Institution: University of Cambridge

Unit of Assessment: UoA 5

Title of case study: Biobullets for the control of invasive species

1. Summary of the impact (indicative maximum 100 words)

The zebra mussel is one of the world's most economically and ecologically important pests, but existing control approaches cause significant deleterious environmental effects. Researchers at the University of Cambridge have developed a 'BioBullet' against zebra mussels, which encapsulates toxins in a harmless edible coat, enabling efficient, targeted product delivery and dramatically reducing environmental pollution. [Text removed for publication] Further successful formulations are being developed by the researchers and the company for fouling in shrimp farms and enhancing shellfish aquaculture.

2. Underpinning research (indicative maximum 500 words)

For the past 12 years, the Aquatic Ecology Group (AEG) in the Department of Zoology has been studying the biology and rapid spread of the zebra mussel, *Dreissena polymorpha*. One of the world's most economically and ecologically important pests, control of zebra mussels now costs an estimated U.S.$5 billion per year in North America, due to its ability to block the raw water cooling systems of power stations and water treatment works.

Led by Dr David Aldridge (Affiliated Lecturer 1997-present), the AEG initially mapped the location and spread of zebra mussel populations in Britain[1], documenting a recent, rapid increase in both abundance and distribution, coupled with deleterious ecological impacts (increased water clarity, changes in community composition, declines in native mussel populations).

Although chlorination is a widespread and licensed control technique, it is non-specific; application in an open ecosystem therefore has devastating effects on non-target species. Also, zebra mussels can sense chlorine and other toxins in the environment and respond by closing their valves; effective treatment therefore requires prolonged dosing. However, prolonged chlorine dosing in raw water produces trihalomethanes by reaction with organic material; these are toxic to both humans and other animals, restricting the doses that can be applied. As a result, there has been continued tightening of regulatory controls on the discharge of chlorine into the environment (e.g. the European Water Framework Directive 2000/60/EC).

Dr Aldridge, in collaboration with Dr Geoff Moggridge (Department of Chemical Engineering and Biotechnology), theorised that toxins could be delivered to zebra mussels in an edible coating, overcoming the valve closure response, and requiring smaller doses to be effective. An umbrella patent, providing broad IP protection for the encapsulation of any material for delivery to filter feeders, was granted to Aldridge and Moggridge in Europe in 2003 and in the US in 2008. Commercial development was supported by winning the first BBSRC Bioscience Business Plan Competition, with 'BioBullets Limited' founded by Aldridge and Moggridge as an independent company in 2000. In February 2001, Aldridge and Moggridge, via BioBullets Ltd., began a collaboration with Anglian Water to better understand the effect of encapsulated products on zebra mussels, and in 2003, a DTi SMART Award enabled various coating formulations to be tested [Text removed for publication].

Whilst refining the capsule, the AEG also determined which toxin should form the core of the 'BioBullet'. They initially chose potassium chloride (KCl), having demonstrated that it is particularly toxic to freshwater bivalves [Text removed for publication], but at low doses is inert to most other organisms[2]. The mussels' natural filtering behaviour internally concentrates the toxin, reducing the quantity of active ingredient required, and it is effective as a one-off treatment, rather than needing continuous dosing.

Further academic work by the AEG demonstrated that zebra mussels show seasonal peaks of increased susceptibility to toxins[3], which has implications for the overall design of chemical control

strategies, and for the amount of toxin that needs to be released into a water system to achieve the desired effect. Subsequent studies to understand the filter-feeding behaviour of zebra mussels have identified methodologies for indirectly quantifying fouling levels in inaccessible pipelines, and demonstrating the potential of mussels as bioremediation tools within nutrient-enriched reservoirs[4]. Additional studies by the group demonstrated that multiple active agents, with differing physiological impacts on zebra mussels, can have synergistic effects, thereby reducing the amount of product needed to control pest species[5].

