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SHORT COMMUNICATION

Some key emerging food safety issues

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Abstract

Food scares lead to loss of consumer confidence and trust and to new challenges for industry and policy makers alike. Being able to react fast, efficiently and effectively in times of a (potential) food safety crisis is therefore very important. This article describes some key emerging food safety and quality topics that have been identified by the MoniQA emerging issues working group. These include the 2008 melamine crisis, the detection of dioxin in Irish pork, clenuterol and nanotechnology/nanofoods.

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Introduction

Globalized trade in food means more choice for consumers. But, while the European food chain may be considered as one of the safest in the world, European consumers show little confidence in the safety of their food supply and remain sceptical and distrustful of the procedures currently in place or the institutions that implement them (Cnudde, 2005). Recent years have seen an increasing number of food safety incidents or 'food scares' (e.g. Foot-and-mouth disease, Bovine spongiform encephalopathy and Polychlorinated biphenyls), which have received a considerable amount of attention in the media and have resulted in a decline in consumer trust, perhaps exacerbated by the ongoing debate over the introduction and safety of genetically modified crops.

It is therefore of the highest importance that food scientists are able to react fast, efficiently and effectively in times of (potential) food safety crises. A number of previous initiatives have attempted to lay down frameworks for early detection of emerging risks in the food chain, for example the EU-funded project Safe Foods (http://www.safefoods.nl). The consortium of the MoniQA (http://www.moniqa.org) decided early on to establish an emerging issues working group which offers information, expert advice and decision support on current or upcoming food safety and quality issues. The wide range of expertise in analytical techniques, developmental abilities, socio-economic analysis and technology transfer means that MoniQA is ideally placed to offer a comprehensive role in the identification and reaction to emerging food safety issues. Among the issues which have been identified and discussed in detail are:

1. *Melamine*: the melamine crisis was reported extensively in the media in 2008 and has affected Asian and Western countries alike
2. *Dixon in Irish Pork*: this was an issue, which was on the agenda around December 2008 and January 2009

3. *Clenbuterol*: another food safety issue, which has implication both for China and in the European context
4. *Nanotechnoloy and nanofoods*: an issue that is currently debated extensively in Europe and elsewhere and it will remain an important issue in the years to come.

In the following, this article discusses key findings and MoniQA activities in these areas. Please note that the discussion below is meant to highlight salient features of the different topics but is not an exhaustive description of each issue.

The melamine crisis

Melamine is an organic compound. Synthesised in 1834 by German chemist Justus von Liebig, it forms a very durable thermosetting plastic (melamine resin) when combined with formaldehyde, and has been used in products such as housewares (cookware, appliances, lighting, etc.), fertilizers, countertops, flame retardants, glues, fabrics and dry-erase boards (white boards). Because it consists of 66% nitrogen, melamine was also used as a so-called non-protein nitrogen source in cattle food from 1958 onwards, until this was judged as unacceptable in 1978.

Melamine is non-toxic in low doses. However, in combination with cyanuric acid, it can form insoluble crystals, leading to the formation of kidney stones, which can cause kidney failure and ultimately death, particularly in vulnerable individuals such babies and young children. For adults, melamine is only dangerous in relatively high concentrations – the US Food and Drug Administration (FDA) set a concern level of 0.5 mg kg^{-1} body weight (Figure 1).

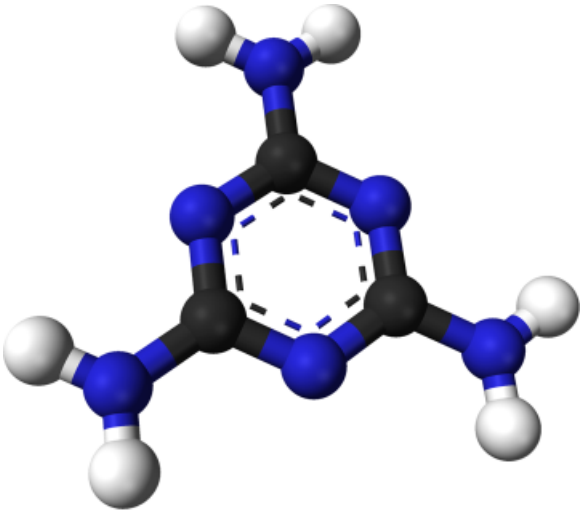

Figure 1 The Melamine Molecule $C_3N_6H_6$.

