

*Boehringer Ingelheim Animal Health*



*Dedicated to Research for Animals.*

3	Commitment
5	Ambition
6	Introduction
8	History
10	Dedicated to Research for Animals
34	Outlook
36	Business
38	Worldwide Presence
40	Closing Remarks

## Contents\*

\* This brochure is intended exclusively for the purpose of presenting our company and showing facets of our success and how we work. The contents should not be used for information on medical or product usage. For product information, please refer to local prescribing information, scientific literature or advice from a veterinarian.



## Commitment



Christian Boehringer  
Chairman of the Shareholders' Committee

The vision of the Animal Health business is to foster the health and well-being of mankind by contributing to an adequate supply of safe, nutritious food and by promoting the emotional and physical benefits arising from the human animal bond.

For more than 50 years our Corporate Division Animal Health has been providing solutions for the prevention and treatment of diseases in animals.

The sound expertise in scientific research at Boehringer Ingelheim allows us to explore innovative technologies to develop tomorrow's drugs to the benefit of both animals, and ultimately, humans. The shareholders of Boehringer Ingelheim firmly believe that contributing to the supply of high-quality animal protein is becoming an increasingly challenging task in times where the world population is growing and global competition for agricultural products is becoming increasingly fierce. In our constantly changing society, the role of companion animals and their significance for the well-being of their owners is assuming ever more importance. The transfer of scientific concepts from human medicine to Animal Health continues to enrich our Animal Health portfolio. Research is the driving force behind future success – for the benefit of animals and ultimately the health of mankind.

## Ambition



Joachim Hasenmaier  
Managing Director

Based on our own research and the synergy with our human pharmaceutical expertise, Boehringer Ingelheim Animal Health delivers leading solutions to prevent, treat and cure animal diseases. We believe that it is necessary to focus to be world class. Therefore, we have made a conscious decision to focus on specific diseases and animal species, such as small animals, cattle, pigs, horses and poultry. We strive to set standards and provide for unmet medical needs. We are driven by the wish to improve animal welfare as an integral part of a healthy future for mankind.

Over the past years, Boehringer Ingelheim Animal Health has continually been one of the fastest growing international companies in the animal health industry.

An achievement that further motivates our teams on the path to our common goal: to become a world-class leader in the prevention and treatment of animal diseases. We can consolidate the success of our company by further exploring vaccination strategies across all major species and by providing novel therapeutic solutions for chronic diseases in companion and food-producing animals. For the future, we subscribe to the belief

that only innovation can make a genuine difference for animals and their owners, thus building trust on the part of our customers in the long term. With professional research teams and valuable networks, combined with our sound knowledge of the markets and our corporate culture, we will continue to research and develop optimum solutions for animals in need of our help.

## Introduction



Albrecht Kissel  
Head of Business Development

The following pages describe a collection of achievements originating from the company's Research and Development (R&D) teams who have established the basis for the success of Boehringer Ingelheim Animal Health.

The people presented are responsible for scientific breakthroughs and the stories provide a feeling for the atmosphere in which this was possible. Dedication, curiosity, teamwork, scientific expertise, inspiration, vision and striving for success are some of the characteristics of those people working in and for Boehringer Ingelheim Animal Health.

Despite the enormous challenges presented by nature, trials that fail time and time again, or a disease that appears to resist all efforts,

the persistence and winning spirit of Boehringer Ingelheim Animal Health's employees and teams made it possible to come up with products and solutions to improve the health of animals and, ultimately, the health and well-being of mankind.

The teams are interdisciplinary and international. They are proud of their results and are committed to delivering more.

Although the people named personally in this brochure have contributed significantly to the success of Boehringer Ingelheim Animal Health, they are just some representatives of highly-committed teams. And while R&D is the backbone of Boehringer Ingelheim Animal Health, all other functions have made their own indispensable contribution to the company's success. It is

impossible to name all the colleagues and functions here, but they are all part of Boehringer Ingelheim Animal Health and all deserve acknowledgement for their contributions to innovation.

**And while R&D is the backbone of Boehringer Ingelheim Animal Health, all other functions have made their own indispensable contribution to the company's success.**

Since the early days, innovation and research have always gone hand in hand at Boehringer Ingelheim. This also applies to the Animal Health division which has formed part of Boehringer Ingelheim's core business activities for over 50 years. Meanwhile, Boehringer Ingelheim Animal Health has become one of the top 10 animal health companies in the world.

It all started in 1955 when the company's crop protection affiliate was integrated into the business. This paved the way for activities in animal health. From the very outset, Boehringer Ingelheim Animal Health has always put emphasis on offering scientific support for their customers – veterinarians and farmers – while providing innovative solutions in the form of animal health products.

Pioneer products included LOBELIN® and VOREN®. In the wake of the post-war economic upswing, both the demand for meat and the number of pets grew steadily, raising the demand for animal health products.

In the 1960s, Boehringer Ingelheim Animal Health activities were further expanded across Europe, creating the basis for its global animal health business. In the early 1980s operations were established in the United States. The acquisition of Fermenta and NOBL constituted further strategic steps in the world's largest market for veterinary products.

Subsequently, production of global biological pig vaccines was started up successfully in St. Joseph, Missouri, USA. Important products manufactured at this site include INGELVAC CIRCOFLEX®, INGELVAC® PRRS, INGELVAC® M.HYO, ENTERISOL® ILEITIS, INGELVAC® AUJESZKY, ELITE® and EXPRESS®.

