestinal contents during slaughtering and to dry meat surfaces being unfavorable for *Campylobacter* survival.

Campylobacter is the most frequently implicated zoonotic agent in human disease reports in the EU, *i.e.* 51.6 incidences per 100,000 population, followed by *Salmonella* with 38.2 incidences. Both in *Campylobacter* and *Salmonella*, fluoroquinolone resistance has been observed, about which EFSA expresses concerns, given the therapeutic importance of these antibiotics (EFSA, 2006b).

Another interesting observation was that populations of the red fox, which is an important carrier of the lung-disease-causing parasite *Echinococcus multilocularis*, increase and move into urban areas, adding to the likelihood of human exposure (EFSA, 2006b). This is similar to the notion that dwindling habitats for wildlife may increase exposure of livestock and humans to carriers of zoonoses, contributing to the emergence of pathogens (see section 6.2.1).

5.2. Food-borne human disease

5.2.1. Surveillance systems

Various systems exist to date that measure the occurrence of food-borne disease, some of which are specifically dedicated to food-borne diseases, whereas others treat these diseases as part of a wider spectrum. Trends in data generated by surveillance may provide indications of the emergence of certain pathogens based on trends towards increased incidences of these pathogens. Apparent increases in incidence reports of food-borne diseases or pathogens may relate to underlying factors other than a real increase *per se*, though. This has been the case, for example, with the increased frequency of isolation of *E. coli* O157 in the US during the 90s, which correlated with the increasing number of US states submitting reports on the *E. coli* O157 isolates (Braden and Tauxe, 2006).

International surveillance is pursued by the WHO, which hosts the International Food Safety Authorities Network (INFOSAN), established in 2000. Through INFOSAN, authorities in member states can exchange information on routine as well as emerging food-borne diseases. These data on food-borne hazards are gathered through national health surveillance and food control activities, as well as from other regional and international organizations. In addition, each member state has a national focal point for dealing with emergency situations, such as in the case of outbreaks. Rapid alert or outbreak situations that are of relevance to international public health should be reported in “real time” through INFOSAN’s computerized Global Outbreak Alert and Response Network (GOARN). Such alerts are then further handled and coordinated by WHO, which can offer technical assistance to member nations experiencing emergencies. Examples of such alerts, of which on average one per month is handled, are norovirus in oysters, *E. coli* in spinach, and *Salmonella* in chocolate. This system is in line with the amended International Health Regulations, which demand that *any* disease of importance for international public health be reported in time, contrary to the previously amended requirement that only three diseases, *i.e.* cholera, plague, and yellow fever, be reported (WHO, 2006).

Braden and Tauxe (2006) describe the various surveillance programs for emerging pathogens in the US. Most of the surveillance of food-borne diseases in the US is done by state and local authorities, while a number of diseases, including food-borne ones, are nationally notifiable in the US, including serotypes of *Salmonella*. Serotyping may allow for the recognition of unusual clusters of infection, *i.e.* the same serotype associated with multiple food poisonings. Modern molecular methods are currently also being used for typing of implicated food pathogens and cluster analysis of outbreaks.

An example of such a surveillance program is PulseNet, which is a collaboration of US state public health laboratories, the national Centers for Disease Control and Prevention (CDC), and other federal agencies that employ pulsed-field gel electrophoresis (PFGE) of seven food pathogens (Gerner-Smidt et al., 2006). The CDC coordinates this network and owns a database of PFGE profiles, while each of eight PulseNet regions that span the whole US is led by a regional PulseNet laboratory that cooperates with the participants within that particular region. The seven pathogens detected by PulseNet include *Salmonella enterica*, *Shigella* spp., *Listeria monocytogenes*, thermotolerant *Campylobacter* spp., *Clostridium perfringens*, *Vibrio cholerae*, and Verocytotoxin-producing *Escherichia coli* O157 (VTEC O157; VTEC is synonymous to Shiga-toxin-like-producing *E. coli* or STEC). Each week, clusters in the reported PFGE-patterns of these pathogens over the last 60 days are screened for. The patterns obtained by PFGE are processed into the database with dedicated software and codes are assigned to distinct patterns, based on the microorganism tested, restriction enzyme used, and banding profile of the electrophoresis gel, in addition to a code for the outbreak with which the microorganism is associated (Gerner-Smidt et al., 2006).

PulseNet cooperates internationally with several laboratory networks outside the US, including fellows in Europe, Canada, Japan, and other Asian-Pacific and Latin American countries. Within the EU, PulseNet Europe carries out PFGE research on outbreaks of zoonoses, in particular *Salmonella*, *Listeria monocytogenes*, and STEC. This research is carried out under the umbrella of the EU-sponsored MedVetNet program. Interestingly, a Danish study on PFGE with STEC in Denmark during the period 2003-05 gives an account of time saved by using PFGE for more rapid identification of the common cause of an outbreak in the period covering the last months of 2003 and the first of 2004 (Møller-Nielsen, 2006).

An example of another relevant joint initiative the US CDC, FDA, and USDA is the National Antibiotic Resistance Monitoring System for Enteric Bacteria (NARMS-EB), in which food-borne pathogens are followed for their antibiotic resistance. Another initiative of the same organizations is the Food-borne Disease Active Surveillance Network (FoodNet), which actively collects data on cases of food-borne disease from laboratories and health professionals in 10 sites covering 13% of the American population (Braden and Tauxe, 2006).

The WHO Surveillance Program for the Control of Food-borne Infections and Intoxications in Europe involves national food-borne disease outbreak surveillance activities of European and Central Asian countries. Member states report to this program using a standardized format into which data have to be added concerning, among others, the number of patients, the cause, the food involved, location of food handling, location of purchase, and any additional factors that contributed to the outbreak occurring. These data facilitate the conduct of outbreak trend analyses, the epidemiology of food-borne diseases, and the identification of sources of outbreaks. The outcomes show, among others, that the importance of factors contributing to the occurrence of outbreaks can vary from nation to nation. These factors include contamination of food through the use of infected equipment, inadequate food storage and processing, and contamination by an infected person (O'Brien and Fisher, 2006).

It is realized though that the methods used by laboratories for identification of pathogens can vary from one nation to the other. Global Salm-Surv is another initiative of WHO in which most of the European network countries participate. It aims at harmonizing surveillance data on serotypes and antibiotic resistance of *Salmonella* through training and laboratory quality assurance.

Enter-net, an initiative sponsored by the European Commission, brings together the microbiological and epidemiological services from its members' nations and also collaborates with various international partners, including the CDC mentioned above. The participants identify the types of *Salmonella* and STEC bacteria that are involved with outbreaks, as well as the antibiotic resistance of *Salmonella* isolates. The data thus collected enable the conduct of a trend analysis of *Salmonella* and STEC outbreaks, while these data serve as supplement rather than a substitute to national activities. The international collaboration allows for the accumulation of sufficient data that member nations may not be able to do on their own, so that an outbreak can be recognized earlier (O'Brien and Fisher, 2006).

Additional research projects sponsored by the European Commission include Food-Borne Viruses in Europe (FBVE) and Diagnosis, Viability, Networking, and Epidemiology (DIVINENET). These projects focus on new virus detection methods, data exchange, outbreak research, and mechanisms of emergence of new viral diseases. The Salm-gene project aims at strengthening the surveillance of *Salmonella* by standardizing molecular identification methods such as PFGE in Europe (O'Brien and Fisher, 2006).