The melamine crisis: from China to the world

Chinese melamine production started in 1958. Today, China is the largest melamine exporter, globally. In 2007, melamine was discovered in pet food imported from China by the United States. It caused the death of 16 pets, and the recall of 60 million pet food packages. The first baby affected by melamine was diagnosed in Nanjing in March 2008. In September 2008, the Sanlu Group admitted deliberate contamination of milk powder with melamine, in order to artificially boost its apparent protein content. In total, 54 000 Chinese babies have been affected; 6000 were seriously ill and four died. As a result of the crisis, consumption of milk in China dropped significantly, and farmers were forced to dispose of milk they could not sell and reduce cattle numbers through culling. Chinese authorities dispatched medical teams across the country and encouraged free screening of babies in local hospitals. New regulations and quality standards have also been implemented.

On 23 September 2008, the Canadian Food Inspection Agency first found melamine in some instant coffee products. The products were recalled in Taiwan and Canada. Melamine was also detected in a Canadian chocolate brand, on 8 October, leading to its recall. On 24 September 2008, melamine-contaminated confectionary was discovered in Australia and New Zealand. Cadbury Schweppes plc. recalled all of its chocolate products made at the Beijing plant on 29 September 2008. In total, 11 chocolate products, exported to Hong Kong, Taiwan and Australia, were withdrawn from the market. At the end of October 2008, and just as the crisis seemed to be contained, health authorities in Hong Kong found eggs containing melamine after chickens were fed with melamine-contaminated feed (http://www.moniqa.org).

These instances have had recriminations on these European market as well. Although the EU does not import milk or other dairy produce from China, processed foods such as biscuits and chocolates might contain traces of milk powder. In fact, contaminated biscuits were detected on 3 October in the Netherlands. The biscuits in question were also recalled in the UK by the Food Standards Agency.

In response to the crisis the European Commission decided that composite products, including feed, that contain milk products originating in or consigned from China need to be analysed (Commission Decision 2008/798/EC) and that products containing more than 2.5 mg kg^{-1} are to be immediately destroyed. The Joint Research Centre (2008) has reviewed existing analytical methods for the detection of melamine in food and feed and has organised a proficiency test to benchmark laboratories ability to detect melamine in

food and feed. The results of the study were that 74% of the 114 results for milk powder and 73% of the 112 results for the baking mix were within the acceptable range (defined by common international measurement guidelines). These figures are in line with other similar tests that benchmark measurement competence among analytical laboratories (see JRC IRMM Melamine website).

MoniQA and melamine

The melamine issue was discussed extensively during the MoniQA consortium meeting and the First International MoniQA Conference in Rome (Italy) in October 2008, with presentations on the current state-of-play by Xioafang Pei and Lishi Zhang from Sichuan University (Yang *et al.*, 2009). Samuel Godefroy from Health Canada also spoke, outlining a regulator's perspective and summarizing the global response. Melamine was also one of the topics of a MoniQA Food Scientists' Training workshop on 'Food Safety and Risk Assessment,' which took place in Nanjing (China) in October 2008. This event brought together experts from European organizations (Institute of Food Research – UK, International Association for Cereal Science and Technology – Austria) as well as Asian institutions (Jiangsu Entry–Exit Inspection, the Quarantine Bureau of China and the Nanjing University of Finance and Economics). The Institute of Environmental Science and Research has been able to provided valuable input on the situation in New Zealand. As a result of these events, interviews with MoniQA experts were broadcast on Italian National TV (Rai 3) and a Chinese provincial television station.