As a division within a successful human pharmaceutical company, Boehringer Ingelheim Animal Health benefits from continuous access to high-quality molecules generated by human pharmaceutical research and development. Key products originating from that source include METACAM®, VETMEDIN®, VENTIPULMIN® and VOREN®.

Research cannot be successful if it is limited to within the walls of Boehringer Ingelheim alone. Research is only possible if a group of highly-qualified and dedicated researchers cooperate in the search for solutions to medical needs. It also requires international networking with high-ranking academics and research institutes in various countries. In addition, Boehringer Ingelheim Animal Health has successfully complemented its inhouse R&D efforts by licensing activities. Colleagues are, therefore, committed to scientific exchange and fruitful cooperation in their respective fields.

Research is only possible if a group of highly-qualified and dedicated researchers cooperate in the search for solutions to medical needs.

Boehringer Ingelheim Animal Health –  
a business from scratch



## Curing by curiosity



Hubert Hummelt

In 1986, there was a proliferation of mysterious reports about sick pigs in the USA. Anorexia, abortion, stillbirths, mummified fetuses, weak piglets – the symptoms varied and researchers across the continent were struggling to find the cause: a bacterium, a virus, a fungus?

Speculation was rife, there was not even a consistent name for the problem. Various acronyms began to appear such as MSD (Mysterious Swine Disease), MRS (Mysterious Reproductive Syndrome) and PEARS (Porcine Epidemic Abortion and Respiratory Syndrome). In order to cope with the host of different names, researchers at Boehringer Ingelheim Animal Health soon called all of these: Multi Acronym Disease or “MAD” for short. “Magic” diseases like the one above provoke the curiosity of dedicated scientists.

Eventually, a talented scientist at Boehringer Ingelheim Vetmedica, Inc. in St. Joseph, USA, was given a tissue sample from an affected pig. Curious as to why his friends at the University of Minnesota were unable to identify the pathogenic agent, he invested enormous effort until he eventually isolated the previously unknown virus, now known as Porcine Reproductive and Respiratory Syndrome Virus (PRRSV).

But was it worth continuing research? Or were these cases simply isolated outbreaks that would not justify the development of a new vaccine at commercial level? Although investment was considered “MAD” by some, Hubert Hummelt, Head of R&D in those days, and his colleagues persisted and were finally given the go-ahead – their curiosity feeding their motivation.

Then suddenly, an epidemic broke out in many pig fattening farms in northern Germany and the Netherlands, affording the project a completely new dimension. Since the key problem in PRRS research, identification of a cell line that could propagate the PRRS virus, had been solved earlier by the colleagues in St. Joseph, the researchers had a sound basis from which to continue with their work towards an efficient vaccine. Hubert Hummelt was now coordinating research in various working groups on both sides of the Atlantic, and feverish research eventually produced an attenuated PRRS vaccine strain.

Only three years were needed between isolation of the pathogen and vaccine approval in the United States, and two more years before INGELVAC® PRRS was available to German veterinarians and farmers. This was an extremely short development

period and a marvellous example of how curiosity can lead to innovation and the introduction of an effective vaccine in record time.

Active immunisation with INGELVAC® PRRS MLV is now a standard in modern pig farming around the world and has only recently saved thousands of piglets in East Asia where a new and devastating outbreak occurred.

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## Why would you find pigs on the third floor?



Volker Ohlinger

When the Porcine Respiratory and Reproductive Syndrome (PRRS) broke out in Germany in the early 1990s, top priority was given not only to the search for an effective vaccine, but also to the search for a reliable diagnostic method.

Therefore, when a protective vaccine became available, diagnostic know-how and capacity had to be developed. This prompted the foundation of the bioScreen European Veterinary Disease Management Center in Münster which is ideally located in a region renowned for being the “pig belt” of Germany. The centre is led by virologist Volker Ohlinger.

Although a serological test had rapidly been launched on the market, identification of early infection required a molecular diagnostic procedure. This proved very challenging. At the peak of the epidemic, Volker Ohlinger and his team established an innovative procedure which not only allowed various types of PRRS virus to be

**bioScreen quickly earned a reputation as a flexible and highly efficient diagnostic centre of excellence for infectious animal diseases.**

differentiated, but also virus evolution in the field to be monitored. bioScreen quickly earned a reputation as a flexible and highly efficient diagnostic centre of excellence for infectious animal diseases. Interestingly, the other occupants of the building in the biotech park quickly got used to sharing the elevator with farmers bringing a litter of newly-born piglets along for examination at bioScreen on the third floor!

In more than ten years since it was established, bioScreen has supported the development of most of Boehringer Ingelheim Animal Health’s pig vaccines, namely INGELVAC CIRCOFLEX®, INGELVAC® PRRS, INGELVAC® M.HYO and ENTERISOL® ILEITIS. In addition, bioScreen provides essential support in the clinical development of new vaccine research projects. For veterinarians and farmers from most European and some Asian countries, bioScreen has become a valuable centre for diagnostics.

Anyone who has ever worked on a pig farm knows how exhausting and stressful an injection is, for both the animals and the farmers. Based on this experience, researchers all over the world are working constantly on solutions to reduce the stress of vaccine injections – especially for widespread diseases that affect thousands of animals.

*Mycoplasma hyopneumoniae* (M.hyo) is one of the most common pathogens in pig farming that makes farmers' lives difficult. Apart from causing the animals to suffer from cough, fever and secondary infections, it also lowers performance – the animals show reduced growth and need more food. The infectious agent spreads very easily through the air, even over distances of up to three kilometres. Moreover, infection of entire herds is possible simply by adding a few newly-

infected animals to the group. In an effort to control the disease, preference is given to prophylactic vaccination rather than treating the animals with antibiotics.