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

1. Aldridge, D.C., Elliott, P. & Moggridge, G.D. (2004). The recent and rapid spread of the zebra mussel (*Dreissena polymorpha*) in Great Britain. *Biological Conservation* **119**: 253-261. DOI: 10.1016/j.biocon.2003.11.008
2. Aldridge, DC, Elliott, P, Moggridge, GD (2006) Microencapsulated BioBullets for the control of biofouling zebra mussels. *Environmental Science and Technology* **40**: 975-979. DOI: 10.1021/es050614+
3. Costa, R, Aldridge, DC, Moggridge, GD. (2008) Seasonal variation of zebra mussel susceptibility to molluscicidal agents. *Journal of Applied Ecology* **45**, 1712-1721. DOI: 10.1111/j.1365-2664.2008.01555.x
4. Elliott, P, Aldridge, DC, Moggridge, GD (2008) Zebra mussel filtration and its potential uses in industrial water treatment. *Water Research* **42**, 1664-1674. DOI: 10.1016/j.watres.2007.10.020
5. Costa, R, Elliott, P, Aldridge, DC, Moggridge, GD (2011) Enhanced mortality of the biofouling zebra mussel, *Dreissena polymorpha*, through the application of combined control agents. *Journal of Great Lakes Research* **37**, 272-278. DOI: 10.1016/j.jglr.2011.01.005

Funding:

- "Silver bullets for zebra mussels" (GR/R27723/01) - EPSRC (Anglian Water Services as Project Partner). 2001-2004, £238,100: Geoff Moggridge (PI), David Aldridge (coI)
- DTi SMART Award in collaboration with Thames Water Utilities, Ltd. (£10,000, 2003) (awarded to David Aldridge and Geoff Moggridge)

Awards

- Mar 2000: BioScience Business Plan Competition (sponsored by BBSRC, MRC, GlaxoWellcome and the Gatsby Foundation) - £25,000 (awarded to David Aldridge and Geoff Moggridge)
- Oct 2007: Institute of Chemical Engineering (IChemE) Entec Medal, the highest award given at their annual awards ceremony (awarded to David Aldridge)

[Text removed for publication]

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

Impacts on production: decisions by regulatory authorities have been influenced by research

In December 2008, the GB Drinking Water Inspectorate (DWI) approved the BioBullets product Silver Bullets 1000 for use in public water supplies [Text removed for publication]. A second formulation suitable for very large water volumes and carrying a different active ingredient (currently confidential), Silver Bullets 2000, was approved in April 2011 [Text removed for publication]. These approvals demonstrated the environmental safety of the products, and enabled them to be tested within operational drinking water plants. The Environment Agency has also provided permits for discharge of Biobullets' products into recipient streams and rivers, with monitoring of riverine biota before and after dosing trials repeatedly showing the broken-down product to have no measurable impact on aquatic biota[8], and regards "*The biobullet formulation [as] an essential management tool in our response to a variety of priority invasive non-native species*."[8]

Impacts on production: costs of [drinking water] production have been reduced

Since the 2008 DWI approval, eight full-scale trials have been conducted within the impact period in seven UK waterworks, belonging to Anglian Water[9], South Staffordshire Water[10], Thames

Water[11], Severn Trent Water and Welsh Water. Dosing of Silver Bullets 1000 [Text removed for publication] has yielded highly successful results [Text removed for publication]. Removal of mussels from raw water pipes has resulted in reduced pipe restrictions, with related savings on pumping costs. For example, a representative of Anglian Water said: *"There had been a significant loss of performance at our water treatment works in Covenham due to large numbers of zebra mussels blocking the pipes feeding the plant. Use of BioBullets significantly reduced the number of mussels, demonstrating a cost effective solution to the problem".*[9]

The potential financial impact of BioBullets' products on the UK water industry is very significant and has already been recognised. For example, Thames Water spent £1m in 2010 alone clearing zebra mussels from their raw water pipes[11]. Anglian Water reported in 2011 that the increased pressure required to pump water through zebra mussel-infested pipes is costing them £500K per annum in additional energy costs[11]. Following trials of BioBullets, the companies stated:

- "*We believe BioBullets will save hundreds of thousands of pounds in operational costs in a way that has no adverse impact on the environment*."[11]
- *We are very hopeful BioBullets are the solution we've been looking for having trialed them at our treatment works at Alton in Suffolk and Pitsford in Northamptonshire. In both cases we saw a significant reduction in the numbers of mussels without any impact on the treatment process or the environment.*"[11]

Currently, BioBullets is currently negotiating commercial terms with a service provider [Text removed for publication] to deliver the product across the UK water industry.