During the crisis, stringent controls were introduced in many importing countries. For example, within the EU, any products containing milk, milk products, soya or soya products intended for the particular nutritional use of infants and young children originating or consigned from China were immediately withdrawn or destroyed. A maximum level of 2.5 mg kg^{-1} was set for all milk and milk products, including milk powder, originating from China, together with any composite food product containing milk products, or with a high-protein content, originating from China. The same level was also set for ammonium bicarbonate intended for food or feed originating in or consigned from China. Furthermore, in the light of a new tolerable daily intake (TDI) of 0.2 mg kg^{-1} body weight per day set by the World Health Organization's scientific experts, Health Canada has taken the additional measure of lowering its allowable level for melamine in infant formula from 1 to 0.5 mg kg^{-1} in order to ensure that exposures remain below this new TDI. The new 0.5 mg kg^{-1} standard for melamine applies to all infant formula products.

Decision-support and information resources for melamine are available on the MoniQA website at http://www.moniqa.org/melamine. Information about melamine regulations as well as current validated methods can be accessed through the MoniQA database with links to the EU's Rapid Alert System for Food and Feed. MoniQA also provides links to scientific papers about melamine from European Food Safety Authority (EFSA), FDA and other organizations. MoniQA experts are collecting analytical methods for melamine, and analysing validation levels and requirements in addition to providing background information.

Socio-economic ramifications and future challenges

The death of infants, loss of consumer trust, a drop in revenue for export companies, and lower income for farmers – these are only some of the social and economic ramifications of the melamine crisis (Yang *et al.*, 2009). MoniQA addresses the socio-economic implications of the crisis through a Compliance Case Study, focusing on changes in the Chinese food safety regulatory framework towards alignment with standards existing in the European Union. The research will compare the costs and benefits of different policy options and, more specifically, the slow or fragmented implementation of new legislation as opposed to a phased but careful implementation of safety legislation. The study will focus on the impact on consumers, the food industry in terms of re-structuring, and international trade.

EU Food Law Weekly reports that Chinese officials shut down a suspect dairy only in January 2010, after waiting nearly a year before taking action (EU Food Law Weekly, 2010: p. 33). This indicates that the melamine crisis and its repercussions are not over – current challenges include analytical methods and validation (compare the work undertaken by the JRC IRMM as described above), analytical results for 'low background' levels, hazard characterization (effects of other structural related chemicals), and the detection of other foods where melamine may have been used to artificially boost the apparent protein content. MoniQA continues to monitor the situation and publishes news on ongoing developments, such as detection methods, on the MoniQA melamine page (http://www.moniqa.org/melamine).

Dioxin contamination of Irish pork

Dioxins, furans and polychlorinated biphenyls (PCBs) are a group of toxic and persistent chemicals whose effects on

human health and on the environment include dermal toxicity, immunotoxicity, reproductive effects and teratogenicity, endocrine disrupting effects and carcinogenicity. An increase in the presence in the environment of these substances coupled with several accidents (Yucheng, Taiwan, Hsu *et al.*, 1994; Yusho, Japan, Kuratsune *et al.*, 1996; Seveso, Italy, Homberger *et al.*, 1979 and Belgium, Bernard *et al.*, 2002) have triggered a deep concern from the international community for their reduction and control. Moreover, there is considerable public, scientific and regulatory concern over the negative effects on human health and on the environment of long-term exposure to even the smallest amounts of dioxins and PCBs.

Over the past two decades the Commission has proposed wide ranging legislation aimed at directly or indirectly reducing the release of these compounds into the environment, with the objective of reducing human exposure and protecting human health and the environment. Recent exposure data show that measures introduced to control dioxin releases have resulted in a substantial reduction in intake of these compounds: levels in humans are decreasing since the mid-1980s (Startin & Rose, 2003). However, since 1995 this tendency has levelled out, even slightly rising levels have been observed (Fernandes *et al.*, 2004).

On 6 December 2008 the Irish Government announced that laboratory results on animal feed and pork fat samples, tested by the Food Safety Authority of Ireland (FSAI), confirmed the presence of dioxins. The FSAI required the food industry to recall from the market all Irish pork products produced from pigs slaughtered in Ireland. This recall involved retailers, the hospitality sector and the Irish pig processing sector. The FSAI evaluated samples taken from affected herds and was satisfied that these samples raise no public health concern.