Other European initiatives include the Basic Surveillance Network, which has its origin in EU regulations requiring that a European-community-wide surveillance network be set up for 40 diseases. The network aims to develop standards for minimally required reporting data, which can be collected from national reports, so that all member states' data can be harmonized. Various of the 40 diseases mentioned above are food-borne infectious diseases, such as caused by *Salmonella*, *Campylobacter*, and *Listeria*, among others. For the epidemiological surveillance of variant Creutzfeldt-Jakob (vCJD) disease, EUROCJD / NEUROCJD focus on the diagnostics and epidemiology of vCJD. These networks include participants from all EU member states, as well as some associated non-EU nations. The coordination of most of the EU initiatives mentioned has been conveyed to the recently established European Centers for Disease Control (O'Brien and Fisher, 2006).

5.2.2. Retrospective studies on trends

As noted above for the various initiatives on surveillance, besides rapid identification of the source of an outbreak, surveillance data may also serve the analysis of trends over longer periods of time in order to reveal possible increases in existent hazards or appearance of new hazards. This particularly pertains to the surveillance of microbiological pathogens, which may reflect the dynamics of such pathogens and the evolutionary changes they thus may undergo. Various studies on the changing incidences food hazards have been carried out. Such studies may provide insight into the feasibility of discerning trends that are of importance for the study of emerging food-borne diseases.

Gillespie and co-workers (2006) have carried out a retrospective study on the incidence of listeriosis, *i.e.* a disease caused by food-borne *Listeria* bacteria, in Wales and England in the period of 2001 till 2004. Before this period, in the 90s, listeriosis has occurred at a comparatively constant level, whereas an increase is observed from 2001 till 2004. Possible links of listeriosis with ethnicity, age, socio-economic status, and residential home *versus* care center have been explored. The authors have not included clusters of outbreaks with multiple disease reports related to a single common cause, such as consumption of contaminated sandwiches. Therefore, only sporadic cases have been considered. The results show that the risk of listeriosis has increased in patients aged over 60 years in the 2001-2004 period compared to that of 1990-2000, or compared to younger generations. This increase appears to be real and it is considered likely that it is caused by changes in behavior, although no change in intake of the major food groups have occurred.

Another study of relevance to emerging hazard identification considered the detectability of cryptosporidiosis, which is the disease caused by the protozoan pathogen *Cryptosporidium*. A particular property of *Cryptosporidium* is its long incubation period. The study particularly addressed the question as to whether it could have been detected through reporting of nurses reporting diarrhoea in patients to the UK National Health Service (NHS) Direct Call system. This system has monitoring algorithms in place in order to follow particular diseases, such as influenza. Data from an outbreak of *Cryptosporidium* as well as numbers of total calls coming in at an NHS center were used to create a simulation. In this simulation, it was checked what the likelihood was of observing an increase over the background level caused by Cryptosporidium. The data exceeding the threshold level imposed by the detection algorithm were considerably more numerous if 90% of the cases had been reported instead of the 10% initially considered (Cooper et al., 2006). This study also shows that discerning an emerging disease may be less demanding if the reporting rate is high.

6. Identification of hazards in the surrounding environment

6.1. EMRISK: Holistic-approach-based indicators

6.1.1. Background of the EMRISK project

The EMRISK project provides an interesting perspective on the collection and use of indicators from a holistic perspective. This European project was funded by EFSA and was carried out under the supervision of the Dutch national Food and Consumer Product Safety Authority (VWA). EMRISK participants included EU member state authorities and institutes involved with food safety, as well as international organizations. EMRISK extended the work that had previously been done under VWA's supervision by the PeriApt project, which had been supported by the European Commission's research funding as a specific supportive action in the frame of the ERANET program for linking national research activities with the aim of establishing a research area at the European level. Both the EMRISK report & annexes, and the opinion of EFSA's Scientific Committee based on the outcomes of the report, have been posted on the EFSA website (EFSA, 2006a; VWA, 2006).

Within PeriApt, a holistic model has been developed, which takes into consideration that hazards within the food production chain may originate from - or be influenced by - events and developments that take place within influential sectors outside the food sector. This model of a "host environment" analysis builds upon previous outcomes of broadly focused OECD activities on future risks. OECD has discerned four influential sectors, within which critical factors can be further identified and the indicators linked to these critical factors. PeriApt has expanded this range to eight influential sectors based upon the outcomes of three case studies and consultations with stakeholders. These eight sectors include agriculture, technology & industry, government & policy, economy, nature & environment, information, consumer behavior, and culture & demography. Two additional retrospective case studies have also considered the influence of human behavior aspects in the development of past food safety incidents, mad cow's disease (BSE) and the formation of the potentially carcinogenic compound acrylamide in heated products. The PeriApt project recommends reiterating the exercise of identification of influential sectors with stakeholders, as well as building European and national networks to harmonize indicators and to collaborate with international organizations like FAO, WHO, and OECD on issues such as surveillance (VWA, 2005).

EMRISK has extended upon PeriApt, providing recommendations and a blueprint to EFSA on how to build a "pre-early" warning system for the timely, anticipatory, and pro-active detection of emerging food safety hazards in an early phase of their development. Therefore this system is different from the monitoring and surveillance systems that are currently in place to detect known hazards.

6.1.2. EMRISK activities and definitions

EMRISK has carried our various activities, including:

i) a "bottom-up" review of five retrospective case studies, leading from specific cases to identification of indicators and information sources, was intended to provide insight as to how a proactive system could have used indicators and information sources to prevent these incidents, covering the a) discovery of formation of acrylamide in heated products, b) the avian influenza epidemic in poultry livestock in Holland in 2003, c) the BSE incident in the United Kingdom, d) poisoning with aflatoxins in Africa, and e) the discovery of semicarbazide as a food contact substance derived from blowing agents used for the production of jar lids;

ii) an inventory of activities within EU-sponsored research projects pertaining to emerging hazard identification; and

iii) "top-down" identification of information sources and their quality and accessibility, starting from general conclusions via generic indicators towards these sources, by stakeholders with broad expertise invited to workshops specifically organized for this purpose by EMRISK.

In the conclusions to the case studies, it is mentioned that for each case a combination of factors has been important in the development of the case. The use and weighing of multiple indicators could therefore provide be a useful tool (see the traffic light approach below). It is also realized that indicators may not always be quantitative, and that qualitative indicators should be regarded as indicative. Both case-specific and more generic indicators have been identified in the case studies, of which the generic indicators have been further explored for their usability in the approach to be recommended by EMRISK (VWA, 2006).

EMRISK proposes some revisions to the set of influential sectors previously defined by PeriApt in order to align these better with the definitions used by other EU and international institutions. EMRISK also distinguishes between primary and secondary influential sectors, with the latter positioned further away from the food sector than the first. The revised set of primary influential sectors consists of science & technology, environment & energy, health, agriculture, economy & finance, and industry & trade. The three secondary influential sectors thus included government & politics, population & social conditions, and information & communication.

EMRISK also makes a distinction between primary and secondary information sources that provide information for identification of hazards. Primary systems are directly linked to food production, such as the monitoring and surveillance systems that have evolved over time, based on experiences with known hazards. In addition, more responsibility is currently put on the producers themselves, having to fulfill requirements of good and hygienic production and to perform their own risk assessments as part of the HACCP. National regulatory and food control agencies subsequently verify if the right checks are in place and carried out according to the regulations. An example of a primary system is an early-warning database such as the RASFF system where members report detected hazards in food and animal feed that are of relevance to other members. These members include the European Commission, EU member state authorities, and the EFTA Surveillance Agency (ESA). Other examples of primary information systems are expert networks, stakeholder groupings, scientific panels, public media networks, consumer help services, and scientific conferences. These systems bear several limitations including the focus on known hazards, the non-consideration of factors outside the food sector, and economic and societal factors that may influence the response towards a certain hazard. EMRISK recognizes the importance of primary systems in providing information across nations, although these data may be focused on one sector only.

