

First ileitis vaccine

A symposium organized in October by Boehringer Ingelheim Animal Health signalled the official introduction of the company's ileitis vaccine across 19 European countries. The audience of over 150 veterinarians were reminded how researchers strove for 20 years to discover *Lawsonia intracellularis* and how their efforts triggered the work that really matters to producers – control of the disease.

By Anabel Evans

The first presentation at the European Enterisol® Ileitis Symposium was by Prof. Dr Hans-Wilhelm Windhorst from the ISPA University of Vechta, Germany, whose analysis of global pigmeat production and trade indicated that the increasing surplus in countries with considerably lower production costs than the EU will put continuous pressure on the price for pigmeat; the banning of antibiotic growth promoters adding to EU producers' problems as can be seen from the recent developments in piglet production in Denmark.

Prof. Dr Pedro Rubio Nistal from the University of León, Spain then highlighted the distribution and incidence of porcine proliferative enteropathy (PE, ileitis) saying, "PE has a world-wide distribution and it is very difficult to find negative farms including those with a high sanitary level. Prior to the launch of Enterisol Ileitis the presence of antibodies against the causative agent, *Lawsonia intracellularis*, has been investigated in several hundred farms within the EU. The percentage of seronegative farms among the countries was always below 2%; and they were always in farms with special characteristics like systemic weaning in three-site systems.



The oral vaccine is licensed for grower/finishers, breeding sows and gilts.

Dedicated research

Today's ability to make such detailed PE surveys must be credited to more than two decades of research by dedicated groups. Dr Steven McOrist of QAF Industries, Australia explains: "It was back in the 1930s when Harry Biester and others first described the lesions of PE in pigs at the Veterinary Medical Research Institute in Ames, Iowa. Subsequent workers throughout the 1950s have provided a series of case descriptions in Scandinavia and elsewhere, also focusing on pathologic discussions. In the late 1960s, intensification procedures started to get into swing in the pig industry and in-feed antibiotics, such as tylosin, also started being widely registered and used. It is likely that these changes led to both an upsurge in *Lawsonia* transmission and susceptible pig populations. This in turn led to further clinical and pathologic descriptions, with the workers at the University of Edinburgh: Alan Rowland, Giles Rowntree and Gordon Lawson investigating major outbreaks occurring in the UK. As part of this, they developed a productive research program and discovered that small, curved intracellular bacteria were consistently present within the abnormal proliferating cells (Rowland and Lawson 1974). An early

transmission experiment was successful (Roberts et al. 1977), suggesting these bacteria were the causative agent of the lesions. However, a number of attempts to repeat this work, even with the same inoculum by the same workers, failed. A string of failed experiments expended most of the 1970s and 1980s.

"The identity of these bacteria and their etiologic role in PE in pigs were finally resolved in 1993 with successful co-culture of the intracellular organism and the reproduction of the disease in pigs using a pure culture of this agent (Lawson et al. 1993 and McOrist et al. 1993). The name *Lawsonia* was chosen to reflect the key role and persistence of the Scottish veterinarian, Gordon Lawson in its discovery."

Commercial control

Once the causative agent of PE became clear in the mid-1990s, as Steve McOrist says, the groups mentioned and many new groups in Europe and North America were able to start working quickly on aspects of the disease that really mattered to their pig industries. So the susceptibility of *Lawsonia* to various antibiotics, its epidemiology within and between pig farms and methods of diagnosis in live pigs and many

related topics were all taken up for research (Knittel et al. 1998).

It was in 1994 that the work commenced on a vaccine for ileitis, finally resulting in Enterisol becoming the first registered vaccine in 2001 and licensed in North America; it is furthermore licensed in Mexico, Brazil and the Philippines. Steve said, "This successful vaccine is now widely registered and used around the world."

Following the enlightening historical summary by McOrist, Dr Connie Gebhart from the University of Minnesota, USA, commended Boehringer Ingelheim for having the foresight to develop a vaccine. From her own research experience into the pathogenesis, immunology and diagnosis of PE, she highlighted that "it is not an easy bug". She said: "*L. intracellularis* is a unique bacterium, which causes an unusual pathology in infected animals. Limited knowledge of the pathogenesis of *L. intracellularis* suggests that this organism has adopted mechanisms of survival and pathogenesis unique from those utilized by other bacterial pathogens."

