Institution: University of Nottingham

Unit of Assessment: 6; Agriculture, Veterinary and Food Science

Title of case study: Advancing analgesic use in cattle

1. Summary of the impact

The use of non-steroidal anti-inflammatory drugs (NSAIDs) for their pain-relieving properties in cattle medicine has lagged behind that of other species (e.g. companion animals) where analgesic use is now routine. University of Nottingham (UoN) research exploring the attitudes of vets and farmers to the use of NSAIDs in cattle, and subsequent marketing by Boehringer Ingelheim, a multinational pharmaceutical company, has led to a substantial increase in analgesic use. UoN research increased sales for Boehringer Ingelheim and almost doubled the UK market value of NSAIDs for use in cattle. With administration of up to 2 million additional doses per year, the research had clear benefits for animal welfare.

2. Underpinning research

Key researchers:
Prof Jon Huxley: Prof of Cattle Health & Production (UoN; 2006-present)
Prof Martin Green: Prof of Cattle Health & Epidemiology (UoN; 2006-present)
Mr Chris Hudson: Lecturer in Cattle Health & Production (UoN; 2009-present)
Dr Becky Whay: University of Bristol

The use of analgesics in cattle when painful conditions are present has lagged behind that in other veterinary species. The reasons for this are multi-factorial, and include:

1. Their ancestral heritage as a prey species means cattle are stoic, they mask the signs of pain and its implied weakness, making discomfort difficult to identify.
2. Cattle are large animals, the volume of product required means treatment costs are high.
3. Historically analgesic use has not been considered a social norm in the farming industry and veterinary profession.
4. The research literature has lacked evidence of the benefits of NSAID use in the field.

Strict food safety legislation governs the use of medicinal products in food animal species. NSAIDs are the only licensed analgesics that can be practically administered to cattle, so their underuse represents an important welfare problem for the UK's ten million farmed cattle.

UoN research initially used questionnaires to explore the attitudes of cattle veterinarians (641 UK-wide responses; **[1]**) and cattle farmers (1135 UK-wide responses). These studies gathered extensive data on the viewpoints and opinions of vets and farmers to pain in cattle and their use of analgesics. They identified the huge diversity of opinion in this area and recognized some of the barriers to the wider administration of analgesics. This research strategy developed by Prof Huxley and Dr Whay in the UK was adopted in many parts of Europe (including Spain, The Netherlands, Sweden, Belgium, Norway, Denmark, France and Germany) and New Zealand **[2]**. Following this initial attitudinal research, the work focused on addressing some of the knowledge deficits and behavioural barriers that were identified. For example, veterinary respondents to the questionnaire surveys who did not use analgesic agents for a condition, assigned significantly lower pain scores to it. This indicated that one of the key motivators for the use of analgesics was the clinician's perception of the animals' suffering **[1]**. Consequently a project **[c]** was mounted with the aim of improving understanding of the clinical beliefs of farm animal veterinary surgeons, within a Bayesian statistical framework, in order to understand and improve clinical decision making **[5]**. Similarly, hock lesions are very prevalent in UK herds and were deemed of minor significance by the respondents of the farmer surveys despite evidence to suggest they are painful. Studies have further explored the pain associated with, and farmer attitudes towards, hock lesions **[4; a, b]**. Recent work has targeted the lack of field based NSAID efficacy studies. A randomised clinical trial has been conducted to investigating the clinical impact of NSAID treatment on lameness, a key endemic disease **[d]**.

This collective body of research evidence assessed the attitudes of prescribing vets and identified barriers to NSAID usage and how they could be overcome. These and the wider findings from the

work allowed dissemination and discussion of the results at conferences, in continuing professional development programmes and in journals targeted at veterinary clinicians **[1,2,3,4,5]** and allowed the development of training and marketing programmes designed to challenge the prevailing opinions which limited analgesic use (see sections 4 and **Sources 1-7** for evidence and detail).

3. References to the research

The outputs from this on-going research have been published and described in a range of peer-reviewed research and clinical journals.