Secondary systems, on the other hand, are more broadly focused and not only consider the food sector but also the host environment of influential sectors surrounding it. Indicators used by these systems to predict the likelihood of the emergence of a hazard are considered as “indirect” and to be located within these influential sectors.

EMRISK also describes anticipatory systems, which would extend upon the secondary systems by linking all the different kinds of information. It is noted by EMRISK that anticipatory systems are still within their initial phases of formation. Critical factors assigned within an anticipatory system may be strongly linked with each other in a kind of network structure. Assigning importance values to the indicators linked with these critical factors may be necessary, based, for example, upon the importance of detecting a signal for the emergence of a hazard (VWA, 2006).

6.1.3. EMRISK project outcomes

Based upon the outcomes of the various activities, including the case studies and workshops, EMRISK has identified of a set of indicators within the nine influential sectors (VWA, 2006). These indicators are both quantitative and qualitative by nature and have been refined and sized down, based upon a ranking system using defined criteria. These criteria include i) measurability, which is the ability to detect a signal based upon thresholds or ranges for quantitative indicators or upon affirmative or negative outcomes for qualitative indicators; ii) interpretability, which is the ability to observe trends in the outputs from the indicators; iii) directness, which is inversely related to the distance between indicator and emerging hazard, with a high directness signifying a short distance; iv) potential impact, which relates to the potential harm that a particular emerging hazard associated with the indicator may cause to health, as well its degree of dissemination through society; v) comprehensiveness, with generic indicators being preferred over specific indicators; and vi) discriminatory nature, which is indicative of the lack of overlap or duplication with other indicators and which therefore can only be determined in a later phase of the selection procedure.

A team consisting of five experts from three organizations participating in EMRISK has subsequently used these criteria in order to make a selection of the indicators collected. Two paths have been followed, the first being a decision-tree approach in which scores on a scale from 1 (very low) to 5 (very high) were assigned to an indicator’s compliance with each specific criterion. Each score for an indicator has subsequently been transformed into a “yes” for scores 3-5 and a “no” for scores 1-2. For an indicator to be selected, all transformed scores should be “yes.”

Whilst each criterion has been equally weighed within this decision-tree approach, the second approach of a ranking system has applied unequal weights to the criteria. Furthermore, the ranking system has not considered the criteria “interpretability” and “measurability” at the same time, since they are mutually dependent. Therefore, the ranking system has only considered one of both criteria, that is, interpretability. In addition, the criterion "discriminatory" has not been considered either, given the difficulties in assigning scores for this criterion to indicators. A weight factor of 2 has been assigned to "directness" and "potential impact," whereas a weight factor of 1 has been assigned to the other criteria of "interpretability" and "comprehensiveness." Therefore the maximum score that can be assigned to an indicator is 30. The outcomes of the ranking-system approach are more diverse than those of the decision-tree approach, allowing for the grouping of top-scoring indicators.

Based upon the outcomes of the comparison between the decision-tree and ranking-system approaches, EMRISK concludes that a ranking-system approach employing weighted criteria is preferred for the selection of indicators of emerging hazards in influential sectors. In addition, because of the diversity of the influential sectors that had been considered, EMRISK recommends consulting a sufficient number of experts with knowledge of each relevant influential sector. EMRISK also envisions another role for these experts in further steps downstream of the identification of indicators (see below).

Another objective of EMRISK has been to allocate indicators within the influential sectors it has defined so that each sector would be covered well. This objective apparently has been achieved given that the final output amounted to a total of 217 indicators of which 63% are located within the six primary influential sectors, in which the number of indicators per sector range between 10 for science & technology and 36 for agriculture & fisheries. In annex 5 to the report, which features the list with selected indicators, the table provides indicators per class within each influential sector. For each indicator, it is indicated what the main features are and which information sources are available for data on the indicators. For example, within the influential sector "science & technology," there are two indicators that fall within the class of "knowledge-based services." These indicators are "output (results) of risk assessment" and "number of conferences," for which the main features mentioned are "assists to distinguish between true and false emerging risks" and "reflects the scientific attention / focus of selected issues; beware of the impact of the conference science (*e.g.* one big one *versus* lost of little ones)." As key information sources, a variety of national and international scientific institutions, risk assessment bodies, expert networks and Eurostat, the European Commission's statistical office, are mentioned.

The subsequent steps that EMRISK proposes are to further organize the signals coming from the indicators. For this purpose, time-dependent changes in the relevance of indicators should be measured. This can be done by selecting the top-five indicators in each influential sector based on the scores in the ranking system. It should then be checked during each repetition after a certain period of time if changes with regard to the ranking have taken place, that is, if different indicators reach the top-five with each repetition of the ranking procedure. In addition, the signals coming from each indicator can be measured over time and classified to check for possible changes in their magnitude. In order to deal with both qualitative and quantitative indicators and to interpret the meaning of any temporal changes observed, EMRISK proposes to apply the "traffic light theory" for the interpretation of trends associated with changes in signals. With this theory, the direction of trends is indicated by a color similar to traffic lights, with green for positive trends, yellow for intermediate results, and red for negative trends. It is also possible to assign different "urgency" weighing factors to signals with different traffic light colors, reflecting the need for immediate action if negative trends occur. In addition, one signal may be considered to be more important than another and therefore an additional "importance" weighing factor can be assigned to signals. In order to account for the relationships that signals, including those from different sectors, may share with each other, a "relationship" weighing factor can be assigned to these signals.

For the timely acquisition of data, EMRISK notes that preliminary scientific data may not be readily available. In addition, also non-scientific data can provide useful inputs. Knowledge organized within EU research networks is recognized as a possible source of information, where experts would be able to provide signals from selected information sources to which they have access. In addition, EMRISK provides an outline of how automated searches using dedicated search engines can be done for major changes in indicators over time and in the indicators' "space." To this end, "indicative questions" need being drafted by experts with a description of the attributes of the indicators under consideration. Keywords can subsequently be extracted from this indicative question by specialized computed programs in order to enhance the effectiveness of a search on the Internet for data on changes in the indicators. This process of automated searches based on indicative questions and keywords involving both experts and computer specialists may need being reiterated and adjusted several times in order to further improve the quality of the output.

The signals that come out of the system once it has become operational have to be evaluated by scientific experts and information specialists before a "proactive alert" is issued to inform risk managers of an emerging hazard. It is also envisioned that this semi-automatic search system could be self-learning, building upon experiences with feedback from the risk management process following the yield of signals that require further actions by the management.

Stakeholders, such as consumer organizations, may be involved at various stages of the recommended procedure, for example as information source, for the processing of indicative questions, and after the evaluation of signals.