A number of *mycoplasma* vaccines have been available on the market since the 1990s, but these all had to be administered twice, doubling the stress for the pigs.

Although the development of a single-dose product had low priority, Sharlene Miller, a scientist at Boehringer Ingelheim Vetmedica, Inc. in St. Joseph, USA, was fascinated by this concept. She convinced the Head of R&D to put her microbiological expertise to good use by trying to find a suitable formulation to achieve that goal.

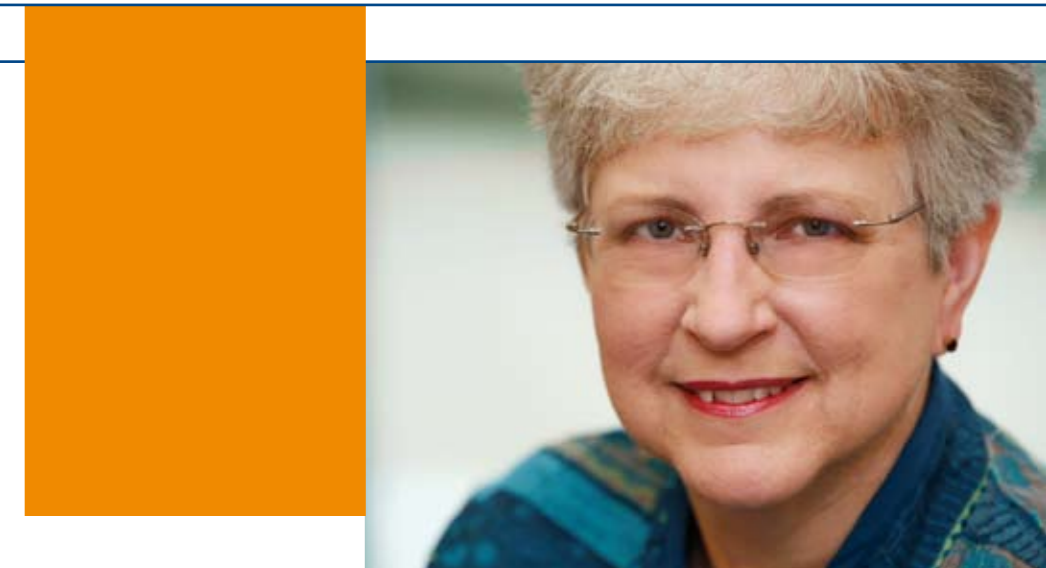
Through optimization and differentiation of an existing product, she found the answer in a special mixture of biologically degradable oils – IMPRAN®.

By means of this antigen depot, a single shot now provides long-lasting protection against M.hyo-induced diseases, cutting the necessary vaccination stress by half.

Based on the same concept, a successor vaccine, INGELVAC MYCOFLEX® has been developed. In the United States the product is licensed for the combination with other Boehringer Ingelheim Animal Health vaccines, which further reduces the stress for animals and farmers.

By means of this antigen depot, a single shot now provides long-lasting protection against M.hyo-induced diseases, cutting the necessary vaccination stress by half.

Give it one shot



Sharlene Miller

Catching two birds with one stone: reduce the need for antibiotics and avoid stress in piglets



Michael Roof



Jeremy Kroll



Knut Elbers

In the early 1990s, there was a marked increase in the number of pigs diagnosed with “hosepipe gut” disease. This disease is characterized by thickening of the gut wall and low performance among fattening pigs. Even worse, this disease occurs in gilts and young boars, causing acute disease and death.

The putative cause of the disease was identified at the University of Edinburgh, United Kingdom, in 1975. However, it took 19 years until it could be proven that a specific bacterium, *Lawsonia intracellularis*, was the culprit.

This is where the team at the Health Care Center in Ames, Iowa, USA, stepped in! The key challenge for the preparation of a vaccine was to propagate *Lawsonia*, an obligate intracellular parasite. Interestingly, *Lawsonia* does not tolerate oxygen well, whereas its host, a mammalian cell,

Unlike the usual vaccines, this product is typically administered with the drinking water, reducing the need for stressful injections.

desperately needs oxygen. This paradox had to be resolved not only under lab conditions, but also on a commercial scale.

The problem was resolved through intensive collaboration between Boehringer Ingelheim Animal Health scientists, academic institutes in Europe and the United States, and biotechnologists. The bacterium was finally attenuated and samples for clinical trials were provided. Michael Roof and Jeremy Kroll were responsible for that endeavour. They were also in charge of clinical development of the product. Following the encouraging results, a vaccine called ENTERISOL® ILEITIS was introduced on the US market.

Further extensive field trials were initiated by Knut Elbers and his team in a move to meet European requirements. This effort surpassed all of Boehringer Ingelheim’s previous vaccine

trials in the animal health business and proved clearly that vaccination against ileitis not only reduces the need for antibiotic treatment, but improves the most important production parameters. Unlike the usual vaccines, this product is typically administered with the drinking water, reducing the need for stressful injections.

The enormous amount of physical work was only possible with the joint and unconventional voluntary support of colleagues from all the departments at Boehringer Ingelheim Animal Health who helped by teaming up with the researchers: controllers in wellies, secretaries weighing piglets, and sales managers counting blood samples!

