Institution:
University of Cambridge

Unit of Assessment:
UoA12

Title of case study:
BioBullets

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

The zebra mussel is one of the world's most damaging invasive species, but existing control approaches cause significant environmental damage. Researchers at the University of Cambridge have developed the patented 'BioBullet', which encapsulates a toxic active ingredient in a harmless edible coating, enabling efficient, targeted product delivery and dramatically reducing environmental pollution. [Text removed for publication]

2. Underpinning research (indicative maximum 500 words)

Since 1999, Dr Moggridge (joined UoA12 as an Assistant Lecturer in 1995, now Reader) and Dr David Aldridge (Department of Zoology) have collaborated to study the zebra mussel, *Dreissena polymorpha*, and to develop a method for controlling its population. One of the world's most economically and ecologically important pests, the damage caused by zebra mussels now costs an estimated U.S.$5 billion per year in North America alone, due to their ability to block the raw water cooling systems of power stations and water treatment works.

Their research has mapped the location and spread of zebra mussel populations in Britain (ref 1) and the damage caused to water installations, documenting a recent, rapid increase in both abundance and distribution, coupled with deleterious ecological and industrial impacts.

Chlorination is a widespread and licensed control technique, but is non-specific; and 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, which produces trihalomethanes by reaction with organic material. Trihalomethanes are toxic to humans and other animals, so there has been continued tightening of regulatory controls on the discharge of chlorine (e.g. the European Water Framework Directive 2000/60/EC).

Moggridge, in collaboration with Aldridge, theorised that toxins could be delivered to zebra mussels sequestered in an edible coating, overcoming the valve closure response – a 'Trojan horse' approach to active ingredient delivery. Broad patent protection has been granted (ref 3).

Dr Moggridge's contribution focussed on the chemical composition, formulation and manufacture of the BioBullet particles. A key formulation decision was which toxin would form the core of the 'BioBullet'. KCl was initially chosen, after demonstrating that it is particularly toxic to freshwater bivalves [Text removed for publication], but at low doses is inert to most other organisms (ref 2). The mussels' natural filtering behaviour internally concentrates the toxin when it is delivered in appropriate particulate form, reducing the quantity of active ingredient required, and meaning that it is effective as a one-off treatment, rather than needing continuous dosing. Furthermore, the 'BioBullet' is engineered to dissolve completely within a few hours, thus eliminating the risk of polluting the wider ecosystem. The effectiveness of the BioBullet product was improved in 2008 and 2009 by the use of a more potent, yet still environmentally benign active ingredient. Particle optimization has focused on the appropriate balance between a smaller capsule, that will be more easily recognised as food by the mussels, and a larger capsule, that will have a better release time (ref 4).

Working on further aspects of the control strategy, Dr Moggridge's team demonstrated in 2008 that zebra mussels show seasonal peaks of increased susceptibility to toxins (ref 5), which has implications for the overall design of chemical control strategies, and for the amount of toxin required to achieve the desired effect. The team's 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 (ref 6). Additional studies 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 the target species.

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

1) "The Recent and Rapid Spread of Zebra Mussels (Dreissena Polymorpha) in Great Britain" D.C. Aldridge, P. Elliott and G.D. Moggridge, Biological Conservation 119 (2004) 253-261.

DOI: 10.1016/j.biocon.2003.11.008

*2) "Microencapsulated BioBullets for the Control of Biofouling Zebra Mussels" D.C. Aldridge, P. Elliott and G.D. Moggridge, Environ Sci Technol 40 (2006) 975-979.

DOI: 10.1021/es050614+

3) [Text removed for publication]

4) "Preparation and evaluation of biocide-loaded particles to control the biofouling zebra mussel, *Dreissena polymorpha*" R. Costa, D.C. Aldridge and G.D. Moggridge, Chem. Eng. R&D 89 (2011) 2322-2329.