The EMRISK report also lists a number of interesting initiatives, however noting that these systems are retrospective. Initiatives that consider multiple sectors include the completed OECD project on emerging risks in the 21st century and Eurostat's measurement of indicators in various sectors. In addition, the European Environmental Agency and the European Commission's Health Monitoring Program are examples of initiatives collecting information on changes in indicators. Field-oriented, key-word-containing thesauri are compiled by both the European Commission and FAO. Initiatives that provide information sources include two systems of the FAO, the Food Insecurity and Vulnerability Information and Mapping Systems (FIVIMS) and the Global Information and Early Warning System (GIEWS). FIVIMS consists of a structure of national and international databases on food insecurity. GIEWS monitors agricultural production and prices, among others by using satellite data, and also provides inputs to FIVIMS. An early warning system for animal diseases considering both official and unofficial information has been set up by OIE, while the Canadian authorities have established the Global Public Health Intelligence Network (GPHIN) which continually monitors information from global public media, including Internet, for certain relevant events. An example of an initiative involving expert networks is the ECDC bringing together European networks of scientists involved in various fields of relevance, such as research networks on certain pathogenic bacteria (VWA, 2006).

6.1.4. EFSA Scientific Committee's opinion

Based upon the outcomes of the EMRISK project, the EFSA Scientific Committee, in which the chairs of the various scientific expert panels as well as senior scientific staff of EFSA participate, published an opinion on the early identification of emerging risks (EFSA, 2006a). The background for this opinion and the EMRISK project was that the General Food Law, European Community Regulation 178/2002/EC, which provided the basis for the establishment of EFSA, also stipulated that EFSA should install monitoring procedures for the identification of emerging risks within its field of work, that is, food safety. EFSA had requested the Scientific Committee to give advice on systems and procedures for the identification of emerging risks, as well as on networks that could provide information for this purpose. Interestingly, the Scientific Committee provides a definition of emerging risks as issues that may pose risks to humans, animals, and environment in the future. The causes of their emergence are either a significant exposure to hazard that have not been identified earlier or a new or increased exposure to a known hazard. Please note that the definition of risk is thus in line with the notion that this is probability of hazard occurring through exposure. An indicator is defined as component of risk assessment, which can be composed of various qualitative / quantitative parameters, either closely or loosely linked with the food production chain. A signal is defined as a trend in time or space of indicator. Emerging risks may be indicated by single or multiple signals.

The opinion lists both internal and external sources of information that could provide signals of emerging problems. Examples of internal sources are EFSA staff, the Scientific Committee, the Advisory Forum in which member state authorities' representatives take part, the EFSA Scientific Panel experts, and the Stakeholder Consultative Platform. External sources include, among others, the European Commission's Scientific Panels, such as the Scientific Committee on Emerging and Newly Identified Health Risks, as well as the RASFF system. Another source could be Eurostat's "Food: from farm to fork" initiative, which brings together data on food safety monitoring, trade, and public health, with the aim of providing risk managers with a tool. Also the REACH program (Registration, Evaluation, and Authorization of Chemicals) could provide data on chemical substances that may be relevant for food safety as well. Other contacts mentioned include international organizations and other European institutions, such as for medicine registration and the environment.

Besides listing a number of ongoing, related systems for early identification of risks, the opinion also recommends a procedure for the identification of issues and the processing thereof. The opinion foresees the establishment of links between EFSA and other networks that may provide information on emerging risks, rather than a comprehensive network dedicated to this purpose. Besides the contacts mentioned above, these links also include research institutions, national agencies within and outside the EU, external experts, and information sources & search tools. In addition, it is recommended to form an *ad hoc* working group under the umbrella of the Stakeholder Consultative Platform with the aim of preparing for the formation of a stakeholder network dedicated to information exchange on emerging risks. In addition, transparent and clear procedures on how to process and evaluate information regarding emerging risks should be implemented. Furthermore, a database with evaluations of incoming issues should be set up.

With regard to indicators, the Scientific Committee concludes that consulted experts should make an initial selection of a limited number of indicators and, if possible, values triggering follow-up actions. In addition, the extensive list with indicators provided in annex to the EMRISK report is considered to be resource-demanding and a possible target in the longer term. For the shorter term, the Scientific Committee recommends a system designated "ER Resource" and procedure based on expert judgment. Within this procedure, information on emerging risks may be provided to EFSA, although not part of a dedicated screening activity. Such information has to pass an initial filtering by EFSA staff based on relevance of the information, but also on its quality and possible duplication of previous information. A quality index was envisioned that could be affixed to the information so as to reflect, among others, the reliability of the source, the multiplicity (>1) of independent sources, and the way in which data had been produced. If selected for closer examination, a secondary filter will be applied to the incoming information by evaluating it with experts from EFSA Scientific Panels. If information does not pass either one of both filters, it will be stored in the abovementioned database. The selected information that has passed the filtering stages is then considered for the urgency required to handle it further. Whether urgent or not, the information can be assessed either by the existing scientific panels & Scientific Committee or by an *ad hoc* working group established for this purpose. In case the information on the emerging risk gives rise to concerns, EFSA will send an alert to the relevant authorities. In case no concerns are raised, the outcomes will be recorded, relevant parties informed, and the information stored in the abovementioned database. The Scientific Committee acknowledged the importance of rapid follow-up to signals received within this procedure and also that of trust between the cooperating institutions. Research was regarded a key source of information.

In conclusion, the Scientific Committee's opinion highlighted the preference for the use of a limited set of indicators to be selected by experts, but did not specifically mention examples of such indicators. In addition, it identifies many European institutions as potential sources of valuable information on emerging risks (EFSA, 2006a).

6.1.5. Dutch study on indicators for emerging mycotoxin hazards

From the indicators recommended by EMRISK, Park and Bos (2007) have selected a limited number as candidates for the future detection of emerging mycotoxin hazards. Selected indicators linked with the critical factor climate include drought, temperature changes, and rainfall. This is based on the known relationship between growth and mycotoxin production of some moulds, including *Fusarium,* on crops at high temperatures and humidity.

Another critical factor is market and consumer trends, given that sudden changes in demand may lead to the use of high-yielding varieties that are more sensitive towards mould infection or to longer post-harvest storage periods in which mould growth can occur. Indicators linked with market and consumer trends include market prices and crop production, such as reported by Eurostat and FAOSTAT, and trends observed in market research reports.

Similar to the market conditions, the economy is also considered to be a critical factor, for example because the availability of financial resources influences agricultural practices and the quality of storage and transport facilities. Indicators such as gross domestic product and inflation rate are linked to this critical factor.

The critical factors global trade and transportation relate to the conditions of storage of the product, including the transit time, during transport. Indicators linked with global trade include import and export statistics, such as from FAOSTAT, as well as information on trade barriers. Transportation indicators include strikes of transporters and registration of transportation companies. Another critical factor is the introduction of new technologies, including crop monocultures, which may facilitate mycotoxin production and dissemination. The indicators for this comprise scientific and non-scientific (newsletter) journal coverage.

Pest control management is considered another critical factor because damage to crop by pests may provide points of entry for moulds, besides the mould being a pest in its own right as well, It is realized, though, that measures against pests, such as by spraying fungicides, may not always reduce, but rather stimulate mycotoxin production. Indicators include data on the prevalence of pests, as well as information from scientific literature on the effect of pest control measures on mycotoxin production.

Park and Bos (2007) also identify legislative developments as a critical factor, not only for legislation pertaining to mycotoxins, but also to other issues related to the factors mentioned above, including crop production, pest management, and transport, among other things. As potential future directions for the use of these indicators, these authors mention retrospective analysis of mycotoxin reports, also with regard to the applicability of the abovementioned indicators to the prediction of these hazards. In addition, the indicators could be incorporated into targeted surveillance for mycotoxins during a specified period of time. The outcomes of this experiment should then form the basis for a continuous system to measure mycotoxin hazards.