Even though porcine circoviruses were only discovered in the 1990s and the impact on pigs' health was far from clear, Boehringer Ingelheim Animal Health decided to start investigations into a potential vaccine to control this virus. Despite seemingly insurmountable problems along the way, the global team in Ames, Iowa and St. Joseph, Missouri, USA, as well as Ingelheim, Germany, continued their research and development. Marc Eichmeyer from Ames invested huge effort in integrating the global team with all its engaged individuals.

At the end of the day, the group came up with Boehringer Ingelheim Animal Health's first recombinant vaccine that not only modulated the course of the viral infection, but also resulted in a most impressive increase in productivity.

The manufacturing process of the vaccine was entirely new territory for Boehringer Ingelheim's Animal Health business as it is based on a recombinant viral protein. This protein is expressed in an insect virus that had to be produced on a commercial scale.

Even larger field trials – compared with the testing of the *Lawsonia intracellularis* vaccine – were conducted and demonstrated the safety and efficacy of that product. Motivated by Vicky Fachinger, Boehringer Ingelheim Animal Health colleagues from all disciplines were anxious to help. They enthusiastically collected all the data while investigating and weighing the piglets.

INGELVAC CIRCOFLEX® became firmly established following an acute outbreak of PCV2-associated

disease in the USA and Canada in 2006; this product contributed to stopping the devastating epidemic on many farms efficiently. As a result farmers found that the vaccination had improved their profitability by increasing weight gain, improving feed conversion and reducing the need for using antibiotics. Moreover, the vaccination resulted in a significant reduction in mortality of the pigs. This unprecedented success also means that the company's vaccine manufacturing department had to produce a large amount of product at short notice.

Thanks to efficient teamwork, production capacity was increased to the maximum within a very short timeframe, allowing market demand to be met.

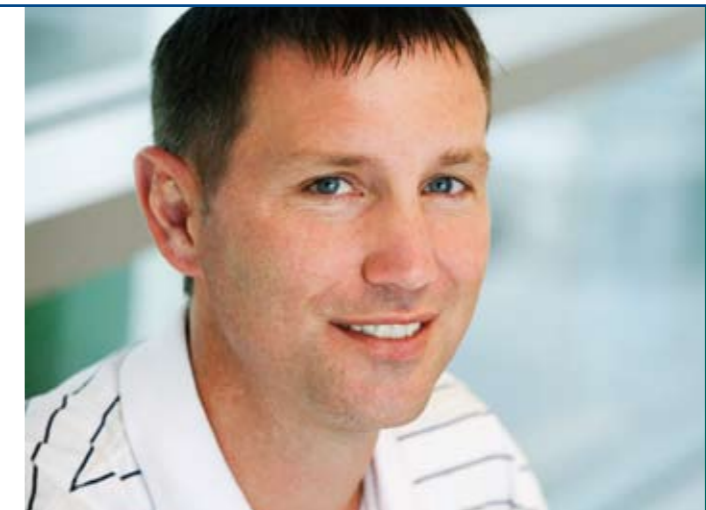
The excellent team spirit within Boehringer Ingelheim Animal Health was demonstrated by research groups pulling together across the Atlantic. Together, they produced the results and evidence necessary for the European introduction of INGELVAC CIRCOFLEX® at the beginning of 2008 – this was a prime example of the potential that can be realized if all employees are united by a common goal.

The excellent team spirit within Boehringer Ingelheim Animal Health was demonstrated by research groups pulling together across the Atlantic.

## Pulling together across the Atlantic



Vicky Fachinger



Marc Eichmeyer

METACAM® became the first blockbuster product of Boehringer Ingelheim Animal Health and is licensed today for a large number of domestic species.

## Challenging a paradigm



Günther Engelhardt

In the middle of the night, when Boehringer Ingelheim office and laboratory staff had already left the Biberach research site for home hours earlier, one light still shone stubbornly.

Pharmacologist Günther Engelhardt, who had been experimenting with non-steroidal anti-inflammatory drugs (NSAIDs) since the 1960s, simply could not find any rest. He was challenging a pharmacological paradigm: “The desirable effects of anti-inflammatory drugs and their undesirable side effects are in a fixed relationship to one another.” However, his own results undermined that opinion. He had discovered substances that were a lot less likely to cause gastric ulcers despite their potent anti-inflammatory effect. Was it possible that the dogma was wrong?

Many other scientists would have doubted their own results and stopped their research – after all, the textbook opinion was based on statements by the Nobel Laureate Sir John Robert Vane! But Günther Engelhardt was of tough stock. In the end, it took more than a decade of trial and error before he found an oxicam that promised to deliver the required effectiveness. Meloxicam provided a strong and long-lasting anti-inflammatory effect whilst simultaneously allowing for good gastric tolerability. The timing was unfavourable, however, as Günther Engelhardt was fully occupied with a number of other projects.

Nevertheless, he continued to work on the substance together with a group of like-minded allies – the so-called “meloxicam gang”. Their investigations turned out to be immensely labour intensive and required that the entire team

worked in shifts seven days a week. Finally, in 1982 the great breakthrough! The team managed to prove that meloxicam was not only effective, but also efficient and safe.

This caused a stir, not only at Boehringer Ingelheim, but also among experts worldwide. Finally they had proof at hand which would change the textbook paradigm that had cost Günther Engelhardt so many sleepless nights back in the 1960s. Having prompted even a Nobel Laureate to rethink, it was comparatively easy to encourage the management of Boehringer Ingelheim Animal Health to pursue development of the substance for animals.