When going into more detail about the research and development of the vaccine itself, Dr Mike Roof, director of Biological R&D Boehringer Ingelheim Vetmedica, Inc., referred back to both Steve and Connie's work when mentioning a key issue that needed to be addressed before vaccine development - *the source of a potential vaccine isolate*. Were there 'strains' or differences between isolates that needed to be considered to develop an effective vaccine? To answer this question, BI scientists used the pure culture isolates from both Steve McOrist and Connie Gebhart to investigate the relevance of strain differentiation in *L. intracellularis*. These represented swine isolates from the US (various locations), Scotland, and Denmark. He said, "Analysis of these isolates along with PCR amplified DNA from clinical samples across the globe indicated 'Lawsonia is Lawsonia' and very conserved at the antigenic level. This allowed BI to focus on an isolate based on safety and efficacy and soon various attenuated live vaccine

Clear vision

Boehringer Ingelheim Animal Health might be a relatively young player in the swine vaccine market but Dr Joachim Hasenmaier, head of corporate division, is clear about the company's target to become the leading swine vaccine company, recognised by their customers for solving problems and providing a product portfolio which can be considered a 'complete tool box' by veterinarians and producers. His welcome speech during the official launch of Enterisol® Ileitis in Europe was sensitive to the image of a corporate company, saying that the committee of private shareholders, who own Boehringer Ingelheim - the largest privately held pharmaceutical company in the world, were committed to both animal health and sustainable practices for future generations. He continued: "The achievement surrounding Enterisol, being the first vaccine against ileitis, continues a trend realised with our PRRS and *M. hyopneumoniae*-one shot vaccines." Joachim attributes this success to the business teams, emphasising that the company's key strength lies in providing an environment that fosters innovation. Neither is Joachim ignorant to the position of the producer saying, "There are numerous choices for producers to optimise their herd health status, but nobody can afford to use all the vaccines or antibiotics available. The production management has to be based on a careful analysis of individual farm situations and Boehringer Ingelheim sees its role to provide these tailor made solutions."

candidates were available and tested."

Economical importance

Moving onto the comments relating to the economical importance of PE, Prof. Dr Pedro Rubio Nistal said, "The disease has two different clinical manifestations. The acute form causes mortality, which depends on the immune status of the affected batch, the infection pressure and housing conditions of the animals. The mortality usually does not exceed 50%; however, our laboratory has diagnosed an outbreak in replacement gilts that caused a higher mortality of 70%. It is more complicated to evaluate the losses caused by the chronic form, which principally causes indirect losses due to reduction in average daily gain, increase in feed conversion index, the lacking uniformity of pigs and costs of medication."

Harm Voets from the BI technical service did mention the estimated cost of the clinical and sub-clinical forms taken from work by McOrist et al. 1997 and Veenhuizen et al. 1998: "It is estimated to cost between €1.3 and €18.5 per affected pig, depending on the severity and duration of the disease." Harm also described

Table 1. Economic gross margin in pigs vaccinated with Enterisol Ileitis versus non-vaccinated controls. (€/pig)

Economic trait/group	Vaccination	Control	Difference
Sales (slaughterhouse)	102.3 ^a	96.2 ^b	+6.07
Piglet costs	43.1 ^a	42.3 ^b	0.89
Feed costs	35.5 ^a	34.3 ^b	-1.16
Mortality	2.2 ^a	2.5 ^b	+0.28
Total costs	80.80 ^a	79.03 ^b	-1.77
Gross margin	21.49 ^a	17.20 ^b	+4.29

Different letters indicate significant differences (p<0.01)
Assumptions: €1.40 per kg slaughtered weight; carcass grading grid for all 5 trials adapted to 80% inclusion of slaughter weights in optimal weight window; €17.50 per ton feed; 2.80 kg/kg feed conversion for the Swiss, German trial 1 and Philippine trial whereas for German trial 2 and the Danish trial actual feed conversion was used.

their own field studies to investigate the efficacy and economics of the vaccine. Concentrating on the financial returns, the combined analysis of data from the five trials showed a €4.29 higher gross margin for vaccinated pigs (Table 1).

These results are supported by Nistal's comment, "Although the mortality is more eye-catching, under the actual production conditions in the majority of farms, the indirect performance losses are principally responsible for the costs of the disease." **PP**

In our next issue we will report on how Genetiporc in Canada and Iowa Select Farms in the USA are managing ileitis infections using the new vaccine.