In May 2009, the Irish Parliament (Oireachtas) Committee on Agriculture, Fisheries and Food published a report calling for an urgent overhaul of the current system for Irish pork, which was considered ineffective. In particular it was criticised that although less than 10% of pork products were potentially affected by the contaminated feed, due to the absence of a forensic traceability regime, 100% of products had to be recalled, which proved to be very costly to the Irish taxpayer (House of the Oireachtas, 2009).

The MoniQA Emerging Issues working group has been carefully monitoring the situation at the time of the crisis and has published the latest news on the developments in Ireland. The working group also collected statements from leading scientists in the field and has published all available information on the emerging issues MoniQA homepage.

Clenbuterol

Clenbuterol is a bronchodilator used in asthma medicine worldwide for the treatment of allergic respiratory disease in horses. A common trade name is Ventipulmin. It can be used both orally and intravenously. Clenbuterol is also a non-steroidal anabolic and metabolism accelerator, through a mechanism not well understood, which is why it is used illegally by athletes to build muscle. Its ability, however, to induce weight gain and ensure a greater proportion of muscle makes its illegal use in livestock popular. Clenbuterol accumulates in the human body through ingestion. It is heat stable, only decomposing at temperatures over 172 °C. Thus, cooking cannot easily eliminate toxicity. Long-term consumption can lead to malignant tumours but it also poses dangers to individuals who have high blood pressure or diabetes. Pre-disposed individuals and those with excess intake often share similar symptoms including palpitations, nausea, vomiting, dizziness, chest tightness, anxiety, shaking, weakness and instability. Clenbuterol accelerates the catabolism of fat in pigs and, when added to feed, it not only shortens growth time but also increases the sale price of pork and porcine organs. Meat containing clenbuterol often has a bright red skin with very little fat. However, approval in the EU is for bovine and equidae use only. Maximum residue levels in products of animal origin are set in Regulation (EC) 2391/2000 at the following levels: (Figure 2)

Animal species	Target tissue	MRL ($\mu g\,kg^{-1}$)
Bovine	Kidney	0.5
	Liver	0.5
	Milk	0.05
	Meat	0.1
Equidae	Kidney	0.5
	Liver	0.5
	Meat	0.1

Methods for detection

Clenbuterol belongs to the group of β_2-agonists which include mabuterol, terbutaline, carbuterol, cimaterol, salbutamol, clenpenterol, isoxsuprine, bambuterol and ractopamine. For control purposes the matrices of choice are urine and liver. Clenbuterol can be detected using screening methods based on immunochemical properties, e.g. ELISA or optical biosensors. Alternatively a wide range of β-agonists can be screened and/or confirmed using liquid chromatography (LC) coupled to tandem mass spectrometry (MS/MS). When performing LCMS/MS measurements for

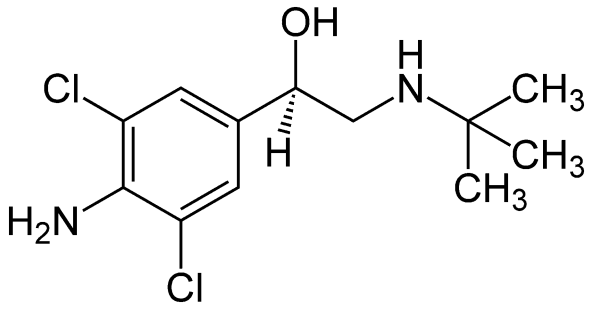

Figure 2 Clenbuterol Molecule.

clenbuterol and a wide range of β-agonists, it is common for deuterated analogues to be used as internal standards.

The case in China and its wider implications

In February 2009, 70 people fell ill after eating pork products contaminated with clenbuterol. The victims, all in Guangdong province, consumed meat bought from markets in Guangzhou, the provincial capital of Guangdong, which came from farms in the neighbouring Hunan province. Since 1998, there have been at least 19 clenbuterol food poisoning cases in China affecting more than 1750 people, including one confirmed death.