The “meloxicam gang” got a go-ahead and now became an official development team. Although the next steps towards licensing METACAM® for dogs followed quickly, it must have seemed like an eternity, even for the persistent Günther Engelhardt – after all, it had taken more than 20 years from the very beginning to the first launch on the market in 1993. But the effort was worthwhile – METACAM® became the first blockbuster product of Boehringer Ingelheim Animal Health and is licensed today for a large number of domestic species. Inflammation and pain in animals can be treated successfully and much safer, also Günther Engelhardt’s own shepherd dog benefited from this treatment.

It was a challenging task to find the delicate balance for the ideal dose for long-term use in this species.

Are cats just small dogs – or not?



Rüdiger Narbe

The introduction of METACAM® for dogs in 1993 was a groundbreaking success. But instead of resting on its laurels, Boehringer Ingelheim Animal Health with its philosophy and ideals to help both pets and human beings, focused on a new species: the cat. This idea was a new concept at the time. Chronic pain was rarely recognized in cats. Dogs limp visibly when they suffer from osteoarthritis and humans readily understand the symptoms. Cats with pain in their joints, however, just move more slowly or curl up in a corner, leading their owners to believe that they are simply old and tired.

With no reference models at hand, the researchers faced the challenge of measuring pain in cats and proving the success of their treatment. This problem was resolved by Rüdiger Narbe, who was working with the Boehringer Ingelheim Animal Health development team. In collaboration with his colleagues in St. Joseph, Missouri, USA, a suitable test system was established. With joint forces from both sides of the Atlantic, the test system was soon brought to maturity and finally work could begin on finding the optimum treatment dose for cats.



Udo Ehlers

Udo Ehlers, Project Manager for METACAM® at the time, pushed the programme forward persistently. He was strongly encouraged by field reports from practising veterinarians who confirmed the need for pain control in cats. It was a challenging task to find the delicate balance for the ideal dose for long-term use in this species. Subsequent field trials produced excellent results.

This drug approved for control of chronic pain in cats was launched on the market in 2007. Both cats with pain and their owners can now enjoy an harmonious life together once again.

## A coughing race horse recovered again!



Ernst Salamon

Researchers at Boehringer Ingelheim Animal Health always work hand in hand with Boehringer Ingelheim human medicine to make optimum use of synergies. In the early 1970s, when the exposé on clenbuterol, a tocolytic, hit the desk of horse lover Ernst Salamon, he was thrilled.

As it showed a longer and more potent effect, yet did not increase pulse rate as a side effect, it promised to relax the bronchial muscles in case of broncho spasms. Unlike previous beta-adrenergic agents, the heart remained completely unaffected. “Why,” Ernst Salamon asked himself “shouldn’t horses suffering from chronic respiratory disease (also called COPD/chronic obstructive pulmonary disease) also benefit from this effect?”

Although there was a strong belief in the veterinary community that COPD was a rare disease in horses, Ernst Salamon was convinced that this was not the case. Proving it, however, was another

matter. Measuring lung function in horses was not routine in those days. Luckily, Ernst Salamon identified a capable veterinary scientist at the University of Zurich, Switzerland, who helped solve the problem. The first clinical trial was initiated.

Imagine how tedious it was to open up to 100 ampoules, originally intended for human use, in order to treat a single horse. Yet the effort was not in vain as the lung function of affected horses showed a dramatic improvement. Clinical trials initially caused concern among veterinarians who reported that treated horses were producing huge amounts of purulent mucus. It was not easy to convince them that this was in fact a sign of the therapeutic efficacy leading in clinical improvement.

The most extraordinary result was certainly that of a former trotting champion who showed poor performance and the occasional cough. After treatment with VENTIPULMIN® his performance improved and he soon returned to the New York racing scene.

In fact, up to 80% of horses kept in stables or who get in contact with dust and pollen suffer from COPD or milder forms of chronic airway diseases and may benefit from treatment with VENTIPULMIN®. A researcher’s dedication to his idea enabled Boehringer Ingelheim Animal Health not only to discover a widespread disease, but also to provide a successful treatment and improve the daily life of many horses.

Although there was a strong belief in the veterinary community that COPD was a rare disease in horses, Ernst Salamon was convinced that this was not the case.

As with so many success stories, coincidence had led to the development of an innovative vaccine against fungal skin infections. This, however, had a very unusual origin. It also took the dedication of an animal health professional, ever alert to opportunities arising, even when he was far away from his office.

Back in 1993, Joachim Karle, who was working at Boehringer Ingelheim Animal Health, met a Russian veterinarian at a horse dealer's paddock. It was their shared passion for horseback riding that brought them together. In spite of a significant language barrier, they quickly established that they were both equally fascinated by vaccines. As luck would have it, Joachim Karle's

Russian colleague in cooperation with his wife had developed a polyvalent vaccine to fight fungal skin infections in horses and circus animals. It became clear that this was a vaccine with promising potential. Consequently, he convinced his management to pursue the opportunity. Shortly after that decision, the project was taken up by Boehringer Ingelheim Animal Health.

In the course of that development it became obvious that the work was performed in a completely exotic environment. The vaccine was examined in Russian circus animals, including lions, tigers, coatis, camels and polar bears. Often, the dangerous animals were treated by the researchers "entering the ring" themselves.

Joachim Karle was later able to share this thrill first hand during a visit to the Russian State Circus – an opportunity not available every day to members of animal health industry.

Although the team was small, it was quickly able to generate the data supporting the marketing authorization for horses, cats and dogs. What had originally started as a hunch finally resulted in a successful vaccine – INSOL® DERMATHOPHYTON.