6.1.6. Dutch policy support project

Hagenaars and co-workers (2006) have recently published a report on emerging risks in food as part of the output of a four-year project supervised by the Dutch Ministry of Agriculture Nature and Food Quality and VWA. The report gives an account in retrospective of six exemplary cases of risks that emerged in food and feed safety, and the way that these risks had been dealt with by both risk assessors and risk managers. These case studies pertain to both new and re-merging risks, as well as chemical and microbiological risks, while their detection has occurred either in time or late.

Although these cases are specific, the inferences made from them are relatively broad, so that they can be applied to a range of other hazards as well. The focus was on the role that pro-activity might have had on the emergence of the risks in retrospect, both from a "holistic" point of view outside the food production chains, and within that chain. In addition, the authors of this study recommend monitoring of various indicators as part of the holistic approach. The six cases and the recommendations include the following:

1. The occurrence of dioxins in pig meat in The Netherlands in 2004. The animal feed for these pigs contained potato peelings that had taken up dioxin-contaminated clay during potato processing. The clay replaced salt that had been previously used for this purpose, because of environmental considerations regarding processing wastewater. It is recommended to monitor changes in production processes, particularly those that have an effect on waste streams. Indicators that could be useful for this purpose include changes in regulations, purchasing patterns of auxiliary materials needed for processing, and market prices for processing input materials;
2. The BSE epidemic among cattle in the UK starting in 1986 and the possible relationship with variant Creutzfeldt Jakob Disease in humans, which was discovered a decade later. BSE has been able to spread by the inclusion of meat and bone meal carrying the BSE-causing agent in the cattle's diet. The authors recommend assessing risks of changes in waste stream processes, while at the same time realizing that it is not certain if this could have averted the BSE crisis with the state of knowledge at the time it occurred;
3. The avian influenza epidemic among poultry and several humans in The Netherlands, a country with high-density poultry farming, in 2003. Highly pathogenic avian influenza had not occurred for 75 years until the epidemic. It is recommended by the authors to consider the increased risk of exposure to certain chemical contaminants and biological agents in outdoor, free-ranging livestock, compared to that kept in-house.
4. Disease in horses, *i.e.* equine leukoencephalomalacia, caused by contamination of feed maize with the mycotoxin fumonisin in the US in 1989-1990. Mycotoxins are formed by moulds infecting the crop under favorable conditions of temperature and humidity.

Horses are particularly sensitive to the action of fumonisin. It is recommended to monitor for indicators of plant stress, as this correlates to increased levels of infections by mycotoxin-producing moulds.

5. Cultured fish containing residues of polychlorinated biphenyls, dioxins, and organochlorine pesticides. These persistent chemical compounds occur in nature in low background levels but tend to accumulate through biological food chains, so that increased levels may occur in fish. Cultured fish may be fed with meal from other fish, so that additional accumulation may occur. Governments already have monitoring programs and regulations in place for these contaminants. Nevertheless, the outcomes of a study published in Science, which used a different calculation method for estimating risks than is commonly used by governments, has raised concerns and triggered consumer backlash in some countries. The authors recommend considering the possibility that standards may change for compounds that are intensively investigated, in particular combinations of compounds. In addition, products that have a strong image of positive health attributes may be particularly sensitive.
6. Contamination of fish with perfluorinated compounds, which are compounds with various industrial and household uses, but also may occur naturally. These compounds are volatile and can be disseminated over large distances before condensing into sea water where they can be taken up by fish. Awareness of the possible toxicological implications of the presence of these compounds has recently started emerging. It is recommended checking the substitutes for the abandoned perfluorinated compounds for any similarity in their toxicity and capacity to bio-accumulate.

In addition, two other general risk indicators are mentioned, namely i) the use of recycled animal material as animal feed, as seen in the cases on BSE and PCBs, dioxins, and organochlorine pesticides in fish; and ii) health effects observed in populations with high exposures to certain agents, as seen in the cases involving perfluorinated compounds and dioxins (Hagenaars et al, 2006).

6.2. Exploration of potential future issues

Anticipation of future issues can be done through “futures research” in which various possible future environments are explored, for example with respect to their consequences for a particular organization. The plural form of “futures” refers to the multiple potential future environments that are usually explored. The envisioned future environments have to be realistic and therefore futures research is not a “crystal ball” or science fiction. Various methods exist for futures research, while it has to be realized that these methods do not exactly predict what the future will be like, but rather help the assessor in preparing itself better for future situations.

Methods for future exploration include analysis of scenarios, road mapping, and trend analysis. For the method involving scenarios, multiple scenarios are generated that aim at facilitating the identification of uncertainties and the ability to prepare for these uncertainties. The scenarios can contain images and stories, each based on, for example, plausible assumptions of how the present situation may develop further. They therefore provide an impression of what the future environments may look like so that subsequently the assessor can position itself within this environment, rather than starting by envisioning the assessor’s own position (Van der Duin and Stavleu, 2006).

For road mapping, the description of the various phases that lead up to a certain future situation forms the main part of the exploration. The road map is a kind of action plan that describes which steps have to be taken in order to arrive at a certain future, taking into account a broad range of factors, including economic and societal issues (Van der Duin and Stavleu, 2006).

Trend analysis is the estimation of future trends or developments in a broad range of fields and an assessment of their possible consequences for an organization with a given problem or query. Such an analysis can be either qualitative, with trends being described in words, or quantitative, with trends expressed in numbers or models of cause and consequence. The trends that are considered actually have already started and have a certain direction, which is extrapolated into the future. Trend analysis may not always take short-lived events into consideration (Van der Duin and Stavleu, 2006).

6.2.1. Trends affecting the emergence of zoonotic diseases

Ackerman (2006) has analyzed a number of trends that may have impacts on threats and vulnerability to the food chain, in particular on the development and spread of zoonotic diseases, that is, diseases that can be transferred from animals to humans. An example of such a trend is the increasing deforestation and urbanization, which may encroach on natural habitats of wild species that are also vectors of zoonotic agents. This may increase the likelihood of contact of humans and animals with these vectors and thus the transmission of disease. Another trend is the globalization of transport of humans and of trade in livestock, livestock products, and exotic species. This globalization may contribute to comparatively rapid dissemination of a disease from one geographic area into other remote areas, which previously might have taken much longer to occur. In addition, this may expose immunologically “naïve” humans and animals to diseases that have previously not occurred in their own habitat, contributing to the potential severity of the impact of the disease.

In addition, Ackerman (2006) notes that societies have become increasingly vulnerable due to dependence on failure-sensitive networks, rapid urbanization, increases in population density, and unfamiliarity with large outbreaks due to a history of well-functioning hygiene and healthcare systems. In addition, populations may be immunologically compromised and appropriate therapies may not always be available. Another threat comes from traditional agriculture in some countries, where the proximity of different species promotes transmission of diseases, combined with international mobility of these diseases through man-controlled transport or migration of animals to areas with intensive farming techniques, where diseases can spread rapidly (*e.g.* avian influenza).

Ackerman (2006) also considers the fact that the causes of the periodic emergence of pandemics and epizootics are not known and that they therefore may re-occur. Another point of concern is the threat of intentional infection of humans and animals by non-state actors that might be motivated to use biological weapons. Finally, it is recommended to consider trends and to develop holistic broad system for preparedness for incidents including unexpected “outliers.” Furthermore, simulations of scenarios are recommended, which should also consider the social and political consequences of zoonotic disease outbreaks. Active- rather than passive-surveillance techniques should be pursued, which may be facilitated by “situational awareness” (described more in detail in section 4.2; Ackerman, 2006).

