

## TRANSCRIPT OF “MODE OF ACTION” VIDEO

Pfizer Animal Health is leading the advance into an entirely new field ... with IMPROVAC®\*—an innovative immunological product that offers progressive pig farmers breakthrough technology and a welcome new way to eliminate the problem of boar taint, without the production losses and animal welfare issues associated with physical castration. Here’s how it works.

As male pigs mature, a series of events occur that control testicular function and contribute to the build up of taint in the boar. The process begins when the pig’s hypothalamus produces gonadotropin releasing factor, also called GnRF, which controls the cascade of events that regulate testicular development and function. GnRF travels through the blood stream to the pituitary gland where it binds to a specific GnRF receptor, triggering the release of two hormones, luteinizing hormone, or LH, and follicle stimulating hormone, or FSH.

These two hormones then travel through the blood stream to the testicles, where they promote secretion of male sex steroids, such as testosterone and androstenone that give rise to natural male-like behaviour and characteristics. One of these steroids, androstenone, is a major contributor to boar taint. The second major taint-causing compound—skatole—is produced by bacteria in the large intestine of all types of pig, whether boars, castrates or females. However, because the steroids released by the testicles reduce the liver’s ability to metabolize and eliminate skatole, this taint-causing compound tends to accumulate in the fat of boars more than castrates and female pigs, current solutions to boar taint are either physical castration at a very young age or slaughtering male pigs at a light weight, before they reach sexual maturity and are at risk of developing taint. Both of these approaches have disadvantages, prompting the search for alternatives, including immunological approaches.

IMPROVAC is the world's first immunological solution to boar taint. Just like disease vaccines that contain antigens to stimulate a specific immune response, IMPROVAC contains two components linked to form an antigen that can be recognized by the pig’s immune system. The IMPROVAC antigen is constructed with a synthetic peptide analogue of the pig’s own GnRF.

These GnRF analogues are linked to the surface of the large carrier protein—a protein that is also used in other vaccines. This presents the GnRF analogues in a form that effectively triggers a significant immune response against GnRF. And the unique IMPROVAC antigen is unable to bind to receptor sites in the pituitary gland, which means IMPROVAC does not have any hormonal activity.

An injector with safety features should be used to administer IMPROVAC. As with many vaccines, the initial injection of IMPROVAC merely primes the immune system without producing a significant antibody response and without hindering the normal physiological growth, lean gain and feed efficiency of healthy boars.

It’s the second injection, given 4 to 6 weeks before slaughter that produces an effective immune response in the boar, leading to antibodies specific to the pig’s own GnRF. The production of GnRF-specific antibodies rises above the effective level at about 1 to 2 weeks and remains effective for a minimum of 8 weeks. By binding to the pig’s own GnRF, these antibodies effectively neutralize it, as the GnRF is prevented from binding to and stimulating pituitary gland receptors—which in turn, prevents the release of LH and FSH.

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\* Originally introduced in 1998 as IMPROVAC®, regulatory considerations have required different names for the same product in other parts of the world. Thus, IMPROVAC may appear in other markets as VIVAX\*, IMPROVEST® and INNOSURE®.

In the absence of LH & FSH, the testicles are no longer stimulated to produce steroids such as testosterone *and* androstenone—one of the primary taint-causing compounds. The other major taint-causing compound—skatole—is also cleared. As the process that leads to the release of testicular steroids is blocked, the liver recovers its ability to eliminate skatole from the pig's body.

In fact, studies show following the second injection of IMPROVAC, and the development of high titers of anti-GnRF antibodies, testosterone, androstenone and skatole levels all drop quickly and remain suppressed for a minimum of 8 weeks. The testicles also temporarily cease to grow, and sexually driven aggressive behavior declines. IMPROVAC thereby effectively reduces the levels of the major taint compounds to levels similar to those in physical castrates.

By using IMPROVAC to control boar taint, physical castration is avoided, and the male pig is allowed to grow as an entire male until a few weeks prior to slaughter. Thus IMPROVAC delivers the following benefits: improved animal welfare, decreased costs, reduced environmental impact, higher carcass quality and an overall higher potential return on investment.

Finally, pig farmers have a profitable, animal-friendly, environmentally responsible way to solve the problem of boar taint—with IMPROVAC, advancing pork production.

**On-screen legal text:**

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