## Take the chance



Joachim Karle

The vaccine was examined in Russian circus animals, including lions, tigers, coatis, camels and polar bears.



## A long and happy life together

### Jürgen Dämmgen

Therapeutic principles in veterinary medicine often stem from similar conditions in humans. In case of VETMEDIN® it was Jürgen Dämmgen's empathy with suffering animals that led to the development of one of the most successful and intensively tested heart medicines for dogs. Indeed, this was based on a rejected therapeutic paradigm from human biomedical research.

Back in the 1970s, new therapeutics were being sought for the treatment of congestive heart failure in humans. In those days, standard therapy was based on digitalis glycosides. This therapy

was frequently hampered, however, by serious side effects. One candidate was pimobendan, a compound combining two interesting mechanisms: like digitalis glycosides, it enhances cardiac contractile force, however, pimobendan is also taking the strain off the failing heart by reducing vascular resistance.

Based on its profile, pimobendan appeared to be a promising therapeutic in canine heart failure. Jürgen Dämmgen, a veterinarian, was at that time still working in Boehringer Ingelheim's human pharma research. He frequently heard of the

animals' suffering in such cases from his wife, herself a clinical veterinarian, and urged his colleagues to do something about it.

He proposed that Boehringer Ingelheim Animal Health pursue this new therapeutic option and quickly found like-minded researchers to support him. The results were exciting and the health status of those dogs that participated in the clinical trials improved considerably. VETMEDIN® is now established as a preferential treatment – a result of the QUEST trial, the largest global study of its kind. The study confirmed advantageous

**The results were exciting and the health status of those dogs that participated in the clinical trials improved considerably.**

properties for VETMEDIN®. Thanks to Jürgen Dämmgen's stamina and empathy for dogs, human and veterinary medicine were successfully aligned. VETMEDIN® is now available in over 30 countries and helps dogs and thus their owners around the world to enjoy a long and happy life together.

Hundreds of thousands of birds  
can't be wrong!



Carlos Gonzalez

In the mid-nineties, Mexican poultry producers reported reduced egg production. Boehringer Ingelheim Animal Health's poultry R&D team in Guadalajara investigated the problem in an effort to establish the cause. Despite countless efforts, the scientists only succeeded in isolating well-known bacteria common in poultry which were not the suspected cause of the disease, namely: *Manheimia haemolytica*, *Pasteurella trehalosi* and *Pasteurella haemolytica*-like microorganisms. None of the suspected pathogens listed in the textbooks proved to be primarily responsible for this issue.

Carlos Gonzalez and his team began to search for an infectious agent that could potentially cause the problem and provide a solution.

Many experts discarded the idea of considering those bacteria as the cause of the disease and searching for a vaccine to control a *Pasteurella*

*haemolytica*-like organism. Fortunately, one of the Mexican key opinion leaders in aviculture showed visionary insight and supported this idea. This saw the start of tests with vaccine prototypes. The results were surprising. The previously encountered loss of productivity in the vaccinated layer birds was effectively controlled. As the investigator put it, "hundreds of thousands of birds can't be wrong"!

With encouraging data at hand, the project now gained significant interest in academic circles. Exciting findings were first presented at an international conference in Copenhagen, Denmark. The team was contacted by a leading Danish research group which was also interested in these "novel" microorganisms. According to their genetic analyses, the hitherto "*Pasteurella*"-like organisms were now thought to be part of a novel family of bacteria called "*Gallibacterium*".

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The emerging scientific support for the novel and significant *Gallibacterium* further encouraged the poultry team to develop a vaccine to control "*Gallibacterium*"-induced diseases, and to establish vaccination programmes in a number of egg- and poultry-producing countries.

This resulted in the registration and successful marketing of the first vaccine for this disease: VOLVAC® GALLIBACTERIUM. In addition, the robust and substantial improvement in egg production after vaccination in farms affected by *Gallibacterium anatis* convinced opinion leaders, poultry producers and scientists of the beneficial impact of this vaccine.

There is now an entire chapter on *Gallibacterium* in the book entitled "Diseases of Poultry", the "Bible" of poultry medicine. Thanks to the persistence of a small but dedicated research team, not only has the cause of this emerging disease been discovered and made public, but a means has also been provided to control it.

In spite of tremendous efforts to improve control of mastitis in dairy cows, this disease is still one of the most common reasons for premature exit from production. In an attempt to offer better options for this challenging situation, Boehringer Ingelheim Animal Health has made significant investments in the search for preventive vaccines. However, immunology and the biological mechanisms behind host defence in that organ are poorly understood.

Moreover, the efficacy of conventional vaccines, e.g. inactivated bacteria, has remained limited at best. The complementary search for novel antibiotic principles has provided limited new approaches for product developments globally.

Facing these challenges, a group of Boehringer Ingelheim Animal Health scientists, led by Gabriele Friton, embarked upon a third route: they studied clinically well-proven antibiotics and their combinations from today's point of view, re-examined their efficacy *in vitro* and *in vivo*, scrutinized their quality and safety with the help of modern methods, and carefully investigated the interactions between the antibiotics used in combination.

In view of the absence of evidence to support the efficacy of antibiotic combinations, the added value of a combination had become increasingly controversial. This sceptical attitude was shared by regulatory authorities, clinical opinion leaders and dairy practitioners.

### The team deliberately took an unconventional and pragmatic approach.

Yet, the Boehringer Ingelheim Animal Health mastitis team was convinced that there was a good rationale for the right combination and chose a product now named UBROLEXIN®, a combination of an aminoglycoside and a lactam antibiotic.

