

<p>Institution: Queen’s University Belfast</p>
<p>Unit of Assessment: 6 - Agriculture, Veterinary and Food Science</p>
<p>Title of case study: Solving the Bangladeshi Crisis of Nitrofurantoin Antibiotic Contamination in Shrimps</p>
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Kennedy and his team helped resolve a massive societal and economic problem for Bangladesh and ensured safer food for consumers worldwide. Nitrofurantoin antibiotics were banned from use in food animal production in the 1990s because of their carcinogenicity. However, large numbers of nitrofurantoin-contaminated shrimp were detected in Europe which originated from Bangladesh. This resulted in massive disruption to their shrimp industry. Kennedy and his team identified the complex cause of the nitrofurantoin problems and delivered a solution saving the shrimp industry from collapse. He then set about resolving a second, knock-on antibiotic crisis in the Bangladeshi poultry industry.</p>
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>Nitrofurantoin antibiotics are extremely problematic food contaminants and were banned from use in animal production due to their carcinogenicity ~20 years ago. Furazolidone, furaltadone nitrofurantoin and nitrofurazone were once used widely as feed additives in pig and poultry globally. However due to their effectiveness in controlling disease and low production cost they remained in use long after the global ban. Another major factor was that the illegal use of nitrofurants was extremely difficult to detect. Work at QUB¹ on detecting furazolidone in food and feed showed, following experimental studies, that it was impossible to monitoring compliance of the nitrofurantoin ban. However, instead of measuring the parent compound, measurement of furazolidone’s tissue bound metabolite (AOZ), enabled the detection of the misuse of furazolidone many weeks post administration². Queen’s researchers were able to demonstrate the effectiveness of the new test and the widespread use of furazolidone in pig production in the UK (17% of kidneys tested AOZ positive), shortly before the introduction of the ban. The Queen’s-led FP5 FoodBRAND team developed new analytical methods, based on LC-MS/MS to detect tissue bound metabolites for all nitrofurants³. These tests were employed to analyse imported shrimp from Asia and large numbers of bound residues were detected. Similar problems were found in chicken imported from Thailand and Brazil, which accounted for ~25% of the chicken consumed in the UK. This rapidly developed into the “global nitrofurantoin crisis” where multiple foods from many countries were embroiled in scares about dangerous chemical residues being found⁴. The Queen’s method is now used globally to control nitrofurantoin misuse. The finding of nitrofurantoin residues in imported foods resulted in the EU imposing severe import restrictions on China, Thailand, Brazil, India and Bangladesh. It appeared misuse across the world was under control and further research identified other markers of nitrofurantoin abuses⁵. However, in Bangladesh, the worst effects of the contamination of aquaculture produce, especially shrimp arose in 2008. Bangladeshi exporters of giant river prawn were rocked by more than 50 rejections of consignments of their product in Europe. This caused the EU to place a ban on their products. Based on Kennedy’s research into the highly complex origins of nitrofurantoin contamination he and his team were able to determine that a Belgian laboratory had made a major mistake in their analytical protocol. Kennedy’s work uncovered that a nitrofurantoin metabolite (semicarbazide) was naturally occurring and was present in the shell of shrimps, without exposure to any nitrofurantoin⁶. In Belgium they included the shell in their testing regime. Beginning in March 2008, Kennedy set out to convince the Belgian authorities to correct the analytical error and to prove that the residues of semicarbazide had occurred naturally in the shell of the river prawn and other crustaceans. This was achieved by carrying out extensive sampling and analysis of shrimp samples from many regions of Bangladesh. The isolation of semicarbazide from shells of shrimps not exposed to any nitrofurants was used as compelling scientific evidence that Europe had mistakenly branded Bangladesh products as contaminated.</p>

3. References to the research (indicative maximum of six references)

1. McCracken, R.J., Blanchflower, W.J., Rowan, C., McCoy, M.A. and Kennedy, D.G. (1995). Determination of furazolidone in porcine tissues using thermospray liquid chromatography - mass spectrometry and a study of the pharmacokinetics and stability of its residues. *Analyst*, 120, 2347-2351
2. McCracken, R.J. and Kennedy, D.G. (1997). Determination of the furazolidone metabolite, 3-amino-2-oxazolidinone, in porcine tissues using liquid chromatography- thermospray mass spectrometry and the occurrence of residues in pigs produced in Northern Ireland. *Journal of Chromatography B, Biomedical Applications*. 691, 87-94.
3. McCracken, R.J., McCoy, M.A. and Kennedy, D.G. (1997). The prevalence and possible causes of bound and extractable residues of the furazolidone metabolite: 3-amino-2-oxazolidinone in porcine tissues. *Food Additives and Contaminants*, 14, 287-294.
4. O'Keeffe, M, Conneely, A, Cooper, KM, Kennedy, DG, Kovacsics, L, Fodor, A, Mulder, PP, van Rhijn, JA, Trigueros, G. 2004. Nitrofurant antibiotic residues in pork The FoodBRAND retail survey. *Analytica Chimica Acta* 520, 125-131
5. Samsonova, J. V., Douglas, A. J., Cooper, K. M., Kennedy, D. G., Elliott, C. T (2008) The identification of potential alternative biomarkers of nitrofurazone abuse in animal derived food products. *Food and Chemical Toxicology*: 46 : 1548-1554
6. McCracken, R.J., Hanna, B., Ennis, D., Cantley, L., Faulkner, D & Kennedy, D.G. (2013). The Occurrence of Semicarbazide in the Meat and Shell of Bangladeshi Fresh-Water Shrimp. *Food Chemistry*. 136, 1562-1567.