In 2006, a series of food borne illnesses in 300 individuals from Shanghai were associated with meals containing pork or pig intestines contaminated with clenbuterol. In June 2006, employees of a hotel in Foshan suffered from clenbuterol poisoning while hundreds of workers in a glass factory in Guangdong Province were also poisoned by clenbuterol in May 2006. Seventy employees at a plastics factory in Jiaxing City, Zhejiang Province were taken ill with clenbuterol poisoning after eating pork in the company cafeteria during November 2008. Between 8 and 18 October 2008, three people were confirmed to have been poisoned by clenbuterol from pork in Guangdong.

The case of clenbuterol, while not currently an export issue, is nonetheless of international importance as cases are not limited to China. Though not recent, four separate cases of acute food poisoning in Portugal, involving 50 people, were caused by eating lamb- or beef-containing clenbuterol between April 1998 and April 2002 (Barbosa *et al.*, 2005). Similar cases have been reported in Spain (Martinez-Navarro, 1990; Garay *et al.*, 1997), France (Pulce *et al.*, 1991) and Italy (Maistro *et al.*, 1995; Brambilla *et al.*, 1997, 2000). The MoniQA Emerging Issues working group has dedicated a web page to the clenbuterol issue where consumers can find further information and a factsheet for download (http://www.moniqa.org/clenbuterol).

Nanotechnology

Nanotechnology (the control of matter on atomic and molecular scale) could potentially revolutionize industry and everyday life. However, there are concerns whether the application of nanotechology is safe. In an own-initiative report the European Parliament has recently decided to consider all nanomaterials as new substances and holds that existing legislation does not take into account the risks associated with nanotechnology. According to the EFSA, in the area of food science, uncertainties in detecting and measuring levels of nanomaterials could make risk assessment of some nanoproducts extremely difficult (EFSA, 2009).

EFSA therefore recommends a case-by-case approach to determining the risks associated with engineered nanomaterials, adding that there is limited knowledge of current usage levels and likely exposure to products in the food area. The agency recommends that additional research is needed to address the many current uncertainties and limitations. An expert group will be established to monitor emerging scientific data. The EFSA opinion (EFSA, 2009) comes at the request of the European Commission, which published an Action Plan (EC, 2005) aimed at promoting the safe growth of nanotechnology and a Code of Conduct for responsible research in nanotechnologies (EC, 2008). This Code of Conduct consists of seven general principles aimed at ensuring that nanoscience research activities are:

1. Comprehensible to the public (Meaning).
2. Safe, ethical, and contribute to sustainable development (Sustainability).
3. Conducted in accordance with the precautionary principle, anticipating potential environmental, health and safety impacts (Precaution).
4. Guided by the principles of openness to all stakeholders, transparency and respect for the legitimate right of access to information (Inclusiveness).
5. Able to meet strict scientific standards, including standards underpinning the integrity of research and standards relating to Good Laboratory Practices (Excellence).
6. Innovative, and encourage maximum creativity, flexibility, and incorporate the ability for innovation and growth (Innovation).
7. Accountable for the social, environmental and human health impacts that their research may impose on present and future generations (Accountability).

The Novel Foods Regulation (EC 258/97) also has important implication for nanofood. It established a community system for the pre-market approval of so-called 'novel

foods,' including a safety assessment (see European Commission, 2002). In September 2008 the Commission proposed to centralize the assessment and authorization procedure for novel foods which would be carried out by EFSA instead of a single member state (EC Press Release, 2008). This proposal is currently being debated in the European Parliament and the Council.

In general, proponents of nanotechnology argue that nanotechnologies could deliver cleaner, safer, more competitive production processes as well as smarter, more durable and more user-friendly products. Opponents, such as the Swedish Green MEP Carl Schlyter, argue there is considerable risk involved and call for tighter controls on nanotechnology, including the application of the 'no data, no market' principle contained in the Authorization and Restriction of Chemicals (REACH) Directive. This means that products containing nanotechnology that are already on the market would need to be withdrawn until safety assessments can be made. The above-mentioned EU's Registration, Evaluation, REACH Regulation, represents a fundamental shift in the regulation of manufactured and imported chemicals in the EU as it effectively shifts responsibility from authorities to industry to gather information on chemical substances and assess their safety. The regulation prohibits the manufacture or sale of any substance not registered with the European Chemical Agency (ECHA) which means that manufacturers or importers of nanoscale substances in volumes of 1 tonne or more per year, will need to register the substance with the ECHA and provide at minimum a technical dossier on the nanoscale substance. However, only few manufactures, importers or producers will actually exceed the tonnage threshold for registration. Nevertheless, the Commission have stated that the authorisation process can be applied to substances of very high concern even below 1 tonne per year (see Ward and Harely, 2009).