Those active ingredients were thoroughly re-investigated – using state-of-the-art methodologies – for their antimicrobial effect on a host of different pathogens, both as single compounds and in combination. The team demonstrated convincingly that the agents indeed act in synergy; this was shown by the fact that the combination did not simply produce an additive effect, but rather potentiated the individual efficacy.

Extensive field efficacy studies were performed in several European countries. The results obtained from those investigations further underlined the value of UBROLEXIN®. Besides the improvement of clinical symptoms, there was also substantial

relief from bacterial burden and a reduction in the number of inflammatory cells. The mastitis team had thus proven that those two “traditional” antibiotics not only cured infected udders, but in combination were extraordinarily effective. The product was thus approved in 27 European countries in 2008.

The pragmatic approach chosen by the team not only resulted in a highly effective antimicrobial medicine for the customers. It also demonstrated that tried and tested products remain an essential tool in the treatment of mastitis.

The team deliberately took an unconventional and pragmatic approach and demonstrated that conventional attitudes towards combination therapy in mastitis can be overcome with good science and solid data. Above all, they were successful!

Established therapies – why not?



Gabriele Friton

## Research and Development at Boehringer Ingelheim Animal Health



Randolph Seidler  
Head of R&D

Innovation is the key to resolving unmet medical needs and making a difference in the health and life of Boehringer Ingelheim Animal Health's patients. Innovative products resulting from the company's research and development efforts are the driving force behind its business success. Over the years Boehringer Ingelheim's Animal Health business has set standards for innovation in many areas such as pig vaccines or heart failure in dogs. As a research-driven company, it continuously invests approximately 13% of its revenues in R&D. This is one of the highest rates in the industry.

R&D efforts at Boehringer Ingelheim Animal Health focus on two target areas: vaccines for the protection of food-producing animals and pharmaceutical products to treat chronic diseases in companion animals. Numerous partnerships with

academic institutions and Boehringer Ingelheim's Human Prescription Medicines R&D, provide an effective scientific environment. High-level research generates novel ideas that result in innovative products for both humans and animals.

Several major developments will provide the framework for the company's R&D activities in the future: vaccines will gain significantly in importance in all species due to the growing realization that, wherever possible, prevention is preferable to therapeutic intervention. As a result, the need for antibiotic treatment and the risk of antibiotic resistance can be reduced. Recent technological progress has significantly enhanced the company's ability to generate vaccines with better and more predictable efficacy. This includes the integration of sophisticated molecular biology and the decod-

ing of the genome of target pathogens. The company further believes that the early identification of emerging diseases, coupled with tools for their control, will help to protect animals and farmers in the future.

In a changing demographic and social environment, pets are increasingly assuming the role of companions and family members. Consequently, they are more frequently given the best health care and treatment, resulting in a longer and happier life. Accordingly, there is a growing need for optimized therapeutics that are safe, effective, and easy to use. Ever closer scrutiny by the expert veterinarian will further increase the need for high-quality clinical trials which will help meet the more stringent requirements to treat according to "evidence-based medicine".

R&D at Boehringer Ingelheim Animal Health is dedicated to providing innovative and effective treatments that make a difference. To achieve this the company has succeeded in attracting very talented scientists and has provided them with an environment in which they can develop and push forward their ideas. Boehringer Ingelheim Animal Health believes that the company is well-equipped to cope with the future challenges in veterinary medicine and that the organization will continue to rank among the leaders in innovation in the animal health industry.

High-level research generates novel ideas that result in innovative products for both humans and animals.

## Boehringer Ingelheim Animal Health – a successful and growing business



Erich Schött  
Head of Area Management Americas & AAA

Over the past 50 years, Boehringer Ingelheim Animal Health has developed into a global business with leading positions in key segments. Boehringer Ingelheim Animal Health has nearly tripled its market share over the last 15 years, primarily through innovation-driven internal growth. The company is now firmly established among the top 10 animal health companies and is represented in all relevant markets across all five continents.

In recent years, the growth has been generated mainly by the successful launch of innovative products, especially vaccines for the prevention and control of pig diseases. INGELVAC® and ENTERISOL® brands account for a significant portion of Boehringer Ingelheim Animal Health sales and continue to show strong development. The other important growth pillar within the animal health segment is and has been the

companion animal business with METACAM® and VETMEDIN® as leading brands. New pharmaceutical specialities providing novel treatment options for cats and dogs will further strengthen the position of Boehringer Ingelheim Animal Health.

The cattle business with MAMYZIN® and UBROLEXIN®, the equine business with VENTIPULMIN®, and last but not least the poultry business with the VOLVAC® product line will continue to be significant, growing lines of business, highlighting the commitment to consolidating Boehringer Ingelheim Animal Health's presence in these segments.

A focused marketing and sales policy, building and promoting strong global brands and supported by a professional technical and scientific service, has improved customer relationship and helped increase profitability.

