

Bulletin

Boehringer Ingelheim Vetmedica, Inc.

TECHNICAL

PCA™ - Purified Circovirus Antigen for superior efficacy and safety of Ingelvac® CircoFLEX™

The virus – Porcine Circovirus (PCV) – 2

Over the last few years PCV-2, the virus causing Porcine Circovirus associated diseases (PCVAD), has been analyzed and its building blocks described. Two major building blocks or open reading frames (ORF 1 and 2) have been revealed. ORF 2 hereby encodes the outer capsid of PCV2 and has been identified as the part which triggers a protective immune reaction. ORF 2 is therefore the antigen part which is most useful for producing a vaccine.

A number of ways on how to mass produce a vaccine containing ORF 2 are theoretically possible. Two main ways used for vaccine production globally are:

1. Culturing of the whole virus, and either producing a live (MLV) or killed vaccine (KV). A live vaccine has been thought of as too dangerous in relation to PCV-2, and killed vaccines unfortunately usually result in low numbers of vaccine doses due to poor growth of the virus in cell culture and the inactivation process.
2. Taking the most important part of the virus (ORF 2), generating this part using a different virus followed by production of the antigen (ORF2 protein). Boehringer Ingelheim has decided to use this newer technique of producing a separate purified antigen in order to receive a highly effective and safe vaccine against PCVAD.

Baculovirus Vector Usage

In order to achieve this highly effective and safe vaccine, ORF2 was isolated from PCV-2. This ORF2 is then expressed using a baculovirus, a non-pathogenic insect virus, which produces large amounts of virus and can be separated from the antigen very effectively with a newly developed method after production. For our product, generating ORF 2 and baculovirus together in insect cells results in large numbers of PCV-2 ORF 2 proteins and baculovirus particles within cells. In the following step the antigen is then fully detached from insect cell and baculovirus to result in a highly concentrated solution of ORF-2 protein.

Purifying the Antigen

The next steps of production involve separation of the PCV-2 ORF 2 protein from unneeded components of the production medium by application of a proprietary purification process. This process produces a highly purified ORF 2 protein solution for the production of **Ingelvac® CircoFLEX™**. This highly technical purification process is a completely new development by the Boehringer Ingelheim R&D team, which means that **Ingelvac® CircoFLEX™** contains a substantially upgraded ORF 2 protein concentration. The presentation of this purified ORF 2 protein to the pig's immune system via the vaccine leads to optimal development of highly protective active immunity.

The Boehringer Ingelheim R&D team has also developed this vaccine in a way that the antigen (ORF 2 protein) assembles into its natural shape during the production process, which makes the antigen appear exactly like a naturally occurring virus particle. These particles have been found to be structurally and antigenically indistinguishable from regular PCV2 capsids. This whole unique process produces an exceptional vaccine, in which the antigen is easily recognised by the pig's immune system to build a very strong and protective immunity. As a result, the vaccine can deliver outstanding efficacy and safety as demonstrated in many laboratory (data on file) and field trials (CA & EU field trial collection) as well as seen in PCVAD affected production units (CA and US field reports, 2007).

In summary, **Ingelvac® CircoFLEX™** contains PCA™, the new Purified Circovirus Antigen, which creates a highly effective and safe vaccine for the control of PCVAD.