Related Research Grants:

EU FP5 RTD project (QLRT-0142). Co-ordinated by QUB/Kennedy. Aim: to develop improved methods for the detection of bound residues of the nitrofurant drugs, banned from use in food-producing animals because of their toxicity. Dates 2000-2006. Value to QUB €260,000.

European Commission Joint Research Centre funded project. Co-ordinated by JRC. Aim: to develop and validate chemical and immunochemical methods for the detection of semicarbazide in eggs. Dates 2004-2006. Value to QUB €80,000.

Food Research Health Initiative (Republic of Ireland): 07FHRITAFRC5 Safe & healthy Foods. Dates 2007 – 2013: Bound residues in pork, poultry and shrimp. Value to QUB €234,100.

4. Details of the impact (indicative maximum 750 words)

Fisheries in Bangladesh is second only to the garment sector in total national export earnings. Shrimp alone accounts for about 80 – 85% of the total export earnings from all fisheries commodities. About 25% of the total shrimp export earnings comes from the Giant Freshwater Shrimp, *Macrobrachium rosenbergii*. Bangladesh is one of the top producers of this shrimp globally. This and other shrimp species exported from Bangladesh are mostly the products of aquaculture. Besides its role in export, the shrimp aquaculture based industry is one of the major sources of rural employments for men and women, supports several categories of rural based ancillary industries – all significantly contributing to the country's overall economic development. Clearly, the success of the shrimp based industry is extremely important for sustained economic development of this country. The yearly total value only from frozen shrimp and fish exports fluctuated between US\$322 million and US\$ 611 million during the last 10 years. Due to the detection of contamination by nitrofurans in large quantities of shrimp by Belgian authorities in 2008, exports fell by approximately 17%, by comparison with the average over the previous 5 years. By 2009 a further 16% deduction in exports resulted.

The nitrofurant incident impacted hugely on the shrimp industry and entire Bangladesh society in many different ways: (i) An immediate export revenue loss valued at many millions of pounds, (ii) loss of Bangladesh image in the international market for Bangladesh fisheries products, (iii) closure of thousands of shrimp farms and tens of hatcheries across the country, (iv) loss of thousands in employment in the sector, (v) a huge economic loss which was felt right across the country, both immediate and fears of even worse long-term damage.

The European Commission, based on Kennedy's research realised the error that had been made and on the 15th November 2011 issued a formal repeal of the emergency measures that had been put in place with regards Bangladeshi aquaculture products. Now, just five years since the 2008 crisis unfolded, due to the research conducted at QUB there is a much stronger case for Bangladesh to be considered as a producer of safe food. Indeed, the Bangladeshi industry now views the future with high levels of optimism. Despite the setbacks of recent years, there is an industry-governmental plan to increase production from 60,000 tonnes of prawn annually from 80,000 hectares of farms. This is double the current output of the country. Kennedy's nitrofurans research has had a massive and positive impact on the livelihoods of thousands of the world's poorest people.

Kennedy's research uncovered the complex cause of the nitrofurans contamination problems. He worked with the Bangladeshi industry and government not only to uncover the true causes of the problem but on a much wider scale to greatly improve the safety and quality of their entire aquaculture industry. Kennedy was able to convince the Belgium government that their laboratories had made a serious error in alerting the entire European Union (and rest of the world) about a contamination that never actually occurred. This had a massive follow on impact of the stance of the European Commission with regards Bangladeshi shrimp imports into Europe. As a consequence of the shrimp crisis in 2010 and further European Commission penalties, the Bangladeshi government banned the use of all antibiotics in all animal feeds as part of their response to the on-going emergency. However, this ban had an unintentional, yet devastating, effect of causing marked increased mortalities in the Bangladeshi poultry industry caused particularly by necrotic enteritis and causing yet more economic losses to the agri-food sector and extreme hardship to subsistence farmers and their families. The profitability of this industry is vital to the nation, as poultry is the principal animal protein source for the Bangladeshi population. At two meetings in Dhaka, (January 2013) chaired by the Minister of Agriculture and the Chief Veterinary Officer, respectively, Kennedy advised relaxing the ban - permitting the use of the four "beneficial antibiotics" in poultry feed. This advice has been accepted and is being implemented via the Bangladeshi parliament, thus averting another food crisis in the region.

The EU's investigations of the shrimp problems did uncover vast gaps in the ability of this country to provide local consumers and export customers with safe food. Through Kennedy's research and high level advice to industry, governmental agencies and government laboratories a much better system is now in place to safeguard citizens all over the world who purchase and consume Bangladeshi produce.

5. Sources to corroborate the impact (indicative maximum of 10 references)

1. Commission Decision 2008/630/EC. Off. J. Europ. Commun, L205, 49-50. Emergency measures applicable to crustaceans imported from Bangladesh and intended for human consumption.
2. Commission Decision 2010/387/EC. Official Journal of the European Communities. (2010), L178, 31.
3. The 2010 Bangladesh Animal Feed Act.
4. Commission Decision 2011/742/amending Decision 2008/630/EC on emergency measures applicable to crustaceans imported from Bangladesh and intended for human consumption.
5. A letter from the Bangladesh Shrimp and Fish Foundation outlining the key role of Kennedy and his group in solving the nitrofurans crisis.