1. Huxley, J.N. and Whay, H.R. (2006) Current attitudes of cattle practitioners toward pain and the use of analgesics in cattle. The Veterinary Record*, 159 (20): 662-668; doi 10.1136/vr.159.20.662
2. Laven RA, JN Huxley, HR Whay and KJ Stafford (2009). Results of a survey of attitudes of dairy veterinarians in New Zealand regarding painful procedures and conditions in cattle. New Zealand Veterinary Journal, 57 (4): 215-220. Available on request.
3. Hudson, C., Whay, H.R. and Huxley, J.N. (2008) Recognition and management of pain in cattle. In Practice* 30 (3): 126 – 134; doi 10.1136/inpract.30.3.126
4. Potterton, S.L., Green, M.J., Millar, K.M., Brignell, C.J., Harris, J., Whay, H.R and Huxley, J.N. (2011) Prevalence, characterisation and significance of hock lesion in UK dairy cattle. The Veterinary Record*, 169: 634; doi 10.1136/vr.d5491
5. Higgins H., Huxley, J.N., Wapenaar, W. and Green, M.J. (2013) Proactive dairy cattle disease control in the UK: veterinary surgeons' involvement and associated characteristics. The Veterinary Record*, doi 10.1136/vr.101692

The journals above were specifically selected by the authors to target veterinary clinicians to ensure the work directly influenced its target audience. The impact factor of these journals is in part linked to the size and relative importance of the veterinary profession. The quality and international reach of the work is demonstrated by its adoption in other countries around the world (e.g. **[2]**). and its recognition by international reports on dairy cow welfare **(Source 1)**.

**The Veterinary Record and In Practice are delivered to all members of the British Veterinary Association.*

***Underpinning research projects*:**

a. 2007-10: "*An investigation into the significance of hock lesions in UK dairy cattle*". CoPI Prof Jon Huxley and Prof Martin Green; funded by the UoN Interdisciplinary Doctoral Training Centre, £52,500.

b. 2007-10: "*An investigation into the significance of hock lesions in UK dairy cattle*". PI Prof Jon Huxley; funded by Boehringer-Ingelheim Vetmedica, £9,538. UoN

c. 2009-13: "*A quantitative (Bayesian) assessment of veterinary surgeons clinical beliefs in order to understand and improve clinical decision-making by farm vets and direct future research*". PI Prof Martin Green, CoI Prof Jon Huxley; funded by the Wellcome Trust, £342,919 to UoN.

d. 2011-13: Work Package 2 "*A new approach to lameness control in dairy cattle: Treatment of individual lame cows and farm level interventions*" in "*Research Partnership: Cattle health, welfare and nutrition*". CoPI Prof Jon Huxley and Prof Martin Green; funded by DairyCo, £245,000 to UoN.

4 Details of the impact

A long-standing and on-going collaboration between research clinicians (Huxley, Green & Hudson) at UoN and Boehringer Ingelheim (BI) has enabled the UoN research to deliver changes in non-steroidal anti-inflammatory drug (NSAID) use for cattle. There are five NSAIDs licensed for use in cattle, in the UK (carprofen, flunixin meglumine, ketoprofen, meloxicam and tolfenamic acid). A surge in the use of NSAIDs, particularly Metacam™, the meloxicam brand sold by BI, has arisen from the research findings and the collaboration between UoN and BI. UoN research was used to inform marketing policy and approach (based on the barriers to use identified in Prof. Huxley's research), leading to considerable gains for animal welfare and clear commercial benefit for BI, the industrial collaborator. Although the research was instigated, designed and independently

conducted in academia, much of the original research represents a true HEI-industrial partnership, which has further developed (for example, BI are the industrial partner on a current BBSRC Industrial Case Studentship on which Huxley and Green are the PIs). BI were instrumental in this research from the start, providing financial and logistical support to the UK and wider European work.