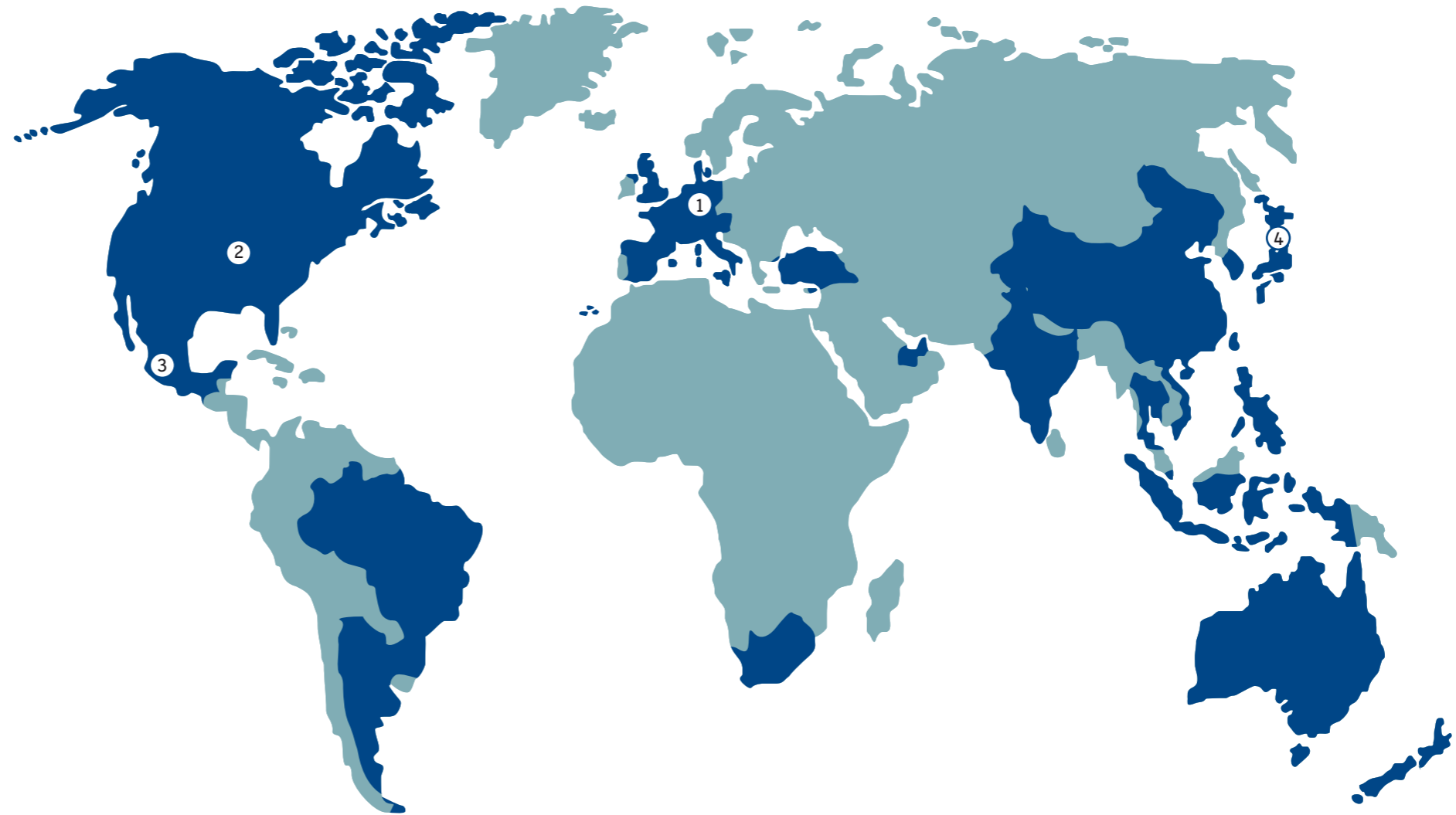
In recent years, Boehringer Ingelheim Animal Health has become a truly global company with a greatly improved position in the US and emerging markets, complementing its traditionally strong EU presence.

Boehringer Ingelheim Animal Health continues to invest significantly in R&D in a move to secure future growth and fulfil its mission: provide solutions for the prevention and treatment of diseases, both now and in the future.

For detailed information about the Boehringer Ingelheim Animal Health business, please see [www.boehringer-ingelheim.com](http://www.boehringer-ingelheim.com).

**Boehringer Ingelheim Animal Health continues to invest significantly in R&D in a move to secure future growth and fulfil its mission: provide solutions for the prevention and treatment of diseases, both now and in the future.**

Dedicated to  
Research for Animals –  
Worldwide



Boehringer Ingelheim Animal Health is represented in all relevant markets on all five continents.

R&D sites:

- ① Boehringer Ingelheim Animal Health GmbH, Ingelheim, Germany
- ② Boehringer Ingelheim Vetmedica, Inc., St. Joseph, Missouri, Fort Dodge and Ames, Iowa, USA
- ③ Boehringer Ingelheim Vetmedica S.A. de C.V., Guadalajara, Mexico
- ④ Boehringer Ingelheim Vetmedica Japan Co. Ltd., Tokyo, Japan

■ Affiliates of Boehringer Ingelheim Animal Health GmbH

## Closing Remarks



Hubertus von Baumbach  
Head of Corporate Board Division Finance  
and Animal Health

Allow me to close by thanking you on behalf of every member of Boehringer Ingelheim Animal Health for your interest in us. In the stories, you have “met” colleagues who have made a key contribution to the success of our Animal Health business. Know-how, dedication and spirit were indispensable factors in their work.

We hope that by now you have a positive picture of what Boehringer Ingelheim Animal Health is all about. The vision of the Boehringer Ingelheim Corporation is to serve our customers by providing “Value Through Innovation”. By combining

this culture with operational excellence in bringing breakthrough products to market, Boehringer Ingelheim Animal Health will continue to serve animals and humans alike.

Innovation is the backbone of our business. We are committed to providing the best solutions for the unmet needs of our customers. Striving for these goals is in our opinion the best preparation for sustainable success in the future.

Join us on this journey.

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