Chomel and co-workers (2007) consider that most of the emerging infectious diseases are zoonotic by nature. These authors review both food-borne and non-food-borne zoonoses and some changing practices underlying the emergence of these zoonoses. As already noted by Ackerman, population expansion, wildlife habitat retraction, and increased contact between pathogen-carrying wildlife on one side and humans and domestic animals on the other side may confer increased likelihood of transfer of zoonotic disease. An example of this is the Nipah virus that was transmitted from fruit bats to non-industrial domestic pigs and subsequently to humans in deforested areas with fruit tree plantings. Another example of increased likelihood of transfer of zoonoses is the increased trade in - and consumption of - “bush meat,” including meat from monkeys that are potential carriers of viruses that also infect humans. “Wet markets” where live animals are traded and come into close contact with each other and with humans have been shown to lead to dissemination of avian influenza. Intensive farming of wildlife species, such as deer, may lead to re-emergence of certain diseases that occur less frequently in wild populations. Other non-food-related factors contributing to zoonosis emergence are import of exotic animals that may be common carriers of zoonoses such as pet reptiles causing salmonellosis, as well as petting zoos facilitating contact between visitors and animals (Chomel et al., 2007).

In a way that is somewhat similar to the domestication of exotic pets, Lubroth (2006) mentions the introduction of non-native species in areas where they can out-compete the native species. This can be an important factor contributing to imbalance of species biodiversity and to proliferation of “vectors,” *i.e.* animals carrying human and animal diseases.

6.2.2. Trends affecting the emergence of food-borne pathogens besides zoonoses

In a recently published book on emerging food-borne pathogens, Motarjemi and Adams (2006) quote six major trends identified in literature. These trends are considered to influence the dynamic relationship between the changing nature and spread of microbiological pathogens; the humans affected by these pathogens; and new niches in changed food production processes where these pathogens can establish themselves. Three of these trends have also been identified by Ackerman (2006, see above), being the mass production and globalization of the food supply; the international movement of people; and transfer of recognized pathogens into new geographic areas.

In addition, the changing demographics of the population include trends towards a higher aged population in the developed world, but also to more immune-compromised and very young people that are more susceptible to infections, including those caused by food-borne pathogens. The trend towards taking meals outside the home, increased traveling, and changes in dietary preferences may also lead to new or increased exposure to food-borne pathogens. In addition, microbial evolution involving changes in the virulence of a given microorganism can result in its development into a new pathogen (Motarjemi and Adams, 2006).

With regard to the aforementioned changes in the virulence of a microorganism, Wren (2006) notes that not only acquisition of new virulence-associated genes through “horizontal gene transfer” between microbiological species, but also loss of other genes through genome downsizing may impart virulence to a microorganisms. Interestingly, this author recommends analyzing for the transfer of determinants of virulence, such as “pathogenicity islands” and antibiotic resistance genes, from one microbiological species to another by the use of, for example, the “active surveillance pathogen (ASP)” DNA microarray.

One of the three key factors for the emergence of a microorganism as a pathogen is its acquisition of virulence, among others through horizontal gene transfer, as defined by Smoot and Cordier (2006). The other two key factors are the susceptibility of consumers and hosts to the pathogen, and the foods in which the pathogen occurs. These authors also assert that zoonotic pathogens are more likely to become emerging pathogens than non-zoonotic ones. As examples of trends that may affect the presence of pathogens in food, these authors name increased growth of toxic algae in warmer seawater; changing agricultural practices including the use of manure; increased globalization leading to spread of unusual pathogens, such as protozoan parasites on tropical fruits; previously unknown associations between pathogens and food products; and changes in food preparation methods, such as substitution of sugar by sweeteners leading to higher water activity and thus bacterial growth.

As information sources for the identification of emerging pathogens, Smoot and Cordier (2006) recommend using information from the Internet, such as RASFF reports, on recalls and outbreaks; information on outbreaks from surveillance reports in different food-related fields and their integration with each other (*e.g.* human, veterinary and wildlife); microbiological risk assessments carried out for good hygienic – and manufacturing – practices (GHP/GMP), and HACCP, taking into account for HACCP what is already known about potential hazards. In addition, post-process contamination is often recognized as cause of outbreaks. GHP/GMP/HACCP can therefore be effective in prevention of the development of emerging hazards.

The role of viruses, such as the Norwalk-like viruses (noroviruses) responsible for “stomach or gastric flu,” as a major cause of food-borne diseases is becoming increasingly evident. Besides the increased identification of viruses as causative agents, also the formation of new virus strains is recognized as a cause of emergence of viral diseases. Such a formation of new strains proceeds through recombination between similar nucleic acid molecules containing the virus' genetic material yielding new nucleic acid sequences, and through “genetic drift,” such as by genetic mutations (Duizer and Koopmans, 2006).

With regard to trends that may affect the emergence of viral food-borne diseases, Duizer and Koopmans (2006) stress the importance of extending current surveillance practices in order to cover food-borne viruses as well. These authors also note that certain new practices, such as mild food preservation techniques and the use of new personal hygiene products, have not been tested for their effects on viruses, so that these may give rise to new problems. The recent finding that hepatitis E virus, which causes symptoms similar to hepatitis A, can be transmitted through food can be considered a token of the increasing knowledge on zoonotic viral agents, which may also lead to the finding of other yet unknown food-borne viruses in future.

Another recent trend in knowledge on emerging pathogens is the discovery of yet unknown reservoirs for these pathogens. An example is the discovery of strains of hepatitis E virus in pigs that are similar to human hepatitis E viruses, which indicates a potential interspecies transfer route of these viruses, possibly by consumption of insufficiently heated pork meat or crops that have into contact with pig manure (Cook and Rzezutka, 2006).

7. Conclusions and common findings

As diverse as the various hazards occurring in food may seem, it is conspicuous that a number of authors mention similar developments that, in their opinion, could lead to the emergence of new hazards to food safety. Globalization of food trade is considered to be able to contribute to more widespread dissemination of hazards. From another perspective, however, globalization may increase the sources of food available to affluent urban populations, which increases their “food entitlements” and thereby decreases their vulnerability to shock in the food supply. Another development that has been pointed at is the emergence of zoonotic agents through increased contact of domestic animals with wildlife, for example through expansion of agricultural activities into wildlife habitats or through increasing wildlife populations moving into human habitats.

Also interesting is the potential link with changes in agricultural practices. Increased use of manure, which may serve as a reservoir of microbiological pathogens, is an item of concern if the manure is not appropriately composted in order to eliminate these pathogens. Intensive livestock husbandry with high animal densities per surface area may be amenable to rapid dissemination of zoonotic pathogens within herds or flocks, once inside these populations. Another concern about intensive livestock husbandry and aquaculture is that they may also lead to the prophylactic use of antibiotics, potentially leading to residues of these compounds in animal edible products. On the other hand, free-range conditions for animals in extensive livestock husbandry practices may increase exposure to zoonotic pathogens from wildlife and to environmental contaminants.

In addition, a number of environmental contaminants that are persistent and tend to distribute over large distances have been found to cause problems due to accumulation through the food chain. This has been observed for dioxins and perfluorinated hydrocarbons in fish, but would also be applicable to contaminants with similar behavior and properties, such as polybrominated hydrocarbons previously used as flame retardants.