The response of BI to the publication of the research findings was to instigate a concerted and on-going marketing campaign, aimed at changing the NSAID prescribing habits of farm animal vets and the attitude of farmers to NSAID use. The material and evidence they used to support this campaign was underpinned by the research on farmer and vet attitudes to pain and analgesic usage and the barriers (both real and perceived) to increased NSAID usage in cattle **(Source 2)**. For example, many veterinary surgeons believed that farmers were not prepared to pay for NSAIDs. The research at the UoN demonstrated this not to be the case, and many cattle farmers stated that vets did not discuss pain control with them as often as they would like. This research was pivotal in changing these attitudes and thus the use of NSAIDs (**Source 2**).

The increase in use of NSAIDs following the UoN research was dramatic. Between 2008 and 2012 the total market value of NSAIDs sold in the UK for use in cattle increased from £4,704,642 to £8,927,556 (a 90% increase; **Figure 1**). Over the same time period Metacam™, the meloxicam brand sold by BI has seen its total market value increase from £1,633,295 to £4,574,484 (a 180% increase; **Figure 1**). It is of note that 81% of the increase in total NSAID growth between 2008 and 2012 was driven by sales of Metacam™, which had a greater than fifty per cent market share in 2012. All other brands in the market place (>20) saw their combined sales rise from £3,071,347 to £4,353,072 **(Source 2)**. In a statement (2013), the Business Manager - Cattle of BI stated, "*Our partnership with Professor Huxley and his team at Nottingham University has been central in moving veterinary opinion and thereby validating our promotional activities. The proximity of this team of researchers to the practising veterinary surgeons and the respect with which their opinion is universally viewed has been, I believe, pivotal in changing attitudes to pain relief and behaviours which have brought about this massive increase in use of NSAIDs in general and Metacam in particular. Since the original collaboration between Boehringer Ingelheim and Professor Huxley and his collaborators to investigate attitudes of vets to the control of pain in cattle, a universally beneficial relationship has been created by way of increased profits for our industry and company, a resultant willingness to invest in on-going internal and third party research with the indisputable improvement in animal welfare for which we can all feel justifiably proud*" **(Source 2)**.

The beneficiaries of this research are widespread. Pharmaceutical companies have benefited from increased sales, which have led to substantial and direct animal welfare benefits via the control of pain and discomfort in treated cattle. It is very difficult to accurately quantify the exact number of additional animals that have benefited (only volume of sales data is available and dose volume is dependent on animal weight). However, if it is assumed that an animal dose has an approximate cost price of between £2 and £20 (calf to adult), in 2012 between 210,000 and 2,100,000 additional animal doses were administered compared to 2008. Consequently farmers, purchasers, consumers and government have benefitted from an improvement in animal welfare and an assurance that every effort is being made to treat and control pain in this key food production species.

Alongside the marketing campaign and in some cases supported by BI, the research clinicians (Huxley & Hudson) have made concerted efforts to raise the profile of this research and pain control in cattle in general **(Source 3)**. Since January 2008 they have delivered eleven training meetings to farmers and industry, three professional development meetings to veterinary surgeons, created an open access webinar **(Source 4)** and presented the work at nine national and international events/conferences attended by the dairy industry and/or veterinary surgeons, reaching an estimated audience of well over 1000 people. Additionally they have publicised the work and the work has been reported directly or indirectly in a wide range of professional journals and industry magazines **(Source 5)**. Finally, based on the interest UoN research generated in this area, XLVets (a veterinary consortium composed of 50 commercial practices across the UK) developed a group-wide training programme (2008-12) to promote the uptake and use of NSAID amongst their farming clients **(Source 6)**. In a statement (2013), the Chief Executive of XLVets said, "*We have greatly appreciated the collaborative approach that you have shown in providing*

not just the science but also practical solutions and key opinion leadership in the development of a better understanding of pain and analgesia in cattle. The impact of your work has been considerably enhanced by your ability to effectively communicate it to the wider audience. We have specifically appreciated the practical help and support that you have provided to us in the development of our campaigns of activity to change mind sets to analgesia. The direct effect of your work can be measured by the significant increase in usage of NSAIDs on farm" **(Source 6)**. The named research clinicians and wider farm animal group at Nottingham have a long-standing relationship with XLVets, based on undergraduate training and knowledge sharing allowing the development and promotion of initiatives such as this. In a similar statement (2013) the President of the British Cattle Veterinary Association (BVCA) stated, *"The reinforcement of appropriate analgesia messages at BCVA CPD and at BCVA Congress in particular has been prominently delivered by the Nottingham team in partnership with BI*" **(Source 7)**.