Other bodies active in nanotechnology include the The European Committee for Standardization (CEN) is active in standardization in the field of nanotechnologies. Activities of CEN/TC 352 include classification, terminology and nomenclature; metrology, measurement and characterization (including procedures for calibration); health, safety and environmental issues as well as nanotechnology products and processes. To work towards this goal, CEN involves other standardization bodies such as ISO, but also collaborate closely with the European Commission.

A variety of projects deal with the challenges and opportunities of nanotechnologies. Framing Nano (http://www.framingnano.eu), for instance, conducted a comprehensive review of existing legislation on nanotechnology and found variation in governance structures across the world. NGOs, including Greenpeace and Friends of the Earth, consider the existing regulatory situation to be inadequate and are urging a strictly precautionary approach. Industry representatives, on the other hand, are seeking the development of specific guidance and standards to support implementation of existing regulations, which are generally seen as adequate. Nanotechnologies are also a topic in iNTeg-Risk (http://www.integrisk.eu-vri.eu), which coordinates research and development sub-projects for improving the management of emerging risks related to new materials and technologies. NanoSafe2 (http://www.nanosafe.org) has even developed a quiz called NanoSmile (http://www.nanosmile.org) on the safety aspects of nanomaterials.

Given the importance of the issues discussed above, MoniQA decided to add nanotechnology to its priority list of emerging issues, which are monitored and explored by the MoniQA Working Group on Emerging Issues. A special sub-site, http://www.moniqa.org/nano, has been created as an information repository, containing important documents by EFSA, the UK Food Standards Agency and the World Nanofood Report.

Conclusion

Various methods and procedures have been developed to try to identify emerging risks in the food chain, ably reviewed by Marvin *et al.* (2009). They conclude that there is a need for a more holistic approach towards early identification of emerging food safety issues, but that no such systems are yet in place which can fulfil this function. While the MoniQA emerging risk-working group in no way currently approaches fulfilling this holistic requirement, the structure of the project and range of capabilities within its partners does provide the opportunity to go beyond the initial stage of simply identifying emerging risks. As a network of excellence, it encompasses partners with the capabilities to respond rapidly to such issues by defining sampling protocols, developing analytical or other identification techniques, transferring technology of such methodologies and training of appropriate persons in their use, as well as undertaking socio-economic assessment of their impacts.

Marvin *et al.* (2009) also point to the importance of stakeholder involvement in identification systems and the MoniQA project has been committed from its inception to the formation of stakeholder groups which will facilitate communication between the different fields of expertise and practitioners along the total food production chain. In all the different subject areas covered by the group dissemination and knowledge sharing has been an important aspect of

the work. So far information has been communicated in the following way:

- A MoniQA webpage on emerging issues, which features up to date information, news and decision support, was set up at http://www.moniqa.org/emerging
- Decision support and expert advice to be provided to regulatory bodies, industry and the research community.
- On some of the issues press releases were created.
- The emerging issues were presented at conferences and in the media.
- A listing of new regulations, available and validated methods was complied.
- The MoniQA databases were extended with relevant information and will be offered for stakeholder use shortly.
- Training courses covering some of the emerging issues were held.

Through this MoniQA ensures that activities on emerging food safety and quality issues are available to a broad audience and thereby ultimately contribute to providing all sections of the food chain with reliable, peer-reviewed information.

It is hoped that this approach will therefore contribute rapidly and responsively to risk assessment and management both in the EU and more globally through the project's non-EU partners and stakeholders.

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