

<b>Institution: Keele University</b>
<b>Unit of Assessment: A5 (Biological Sciences)</b>
<b>Title of case study: Improving fish health and quality using naturally derived products</b>
<p><b>1. Summary of the impact</b></p> <p>Disease severely limits the expansion of aquaculture. Studies on the immune control of infection have led, in association with industry, to the promotion of disease control utilising <math>\beta</math>-glucan feed supplements. Knowledge has, via <a href="#">Keele Water</a>, informed infection control strategies used by UK fish farmers. Studies have provided a legacy of young scientists trained by industry and supported by European funding. Advances made have been embraced in the education of veterinarians in Germany and fish production in Eastern Europe. Close collaboration with government bodies and learned societies has ensured that the work has been recognised by policy makers within the fisheries sector.</p>
<p><b>2. Underpinning research</b></p> <p>Hoole has investigated immunological and pathological interactions between fish and pathogens since 1987, leading to improved fish health in aquaculture and fisheries. Since 1993, aquaculture has been the fastest growing animal production sector. In 2010 59.9M tonnes were produced for human consumption with an estimated value of US\$ 119B. Disease severely limits development and costs the industry US\$ 3B plus US\$ 3M being spent on treatment. The IFAO has highlighted the importance of aquaculture in providing income for an eighth of the global population and the industry contributes to the EU Food Security agenda within the CAP and international support programmes. Initial studies at Keele, in association with Arme, produced the first extensive descriptions of the complex interactions between metazoan parasites and the fish immune system. In addition, the impact of pollution on fish and their interactions with parasites was ascertained in association with the University of London and Environment Agency in Wales (1995-2003). These advances were recognized when Hoole was invited to participate 2002 in a 4 year EU Marie Curie Research Training Network (PARITY) on the immune response of carp to infection. The study, which took a multidisciplinary approach including expertise from the School of Life Sciences at Keele in cancer studies (Williams) and protein crystallography (Greenhough, Shrive), led to the characterization of pathogen interaction at the molecular level with cell death processes in fish, and the isolation and characterisation of innate acute phase immune proteins. This multidisciplinary approach is still ongoing and advances made were noted by 3 international companies involved in the production of immunomodulators (<a href="#">Biorigin</a>), fish feed (<a href="#">Biomar</a>) and the fish ornamental trade (<a href="#">Tetra</a>). These companies collaborated with Hoole to develop a Marie Curie EU Initial Training Network (<a href="#">NEMO</a>) along with 5 European research Institutes (2008-2013). This established optimum protocols for the use of <math>\beta</math>-glucans in the form of MacroGard<sup>®</sup>, a by-product of the bioethanol and yeast fermentation food processes, in the strategic improvement of fish health. Multidisciplinary approaches entailed the formulation of <math>\beta</math>-glucans into fish feed, the determination of adverse effects on cell biology and the assessment of affects on the carp innate immune response. Advantages of pulse feeding compared to continual feeding were confirmed and the possible protective value of <math>\beta</math>-glucan supplements on bacterial and viral diseases of carp (e.g. <i>Aeromonas salmonicida</i>, KHV, SVC) was ascertained. The effects on a range of innate immune parameters such as complement activity, cytokine gene expression and, for the first time, C reactive protein at the gene and protein levels was also determined. The work highlighted the cost benefits of using naturally derived immunomodulators in fish health, allowing farmers to reduce the application of less environmentally friendly treatments such as antibiotics. A more recent collaboration since 2011 with Skidmore, (Life Sciences, Keele University) has led to an association with Biorigin to establish the active ingredient of the <math>\beta</math>-glucan, potentially leading to more effective immunoprotectant. This could reduce the amount being added to feed, thereby reducing costs of protection and increasing product quality control and cost effectiveness of fish farming and other animal production.</p>

### 3. References to the research

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### Key Grants

2000-01	£3,230 - British Council (with Pierce and Dufour, France).
2002-05	£17,250 - Royal Society (with Secombes, Aberdeen and Nie Pin, China).
2002-06	€213,200 - EU Research Training Network Grant.
2008-12	€3,078,798 - EU Initial Training Network Contract.
2012-15	£5,000 - Kurdistan Government (support for Ph.D studentship).
2012-15	£1,500 - Fisheries Society of the British Isles (support for PhD studentship).
2013-date	£7,680 - Biorigin (with Skidmore).

#### 4. Details of the impact

##### *Commercial and International Impact*

(a) The research has been directly applied by industries involved in production of immunomodulators ([Biorigin](#)) and fish feed ([Biomar](#), [Skretting](#)), providing independent verification of the importance and advantages of using [MacroGard](#) in the improvement of fish health. Whilst unwilling to release any sensitive commercial information, Biorigin did provide the following statement "the results from the NEMO project have given us a better understanding of the fish immune system in general and have contributed to the development of new health concepts in the salmon business, where a strong immune response is needed to prevent harmful pathogens. As an effect of these results, Biorigin has significantly increased the sales of MacroGard to the salmon industry". This impact has been extended globally by the use of industrial contacts with fish production and a joint venture between Hoole and Biorigin with ACG, the [Aquaculture Communications Group](#). Since MacroGard shortly loses patent protection, Biorigin are supporting studies on the development of a new generation of immunomodulators based on conformational changes of  $\beta$ -glucan. The advances made by Hoole are also being utilised by partners at Universiti Sains Malaysia in the production of snakehead and other Asian fish.

