



IMPROVAC® Mode of Action

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Introduction

IMPROVAC FOR PIGS, IS A NOVEL VETERINARY IMMUNOLOGICAL, OR VACCINE, FOR THE CONTROL OF BOAR TAIN IN ENTIRE MALE PIGS.

IMPROVAC has been successfully used in Australia since 1998 and as of March 2008 has been approved in 16 additional countries world-wide. The product is being progressively introduced to pig producing markets around the world.

Because IMPROVAC is different to other veterinary products it is important to understand its mode of action and to understand how it can be used to benefit pigs, producers and society in general.

Why control boar taint?

Boar taint is an unpleasant odour and taste predominantly associated with the cooking and eating of pork from some sexually maturing male pigs. An unpleasant experience with boar taint can result in consumer rejection of pork. The main compounds responsible for boar taint are androstenone and skatole.

Androstenone is a steroid hormone produced directly by the testicles of the maturing male pig. It serves as a pheromone and accumulates in the salivary gland. Being highly lipophilic, it also accumulates in fat where it can contribute to boar taint.

KEY POINTS

- IMPROVAC is a novel immunological product for the control of boar taint. It works solely through the immune system of the pig.
- IMPROVAC is not a hormone and has no hormonal or pharmacological activity.
- IMPROVAC is not a genetically engineered product and contains no microbiological agents.
- IMPROVAC has no oral activity if ingested.
- IMPROVAC is as effective as physical castration in the successful elimination of boar taint.
- IMPROVAC vaccinated pigs produce pork with the same high eating quality as pork from physical castrates and female pigs but in a more profitable, humane and environmentally responsible manner than current practices.

Skatole is produced, in boars, castrates and female pigs, by bacterial digestion of the amino acid tryptophan in the pig's hind gut from where it is absorbed and, if not cleared by the liver, accumulates in fatty tissues. In intact male pigs the liver is less efficient at metabolizing skatole than in females or castrated males, leading to an accumulation of boar taint (1). Occasionally, taint caused by skatole is detected in pork from female pigs and physically castrated males (1, 2), particularly when the pigs have been heavily exposed to faecal matter before slaughter as skatole present in faeces can be absorbed through the skin (1),

Boar taint is traditionally controlled by physical castration early in life. However, problems with castration make it undesirable. Compared to intact boars, castrates are less efficient at converting feed into weight gain, are fatter, require more feed and produce more effluent. There are also significant animal welfare concerns with physical castration (1).

External pressures on pig production, from a variety of sources, are putting increasing pressure on pig producers to become more economically efficient, whilst also improving both environmental performance and animal welfare.

IMPROVAC gives pig producers a powerful new tool to control boar taint and benefit from the natural growth and carcass quality advantages of boars.

What is IMPROVAC?

IMPROVAC is a unique immunological product, or vaccine, for the control of boar taint in entire male pigs. IMPROVAC provides an immunological, non-surgical solution for this universal problem in pig production.

As a result of how it works and when it works IMPROVAC:

- Reduces the accumulation of boar taint compounds to the sub-sensory levels typically present in castrated male or female pigs. (3, 4, 5, 6)
- Provides an animal welfare-friendly alternative to physical castration.

- Allows the natural growth of an intact male pig to occur during the fattening period. In other words, it prevents the losses in growth performance and carcass conformation that occur as a direct consequence of physical castration very early in life. (3, 7, 8).
- Eliminates the mortality and morbidity associated with physical castration.

IMPROVAC's only direct effect on the pig is to stimulate specific antibody production that results in the elimination of boar taint.

IMPROVAC does not add hormones to the animal nor does it stimulate hormone production (9). To the contrary, it is simply an immunological way to produce castration.

How is IMPROVAC made?

The antigen in IMPROVAC is comprised of a synthetic, incomplete analogue of natural GnRF (Figure 1) which is conjugated (covalently linked) to a carrier protein (used extensively in human pediatric vaccines).



Figure 1: Schematic representation of natural GnRF and the GnRF analogue in Improvac. The modification to the smaller end of the analogue prevents binding to the GnRF receptor in the pituitary.

By itself, the GnRF analogue is not immunologically active; therefore, it must be conjugated to a larger "foreign" protein to become immunogenic (Figure 2).

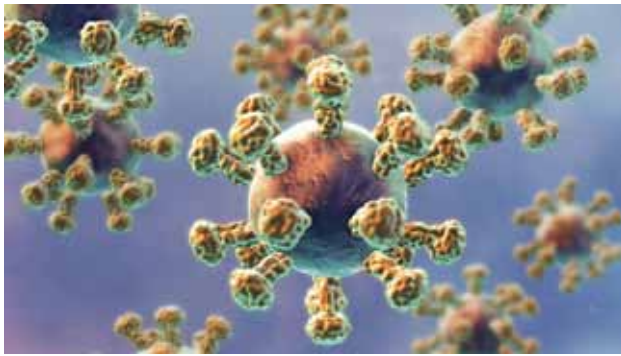


Figure 2: Schematic representation of multiple copies of the synthetic GnRF analogue bound to the surface of a large carrier protein to create the Improvac antigen.

The modification to the analogue followed by the conjugation to the carrier protein prevents any binding to the pituitary GnRF receptor and thus completely eliminates any potential for GnRF hormonal activity.

This antigen is then formulated with an aqueous non-oil based adjuvant into a ready to use injection.

How does IMPROVAC work?