It is clear that the underpinning research from UoN, combined with expertise in clinical practice and collaboration with industry, has driven forward an on-going industry wide promotional campaign to change veterinary prescribing habits and increase analgesic usage on farm. This has led to a substantial change in the use of NSAIDs in cattle and a direct improvement in animal health and welfare in the UK.

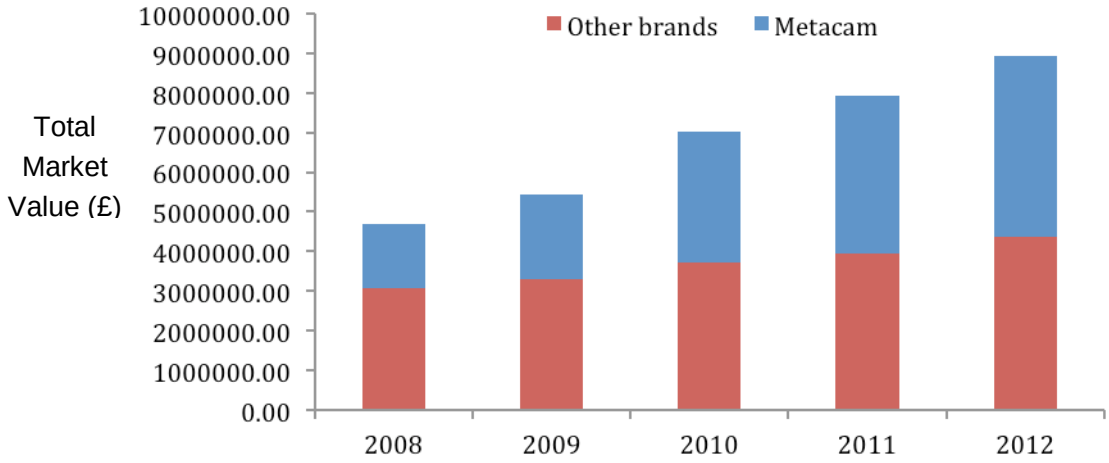

Figure 1:Total market value (£) of Metacam™ (Boehringer Ingelheim) and all other brands of NSAIDs sold in the UK, for use in cattle between 2008 and 2012

5. Sources to corroborate the impact

1. An independent international report on the welfare of dairy cows published by the European Food Safety Authority *cites the barriers to the use of analgesics identified in this research and reports the outcomes of the work more broadly* (http://www.efsa.europa.eu/en/efsajournal/doc/1143r.pdf) 2009.
2. UK Business Manager Cattle, Boehringer Ingelheim Limited (BI). *Provides corroboration for the increased in sales of Metacam due to Nottingham research as well as the creation of awareness on NSAIDs.* 2013.
3. *Provides corroboration for the raising of awareness by the research about the need to provide pain relief for cattle* (http://www.fwi.co.uk/articles/17/10/2008/112682/pain-control-needed-earlier-in-mastisis.htm) 2008.
4. *Open access webinar providing corroboration for the dissemination of research findings on pain relief for cattle* (http://live.webcasts.unique-media.tv/bil039/)
5. *Provides corroboration for the world-wide spread of research work through magazines* (http://edepot.wur.nl/138196) 2010.
6. Chief Executive of XLVets. *Provides corroboration for the impact of research on prescribing habits of vets as well as attitudinal change towards NSAIDs and increased usage.* 2013
7. President of British Cattle Veterinary Association. *Provides corroboration for the promotion of NSAIDs amongst Veterinary practitioners*. 2013