(b) The knowledge acquired by Hoole on fish diseases has been utilised over many years by [Keele Water](#), an environmental consultancy recognised by the Environment Agency to carry out fish health checks under Section 30 of the Freshwater Fish Diseases Act of 1975 and 1983 and "Buyer Beware Policy". Reports produced for fish farmers and fisheries officers, and consultations, have resulted in the implementation of management strategies and biosecurity practices which limit the spread of disease within the fish production sector. Reports also assist the EA to develop strategies and to reassess the threat of individual parasite species to the UK fisheries sector.

(c) The research undertaken has also impacted on the ornamental fish sector, an industry which is considered to be worth globally US\$ 15B. Consultations with the local Koi Carp branch of the British Koi Carp Society have assisted ornamental fish keepers to improve their understanding of diseases and thus implement strategies to improve fish health and biosecurity. In addition, joint studies with [Tetra](#) and [Biomar](#) have supported the scientific rationale for MacroGard being placed in their feed products.

##### *Impact on industrial employment skills*

The EC and Industry are striving to improve the appropriate skills base in academia, the absence of which leads to difficulties in young research scientists initially adapting to, or following, a career in industry. In association with three of his industrial collaborators ([Tetra](#), [Biorigin](#), [Biomar](#)), Hoole has established an industry-based training programme for young scientists working in aquaculture research in academia. Workshops in industrial research training (e.g. Fish Immunology held in the Netherlands, 11th-15th April 2010; Protein crystallography and Molecular Modelling 15th-17th September 2010; Carp Aquaculture held in Poland, 8th-11th May 2011; Proteomics held in Denmark, 14-16th Nov. 2011) resulted in several young scientists acquiring employment or sponsorship within the industrial sector, and have established a legacy of young industry-trained research scientists throughout the European Higher Education sector (see [NEMO](#) web site).

##### *Educational Impact and Raising Awareness*

The research advances made by Hoole and the NEMO Consortium have been adopted in and have modified the educational policy of several European Higher Education and Research Institutes. The work has changed the perception of fish disease control and, in particular, the suitability of using prebiotics and probiotics to improve fish health. Incorporation of the advances made into educational programmes for veterinarian courses in Germany and specialised aquaculture workshops in Poland has impacted on the dissemination of the knowledge base and practice within the fish veterinary sector and the production of carp, particularly in eastern Europe e.g. [Institute of Ichthyobiology and Aquaculture](#), Poland; [AquaCulture](#) Directory (2013), [FEEDINFO News Service](#) (2013), and the [Aquaculture Communications Group](#) (2013).

##### *Impact on policy makers*

Studies carried out by Hoole and the NEMO consortium have attracted the attention of the [Centre for Environment, Fisheries and Aquaculture Science](#). This governmental organisation, which is aligned with DEFRA, is responsible for fish health and associated fish policies within the UK fish production sector and UK territorial waters. A joint meeting has been initiated to assess the impact

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of the work carried out on fisheries research and future policy strategies. This has led to continued discussions with CEFAS and the involvement of the European Association of Fish Pathologists to co-ordinate with Hoole to organise a conference at Keele University in September 2014. In addition, through the Parliament Magazine's Research-European Research & Innovation Review 2010 p26 and reports to the European Commission through the NEMO EU project officer, the advantages of developing natural products as immunomodulators in aquaculture will be assessed by the Commission and will input into the sustainability agenda within the aquaculture fisheries.

**5. Sources to corroborate the impact***Commercial and International Impact*

- (a) Various publications address the use of  $\beta$ -glucan in aquaculture and the impact of the work of Hoole through the NEMO project (e.g. [ORFFA](#)).
- (b) The value and impact of the NEMO project has been highlighted in [FEEDINFO News Service](#) (2013); [ACG](#) (2013) and [Aquafeed](#) (2013).
- (c) Biorigin Scandinavia (independent verification of the scientific advantages of using ( $\beta$ -glucan).
- (d) Tern Fisheries Ltd. (impact of this work on fish health).

*Impact on Industrial Employment Skills*

- (a) Environment Agency (impact of the NEMO Programme on training of EA staff).

*Educational Impact and Raising Awareness*

- (a) University of Veterinary Medicine Hanover (advances in education for veterinarians).
- (b) Institute of Ichthyobiology and Aquaculture (impact of specialised aquaculture workshops in Eastern Europe and particularly Poland).