Specific hazards associated with fraudulent or other illegal activities may be more difficult to predict. In this case, a vulnerability assessment may be helpful to detect the weak spots within the system that are most vulnerable to such illegal actions.

Table 1 provides an overview of various generic indicators located both in the environment surrounding food production and in the food production chain itself. The criterion for their selection was that they had been mentioned in multiple references summarized above and that they could be used for pre-early warning, that is, in an early stage before consumption. Some of these indicators are fairly broad and it may be useful to formulate additional, more specific sub-indicators that would fall within the broad range of the main indicator. Changes measured in these indicators give rise to signals that serve as pro-active, pre-early warnings against the possible emergence of hazards. In addition, combinations of signals derived from of these indicators can indicate a further increased likelihood of the occurrence of emerging hazards. These indicators may serve as a starting point for an exploration of the use of such indicators, based upon which the methods can be refined and additional indicators, including those in the consumption phase, can be formulated. It is obvious that once a signal is detected, various steps may have to be gone through in order to pinpoint at an emerging hazard. For example, if intensification of aquaculture in a certain region is noted, it may be investigated further which aquaculture species this pertains to, if the products are exported to other countries, which diseases may occur within the aquaculture species and which antibiotics are available, if good agricultural practices are followed, and if regulations and law enforcement are in place to comply with food safety standards in importing countries. The table also indicates which particular limitations and / or confounding factors may be associated with each of these indicators and their information sources, suggesting additional, usually less official information sources, if needed.

<< Insert Table 1 around here >>

It is realized that in addition to the formulation of indicators and information sources, also procedures should be established for handling and interpreting signals coming from these indicators. These procedures ideally avoid the generation of “false positive” and “false negative” alerts, in order to enable risk managers to set priorities for the mitigation and prevention of emerging risks. The procedures for processing signals from indicators will be the topic of another report to be prepared within the frame of Work Package 2 of SAFE FOODS.

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Conflict of interest statement

Both authors are employees of RIKILT - Institute of Food Safety and therefore do not have any interests that may conflict with the contents of the article above.

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Figures

Figure 1 Early identification of emerging hazards at different points within the food production chain, consumers, and the surrounding environment

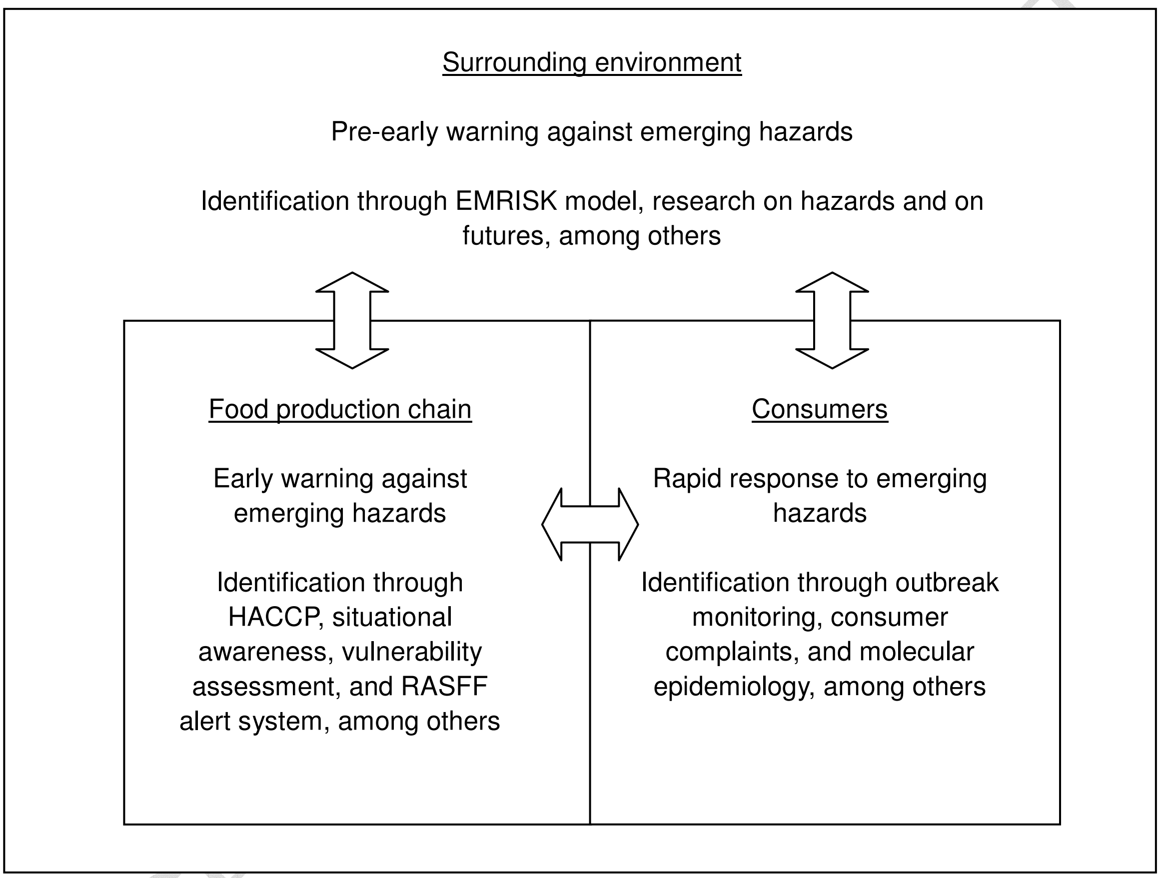

Table 1 Examples of generic indicators for the early identification of emerging hazards

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Climate change, including more extremes	Mycotoxins Zoonosis	Higher temperatures and humidity, as well as drought, favor growth of various moulds that grow on crops in the field or during post-harvest storage Migration of vectors of zoonosis, *e.g.* parasitic insects, to other regions	Meteorological measurements and forecasts Food inspection reports on mycotoxins Animal health service reports Entomological surveys	Limited applicability of predictive models to specific geographical regions and to the for the longer term Inspection, monitoring and surveillance data not be predictive for short-term developments	Scientific and applied literature on climatology Future climate scenarios based on simulations (*e.g.* IPCC) Inspection, monitoring and surveillance data on products / animals from other climatic regions
Intensification of livestock husbandry, including aquaculture	Zoonosis Antibiotic residues	Increased density of animals may lead to more rapid dissemination of pathogens and also to horizontal transfer of virulence and antimicrobial resistance; Corollary increase in disease pressure can also lead to antibiotic use	Agricultural statistics (*e.g.* FAOSTAT, Eurostat); Zoonosis surveillance reports (*e.g.* EFSA)	Other agricultural practices that can mitigate or compound the effect of intensification	National veterinary policy documents

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Livestock husbandry with contact between live animals from various origins and species	Zoonosis	Contact between live animals in farmers’ markets in exporting countries may facilitate transfer of diseases, as observed for avian influenza	Agricultural statistics on national lievstock production and trade (*e.g.* FAO)	Measures possibly in place to ensure sanitary conditions	National/local veterinary guidelines for transport and trading of livestock
Extensive livestock husbandry with contact between free-ranging live domestic animals and wildlife, and between free-ranging animals and a contaminated environment	Zoonosis Environmental contaminants	Increase likelihood of contact between domestic livestock and wildlife or feces from other animals that may facilitate transfer of zoonoses The same for contact with- or uptake of- contaminants from the environment, as observed for dioxins in milk from cows grazing in the vicinity of waste incinerators	National statistics on production of free-range and similar livestock production systems National environmental monitoring data on the level of contaminants in the local environment Biodiversity data, including local wildlife (*e.g.* national clearinghouse)	Risks also dependent on i) the diseases carried by wildlife, and ii) uptake of environmental contaminants by animals Animal and farmer’s behavior difficult to predict	Historical data on livestock diseases under different agricultural practices, *e.g.* before intensification and/or sanitary measures; Wildlife diseases and mortality surveillance data Monitoring data on environmental contaminants reported to occur in wild animals from same region