Immunization with IMPROVAC stimulates the pig's immune system to produce specific antibodies that neutralise its own gonadotropin releasing factor (GnRF) thus blocking gonadal function and the accumulation of boar taint compounds

Gonadotropin releasing factor is the key hypothalamic regulator of testicular function. Endogenous GnRF released from the hypothalamus binds to specific receptors in the pituitary gland (Figure 3) where it stimulates the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH). These hormones then stimulate and control the growth and activity of the testicles leading to sexual maturity, behavioural changes and boar taint in the male pig.



Figure 3: Schematic representation of endogenous GnRF binding to specific receptors in the pituitary gland.

Like many other vaccines, a full immunization course of IMPROVAC consists of an initial priming dose followed by a second dose (at least 4 weeks later). The initial dose primes the animal's immune memory cells but does not stimulate effective levels of anti-GnRF antibodies. Thus, there is no suppression of testicular function and the pig continues to grow and behave as a fully functioning boar, benefiting from its natural growth factors.

The second dose, administered close to slaughter, produces high levels of specific anti-GnRF antibodies. These antibodies bind to and neutralize endogenous GnRF. This temporarily stops stimulation of the pituitary and thus inhibits testicular function. As a consequence, the accumulation of the boar taint compounds (androstenone and skatole), governed by testicular function, is suppressed and any taint already present at the time of immunization is eliminated. The changes in antibody concentration and testicular function and boar taint are depicted in Figure 4.

In the live pig the most visible sign of effective immunisation is that the testicles are smaller compared to non-immunized boars (Figure 5) – but it is important to remember that this is due to a lack of the pig's own hormones and is not a direct effect of IMPROVAC (which has no hormonal activity).

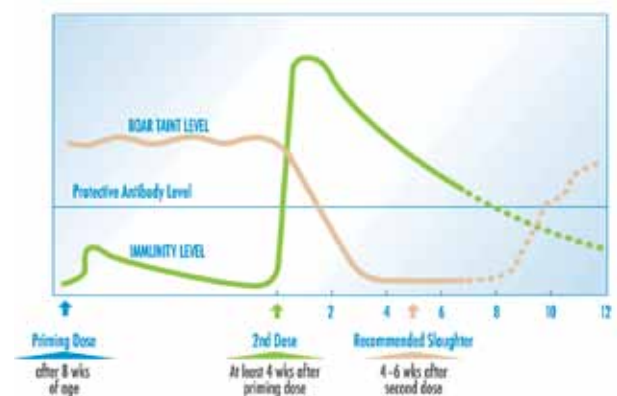


Figure 4: Schematic representation of changes in antibody concentration, and boar taint, following IMPROVAC. The first dose primes the immune memory cells but antibodies do not reach a protective level. The boar continues to grow as a boar. Following the second dose, close to slaughter, there is a rapid and marked rise in circulating antibodies which neutralize endogenous GnRF and thus prevent stimulation of the pituitary. As a consequence, testicular function is inhibited and boar taint is controlled.



Pigs ~100 kg live weight and ~23 weeks of age

Figure 5: Typical testes size in non-immunized boar on left and Improvac immunized boar on right.

As testicular production of testosterone declines so does the production of androstenone, reducing this component of boar taint to equivalent levels found in physically castrated pigs (3, 4, 5, 6). At same time the liver regains its ability to effectively metabolize and clear accumulated skatole and hence this taint compound also decreases to levels found in female and physically castrated male pigs. Clinical studies have show that by 3-4 weeks after the second dose the levels of androstenone and skatole are below the boar taint thresholds (1.0 and 0.2 ug/g respectively) (3, 4, 5, 6).

IMPROVAC has no hormonal activity

IMPROVAC's mode of action, and how it is made, demonstrate how it works just like a vaccine. Moreover, IMPROVAC does not add hormones to the animal nor does it stimulate hormone production. To the contrary, it is simply an immunological way to produce castration.

Professor Iain Clarke from Melbourne's Monash University has demonstrated that the IMPROVAC antigen has no LH releasing ability when injected directly into the blood stream (Figure 6) (9). This study proves that IMPROVAC has no inherent hormonal activity.

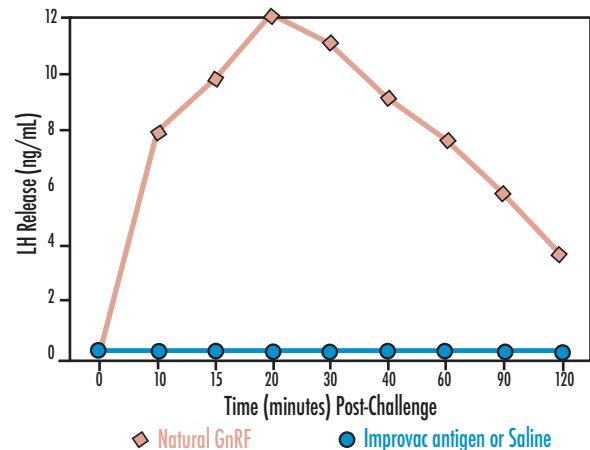


Figure 6: Effect of the IMPROVAC antigen and endogenous GnRF on LH release.

Summary

- Almost 100% of boars are castrated to control boar taint. However, there are consequences: economic losses, reduced animal welfare and increased environmental pollution.
- IMPROVAC: This vaccine alternative offers a safe and effective to castration for controlling boar taint.
- IMPROVAC: Works with the pig's immune system to eliminate boar taint.
- IMPROVAC: The mode of action is no different to other animal health vaccines.
- IMPROVAC: Effectively prevents the pain, mortality and performance losses associated with physical castration.

References

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