DOI**:** 10.1016/j.cherd.2011.02.027

*5) "Seasonal variation of zebra mussel susceptibility to molluscicidal agents" R. Costa, D.C. Aldridge and G.D. Moggridge, J. Applied Ecology 45(6) (2008) 1712-1721.

DOI: 10.1111/j.1365-2664.2008.01555.x

*6) "Zebra mussel filtration and its potential uses in industrial water treatment" P. Elliott, D.C. Aldridge and G.D. Moggridge, J. Water Research 42 (2008) 1664-1674.

DOI: 10.1016/j.jglr.2011.01.005

* References which best reflect the quality of the underpinning research.

Major Grants

Grant 1 Feb 2001-Mar2004: Awarded to Dr Geoff Moggridge; GR/R27723/01 “Silver bullets for zebra mussels”; EPSRC (with Anglian Water Services as Project Partner). £238,100

Grant 2 March - August 2003: Awarded to Dr Geoff Moggridge; “Silver bullets for zebra mussels” DTi SMART Award (with Thames Water Ltd. as Project Partner). £10,000

Grant 3 [Text removed for publication]

Awards

The initial research gained acclaim in the BioScience Business Plan Competition (sponsored by BBSRC, MRC, GlaxoWellcome and the Gatsby Foundation, 2000) - £25,000 and Drs Moggridge and Aldridge received the Institute of Chemical Engineering (IChemE) Entec Medal in 2007, the highest award given at their annual awards ceremony.

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

Impact on production: decisions by regulatory authorities have been influenced

In December 2008, the GB Drinking Water Inspectorate (DWI) approved the BioBullets product Silver Bullets 1000 for use in public water supplies (ref 7). 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 (ref 8). 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 (ref 9), and regards “*The biobullet formulation [as] an essential management tool in our response to a variety of priority invasive non-native species*.” (ref 9).

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

Eight full-scale trials have been conducted within the impact period in seven UK waterworks, belonging to Anglian Water (ref 10), South Staffordshire Water (ref 11), Thames Water (ref 12), Severn Trent Water and Welsh Water. Dosing [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"* (ref 10).

The potential financial impact of BioBullets' products on the UK water industry is significant. For example, Thames Water spent £1m in 2010 clearing zebra mussels from their raw water pipes (ref 12). Anglian Water reported in 2011 that the increased pressure required to pump water through zebra mussel-infested pipes cost £500K per annum in additional energy costs (ref 12). 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*." (ref 12).
- *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.*" (ref 12).

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

Impact on commerce: the performance of an existing business has been improved

In June 2011, a dedicated manufacturing plant for BioBullets was opened in Bristol [Text removed for publication]. The plant has an annual capacity of 5000 tonnes, [Text removed for publication].

International impact on commerce

Based on the original research conducted in Cambridge, 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."* (ref 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.

Building on 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 [Text removed for publication] one formulation yielded 100% mortality of 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) for full-scale field trials. In 2008 a grant to BioBullets from the US National Oceanic and Atmospheric Administration (NOAA) (ref 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* (ref 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 (ref 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 (ref 17). The speed of juvenile shellfish growth is currently constrained by the availability of, and nutrient levels in, algal cells; BioBullets' platform technology

enables them the encapsulation of tailored and optimised nutrient packages for feeding to different shellfish species.

Impact 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, 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*." (ref 9).

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

7) DWI regulatory approval for Silver Bullets 1000 [Text removed for publication]

8) DWI regulatory approval [Text removed for publication] for Silver Bullets 2000

9) Supporting statement from the Senior Technical Advisor on Invasive Species for the Environment Agency

10) Testimonial from Innovation Manager, Anglian Water

11) Testimonial from Southern Production Manager, South Staffs Water

12) www.thameswater.co.uk/media/press-releases/14159.htm

13) [Text removed for publication]

14) "BioBullets for the Control of Fouling Sea Squirts" - US National Oceanic and Atmospheric Administration: US$120,000 Ref. 51710002423, 2008-2009: grant to 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.

16) [Text removed for publication]

17) [Text removed for publication]