Impacts on commerce: the performance of an existing business has been improved; industry has invested in research and development

In June 2011, a dedicated manufacturing plant for BioBullets was opened in Bristol [Text removed for publication]. The plant was part funded through a £500K grant from the Technology Strategy Board [Text removed for publication]. The plant has an annual capacity of 5000 tonnes [Text removed for publication].

International impacts on commerce

Tests and trials have been carried out in other countries: tests in the Netherlands (by [Text removed for publication] a major consultant to the European and Asian power industries) yielded 100% mortality[Text removed for publication]. Trials funded by the Aragon government in Spain in February 2011 resulted in a highly effective removal of fouling zebra mussels and Asian clams (*Corbicula* spp.) within irrigation systems: *"Infestation of irrigation systems by zebra mussels and Asian clams has presented farmers with problems in maintaining adequate water supplies to crops. BioBullets was able to remove substantial volumes of mussels from the irrigation pipes."*[13]
BioBullets is currently in discussion with both the US and Spanish water industries about using their products to control zebra mussels in water supplies in those countries.

Given the breadth of the initial patent, the company has diversified its product range to target a broad range of invasive aquatic species. In 2006, BioBullets started development and testing of a formulation to control fouling by invasive bivalves (*Mytilopsis* and *Perna* spp.) in [Text removed for publication] shrimp farms. In laboratory tests in [Text removed for publication] in 2010, one formulation yielded 100% mortality in mussels, but with no harmful effect on the shrimps. Discussions are underway between BioBullets and [Text removed for publication] two [Text removed for publication] shrimp farming companies [Text removed for publication] for full-scale field trials. In 2008 a grant to BioBullets from the US National Oceanic and Atmospheric Administration (NOAA)[14] enabled the development and testing of a formulation to control invasive seasquirts (*Didemnum vexillum*), pests which threaten the global marine aquaculture industry. Trials of formulations in New Zealand in 2010 produced high mortalities in both *Didemnum*, and a second invasive and economically damaging seasquirt, *Ciona clava*[15].

The underpinning BioBullets technology has become a platform for expansion of the company into other areas. A Feasibility Grant from the TSB in 2011 enabled development [Text removed for publication] to enhance the growth rates and survival of commercial shellfish larvae.[16] [Text removed for publication]. In January 2013, BioBullets led a consortium of three SMEs (the others

being Micropore Technologies, UK, and Scalpro, Norway) in successfully bidding for Eureka Eurostars funding (an EU R&D programme) to develop microencapsulated feed products to enhance commercial shellfish yields.[17] The speed of juvenile shellfish growth is currently constrained by the availability of, and nutrient level in, algal cells; BioBullets' platform technology is enabling them to encapsulate tailored and optimised nutrient packages for different shellfish species.

Impacts on the environment: the management of an environmental hazard has changed

The adoption of Biobullets by UK water companies has changed how the industry approaches control of zebra mussels. The products are reducing the use of chlorine in water supplies on a global scale, and so reducing a major human and animal aquatic toxin: "*Biobullet provides a unique formulation that has the potential to allow us to target a variety of invasive non-native species in a manner that will protect the rest of the ecology from non-target damage*."[8]

Since 2004 research and grant writing has been led by David Aldridge, in his role as Managing Director of BioBullets Ltd. Grant funding has enabled part-time employment of Aldridge and one other person as consultants to the company. [Text removed for publication] BioBullets Limited is expected to become commercial in 2014.

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

6. DWI regulatory approval for Silver Bullets 1000
7. DWI regulatory approval for Silver Bullets 2000
8. Personal communication to Aldridge from the Senior Technical Advisor on Invasive Species for the Environment Agency
9. Description of trial outcomes from Anglian Water
10. Description of trial outcomes from South Staffs Water
11. www.thameswater.co.uk/media/press-releases/14159.htm
12. [Text removed for publication]
13. Description of trial outcomes from Aragon Government, Spain
14. "BioBullets for the Control of Fouling Sea Squirts" - US National Oceanic and Atmospheric Administration: US$120,000 Ref. 51710002423, 2008-2009: David Aldridge (PI, via BioBullets Ltd.)
15. Laing, I., J. Bussell, *et al*. (2010). Assessment of the impacts of *Didemnum vexillum* and options for the management of the species in England. Fera, CEFAS and Natural England: 62. p36

[Text removed for publication]