Porcine pleuropneumonia, induced by Actinobacillus pleuropneumoniae (Ap), continues to be an economically important disease throughout the world. Over 15 different serotypes of Ap have been identified according to their capsular antigens, all belonging to biotype I or biotype II.

Epidemiological surveys have revealed the presence of different serotypes in different countries and regions. The occurrence and prevalence of serotypes evolves and changes over time. A clear shift in predominant serotypes within a specific region compared to previous years can be observed.

There is numerous evidence that even within the same farm multiple serotypes of A. pleuropneumoniae can be present. Chiers (2002) identified four different serotypes in one herd.

Moreover, different serotypes may be isolated within different age groups on the same farm, which makes diagnosis more complicated. Besides antigenic patterns, various serotypes can also be characterised by their difference in virulence.

These differences can be mainly attributed to the production of various combinations of haemolytic and cytotoxic Apx toxins Apx I, Apx II and Apx III. They are produced and released in combinations of two, which are characteristic for each particular serotype.

Serotypes I, 5, 9 and 11 normally produce Apx I and Apx II, while serotypes 2, 3, 4, 6, 8 and 15 have been known to produce Apx II and Apx III (Table 1).

Apx toxins damage the epithelial alveolar cells, endothelial blood vessel cells and macrophages. This direct effect together with the activation of pro-inflammatory cytokines contributes to the local damages of the lung tissue and massive fibrin accumulation in the pleural cavity.

The Apx toxins are immunogenic and can elicit the protective immune response. The advantage is the serotype cross-effectiveness, provided that all Apx I, II and III toxoids are used for the active immunisation. It was also proven that Apx based immunity protects more efficiently than the immunity induced by the whole cell antigens even against the homologous serotype.

It is for this reason several challenge trials have been conducted to assess the effectiveness of Coglapix, a toxoid based Ap vaccine. Ap serotype I strains produce Apx I and Apx II toxins and are therefore usually highly virulent, inducing severe lung lesions and high mortality. In a study evaluating efficacy against Ap serotype I, sero-negative pigs were vaccinated with Coglapix at seven and 10 weeks of age, while non-vaccinated pigs served as the negative control.

All animals were challenged with 5x10^5 CFU of a virulent Ap serotype I strain intranasally at 13 weeks of age and euthanised and necropsied seven days post challenge. Coglapix vaccinated pigs had significantly lower cumulative lung scores than the non-vaccinated controls (p=0.0365). The efficacy of Coglapix was 77%, compared to the non-vaccinated controls, as evaluated according to Jones et.al. 2005; demonstrating protection against Apx I and II toxins. At the same time, vaccination with Coglapix significantly reduced the mortality after challenge with Ap serotype I compared to non-vaccinated controls.

\[
\begin{array}{cccc}
\text{Serotype} & \text{Apx I} & \text{Apx II} & \text{Apx III} \\
1, 5, 9, 10, 11, 14 & 1, 2, 3, 4, 5, 6, 7 & 2, 3, 4, 6, 8, 13, 15 \\
\end{array}
\]

Due to the expression of Apx II and Apx III toxins, Ap serotype 2 is highly virulent and capable of inducing strong lung lesions yet is commonly associated with low mortality. To determine efficacy against Ap serotype 2, sero-negative pigs were vaccinated with Coglapix at six and 10 weeks of age. Non-vaccinated pigs served as the negative control.

All animals were given a high challenge of 6x10^5 CFU of a virulent Ap serotype 2 in an aerosol chamber at 13 weeks of age. The animals were euthanised and necropsied seven days post-challenge.

As a result, Coglapix protected the vaccinated animals even in these extreme challenge conditions. The vaccinated animals had significantly lower cumulative lung scores compared to controls even in the face of a high challenge. Vaccination with Coglapix significantly reduced the mortality after challenge with Ap serotype 2.

Ap serotype 5, producing Apx I and II toxins is relevant in the field and can be highly virulent. In a heterologous serotype 5 challenge study, pigs vaccinated with Coglapix had more resistance against infection with Ap serotype 5, than pigs vaccinated with two homologous bacterin vaccines (both containing serotype 5 bacterin antigens) and the non-vaccinated controls.

In this study, sero-negative pigs were vaccinated at six and 10 weeks of age and challenged three weeks later by aerosol infection with a heterologous Ap serotype strain. All animals were euthanised and necropsied seven days post-challenge.

\[
\begin{array}{cccc}
\text{Total achievable lung score} & \text{Coglapix} & \text{Competitor bacterin vaccine 1} & \text{Competitor bacterin vaccine 2} & \text{Non-vaccinated control} \\
0 & * & 0 & 0 & 20 \\
5 & 0 & 5 & 5 & * \\
10 & 5 & 10 & 10 & * \\
15 & 10 & 15 & 15 & * \\
20 & 15 & 20 & 20 & * \\
25 & 20 & 25 & 25 & * \\
\end{array}
\]

* indicates statistically significant difference (p=0.0156)

\[\text{Fig. 3. Ap serotype 5 challenge: percent of total achievable lung score.}\]

Due to the fact that Coglapix does not contain Ap serotype 5 bacterin antigens it conferred significantly better protection (p=0.0156) than the competitor vaccines containing the homologous serotype 5 bacterin antigens but not containing Apx toxoids. This study confirms the previous experiment conducted by Satran (2003).

Demonstration of efficacy against various Ap serotypes, both homologous and heterologous, producing different combinations of Apx toxins I, II, and III suggests that Coglapix can provide cross protection against all Ap serotypes.

As demonstrated, such cross protection is needed in the field due to the presence of multiple serotypes that can change over time.