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Globalization of trade in food and feed	Zoonosis Other pathogens Chemical residues	More widespread dissemination of hazards from one source into other areas Transfer of hazards into areas with populations that are “naïve” to pathogens and other agents that commonly occur in the area of production	Trade statistics (*e.g.* FAOSTAT, Eurostat, USDA-ERS) Alerts on emerging zoonoses through OIE and WHO-GOARN	Import- or export- controls and other preventive measures that may already be in place; Lack of awareness of hazard outside the exporting region	Data on national control of imports of food and feed (*e.g.* EU FVO; laws and standards) Prospective intelligence of diseases / hazards in other nations (*e.g.* ECDC, USDA)
Increase of wildlife potentially carrying zoonoses in agricultural areas caused by: - wildlife habitat reduction; - expanding and/or moving wildlife populations	Zoonosis	Increased contact of domestic animals contact with wildlife may lead to increase exposure to vectors of pathogens	Wildlife monitoring (*e.g.* EEA) Wildlife disease surveillance (*e.g.* OIE) Zoonosis reports (*e.g.* EFSA)	Passive disease and mortality detection Additional unsuspected reservoirs for the same disease vector Spatio - temporal separation of wildlife and livestock	Comparison of data on local livestock husbandry practices and wildlife behavior
History of no recent incidents with agents that are still endemic in other areas exporting food and feed	Zoonoses and other pathogens	Lack of experience with pandemic and large-scale incidents in well-managed health care and food control systems	Human and animal health statistics of different regions (*e.g.* WHO, OIE)	Underreporting as many carriers in regions of origin may be asymptomatic due to natural selection	Scientific data on predisposition, *e.g.* single-nucleotide polymorphisms;

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Release into the environment of persistent chemicals that are able to spread widely in nature, but for which no regulatory standards or comprehensive toxicity data exist as yet	Chemical residues	Despite low concentrations of some persistent organic compounds, accumulation may take place throughout the biological food chain	UN POP program; WHO IPCS reports; Environmental pollution monitoring reports (*e.g.* EEA)	Lack of monitoring data for novel contaminants	Scientific data on bio-accumulation potential of novel persistent contaminants
Recycling of animal products into animal feed	Biological agents; Chemical contaminants	Bio-accumulating contaminants may further accumulate and infective agents that are not destroyed by processing may multiply through the animal populations being fed the products	Import and trade data on feed commodities (*e.g.* Eurostat); Monitoring data on contaminants and infective agents in the pertinent feeds	Potential lack of data on feed fed to animals reared in exporting countries	Scientific literature reports on the occurrence of contaminants in the specific or similar feeds Applied literature on animal production and animal feed
Recycling of food processing waste streams into animal feed (*e.g.* for reduction of environmental impact)	Chemical contaminants	Recovery of by-products from waste streams may unintentionally concentrate contaminants	Environmental standards for waste streams Monitoring data on contaminants in waste streams used for production of animal feed	Official standards not fully predictive of usage of waste streams Technology important enabling factor	Scientific literature reports on the occurrence of contaminants in waste streams Applied literature on processing and environmental technologies

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Innovations and other changes in food and feed processing and preservation technology	All categories	New conditions may introduce agents (*e.g.* pathogens, chemicals) or favor their survival or establishment more than previously used conditions	Applications for approval of novel foods and processing (*e.g.* EFSA);	Potential lack of regulatory applications for - and assessments of - new conditions and processes	Applied literature on food and feed technology; Scientific literature data on the effects of new conditions on hazardous agents
Introduction of exotic food and feed	All categories	New foods may contain agents, *e.g.* allergens and natural toxins, to which consumers previously have not been exposed	Applications for novel foods (*e.g.* EFSA); Consumption, market basket, and household budget surveys;	Potential lack of regulatory applications for - and assessments of - new foods offered in the marketplace	Applied literature on food and feed; Advertisements; Scientific literature on the characteristics of the new foods
Trends towards changed consumer behavior and preferences	All categories	New food choices and methods of preparation (*e.g.* ready-to-eat meals; minimally processed foods) may alter the profile of hazards to which consumers are exposed	National statistics on financial turnover in various sectors of food production and consumption Consumption, market basket, and household budget surveys	Individual variation in choices and exposure	Applied literature on trends in lifestyle, food industry, retail, and catering; Probabilistic techniques for more realistic exposure assessment
Consumption of foods beyond national oversight and control	All categories	Foreign travel and purchases from foreign vendors through Internet, may expose consumers to foods that are not subject to national controls and regulation	Travel statistics, including areas visited and travelers’ health National standards and monitoring data on food safety and health in visited areas	Local tourist facilities’ compliance with visitors’ standards; Lack of data on Internet sales	Data on local sector-wide quality and safety programs Advertisements for food products on Internet

Indicator	*Hazard*	*Rationale*	*Information source*	*Potential limitations and / or confounding factors*	*Supplementary information sources*
Counterfeiting of food	All categories	Progress in technology and availability of low-cost substitutes may facilitate counterfeiting of added-value food products (*e.g.* non-food dyes in spices and specialty palm oil; replacement of best-before dates)	Crime statistics National food control monitoring data	Responsive but not pro-active systems recording incidences	Applied literature on anti-counterfeiting measures and technology
Sub-optimal functioning or lack of: i) harmonized regulations complying with those of importing nations; ii) effective law enforcement and health monitoring; and iii) quality systems and checks; in exporting countries	All categories	Particularly for those hazards that are differently regulated in importing and exporting nations, frictions may arise; the same applies to products that are prone to contamination with hazardous agents	National standards of importing and exporting nations Reports on national food control systems (*e.g.* EU FVO); Commodity detention data (*e.g.* EU RASFF)	Hazardous agents for which no standards exist Export-oriented private-sector controls compensating for disparities or being more rigorous than government controls	Data in scientific and applied literature on potential occurrence and use of hazardous agent Private-sector international organization standards
Increasing knowledge about new and existing hazards, as well as increasing sensitivity of analytical methodologies to detect them	All categories	Previously unknown or undetected food-borne hazards are discovered, *e.g.* the unexpected presence of components of packaging printing inks in beverages and presence of traces of antibiotics in animal products	Reports from food control authorities, including scope of hazards being measured and analytical methods used	Time elapsed before recognition of hazard and inclusion into food control activities, and before implementation of analytical method	Reports on occurrence of hazardous compounds in scientific literature

Abbreviations: ECDC = European Center for Disease Control; EEA = European Environmental Agency; EFSA = European Food Safety Authority; ERS = Economic Research Service; Eurostat = Statistical Office of the European Communities; FAO = Food and Agriculture Organization; FAOSTAT = Statistical office of the FAO; FVO = Food and Veterinary Office; GOARN = Global Outbreak Alert and Response Network; IPCC = International Panel on Climate Change; IPCS = International Program on Chemical Safety; OIE = World Animal Health Organization; POP = persistent organic pollutant; RASFF = Rapid Alert System for Food and Feed; UN = United Nations; USDA = United States Department of Agriculture; WHO = World Health Organization