Hyogen®

WITH Imuvant™

- A single vaccination at 21 days of age provides early and long lasting protection for up to 26 weeks*
- Contains the highly potent Ceva proprietary strain **BA 2940-99**
- Imuvant™, a unique Ceva adjuvant containing a non-toxic LPS from J5 *E. coli*
- Ceva Lung Program expertise and support with its Lung Scoring Methodology

Enzootic Pneumonia Protection

Species	Administration Route	Dosage
Pigs for fattening	IM	2ml from 21 days of age

ACTIVE SUBSTANCE: Inactivated *Mycoplasma hyopneumoniae* 2940-99 strain. **CONTRAINDICATIONS:** None. **SPECIAL WARNING FOR EACH TARGET SPECIES:** None. **SPECIAL PRECAUTIONS FOR USE IN ANIMALS:** Vaccinate only healthy animals. **SPECIAL PRECAUTIONS TO BE TAKEN BY THE PERSON ADMINISTERING THE VETERINARY MEDICINAL PRODUCT TO ANIMAL: TO THE USER:** This veterinary medicinal product contains mineral oil. Accidental injection/self injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this veterinary medicinal product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again. **TO THE PHYSICIAN:** This veterinary medicinal product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert and PROMPT surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon. **ADVERSE REACTIONS:** On the day of vaccination a transient mean increase in body temperature of about 1.3°C is very common. In an individual pig this increase might reach 2°C, but in all cases body temperature is back to normal the next day. A local reaction at the site of injection in the form of a swelling of a diameter up to 5 cm can be very common, which can last for three days. These reactions are of transient nature and do not need further treatment. Immediate mild hypersensitivity-like reactions may occur uncommonly after vaccination, resulting in transient clinical signs such as vomiting. These clinical signs normally resolve without treatment. **USE DURING PREGNANCY, LACTATION OR LAY:** Not applicable. **INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:** No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis. **AMOUNT(S) TO BE ADMINISTERED TO AND ADMINISTRATION ROUTE:** For intramuscular use. Vaccinate pigs in the side of their neck. Administer a single dose of 2 ml from 3 weeks of age. The data available are not sufficient to exclude the interaction of maternally derived antibodies with vaccine uptake. Interaction with maternal-derived antibodies is known and should be taken into consideration. It is recommended to delay vaccination in piglets with residual MDA at the age of 3 weeks. Shake well before use. Use sterile syringe and needle, respect aseptic conditions of vaccination. **OVERDOSE (SYMPTOMS, EMERGENCY PROCEDURES, ANTIDOTES) IF NECESSARY:** As the vaccine is inactivated, studies investigating the safety of an overdose administration are not required. **WITHDRAWAL PERIOD(S):** Zero days **LEGAL CATEGORY:** UK: POM-V IE: POM **MARKETING AUTHORISATION:UK:** 15052/4078 IE: VPA 10815/026/001

Further information is available on the SPC

* Onset of immunity 3 weeks after vaccination

Reference list

[1]Straw, B. *et al.* Estimation of the cost of pnuemonia in swine herds. JAVMA (1989) 195:1702-1706, [2]Tenk M., *et al.* Imuvant™ - a novel adjuvant; efficacy and safety properties in Hyogen® vaccine. ESPHM 2015, [3]Murphy, K. *et al.* Chapter 2: Innate Immunity. In: Janeway's Immunobiology 7th Ed (2008) p56-59, [4]Lo, D-Y. *et al.* Effect of Immunostimulation by Detoxified *E. coli* Lipopolysaccharide Combined with Inactivated *Propionibacterium granulosum* Cells on Porcine Immunity. JVetMedSci (2009) 71:897-903, [5]Park, B.S. *et al.* The structural basis of lipopolysaccharide recognition by the TLR4-MD-2 complex. Nature (2009) 458:1191-1196, [6]Ceva internal studies, [7]Herczeg *et al.* Onset of immunity after one shot of Hyogen J5® - *Mycoplasma hyopneumoniae* vaccine in pigs. APVS 2011, [8]Tenk M *et al.* Six months duration of immunity of Hyogen® in fattening pigs against *Mycoplasma hyopneumoniae*. ESPHM 2015, [9]Herczeg, J. *et al.* Safety and efficacy field trial of Hyogen® vaccine in finishing pigs in South Africa. IPVS 2012, [10]Christensen, G. Diseases of the respiratory system. In: Diseases of Swine. 8th Ed (1999) p927-928

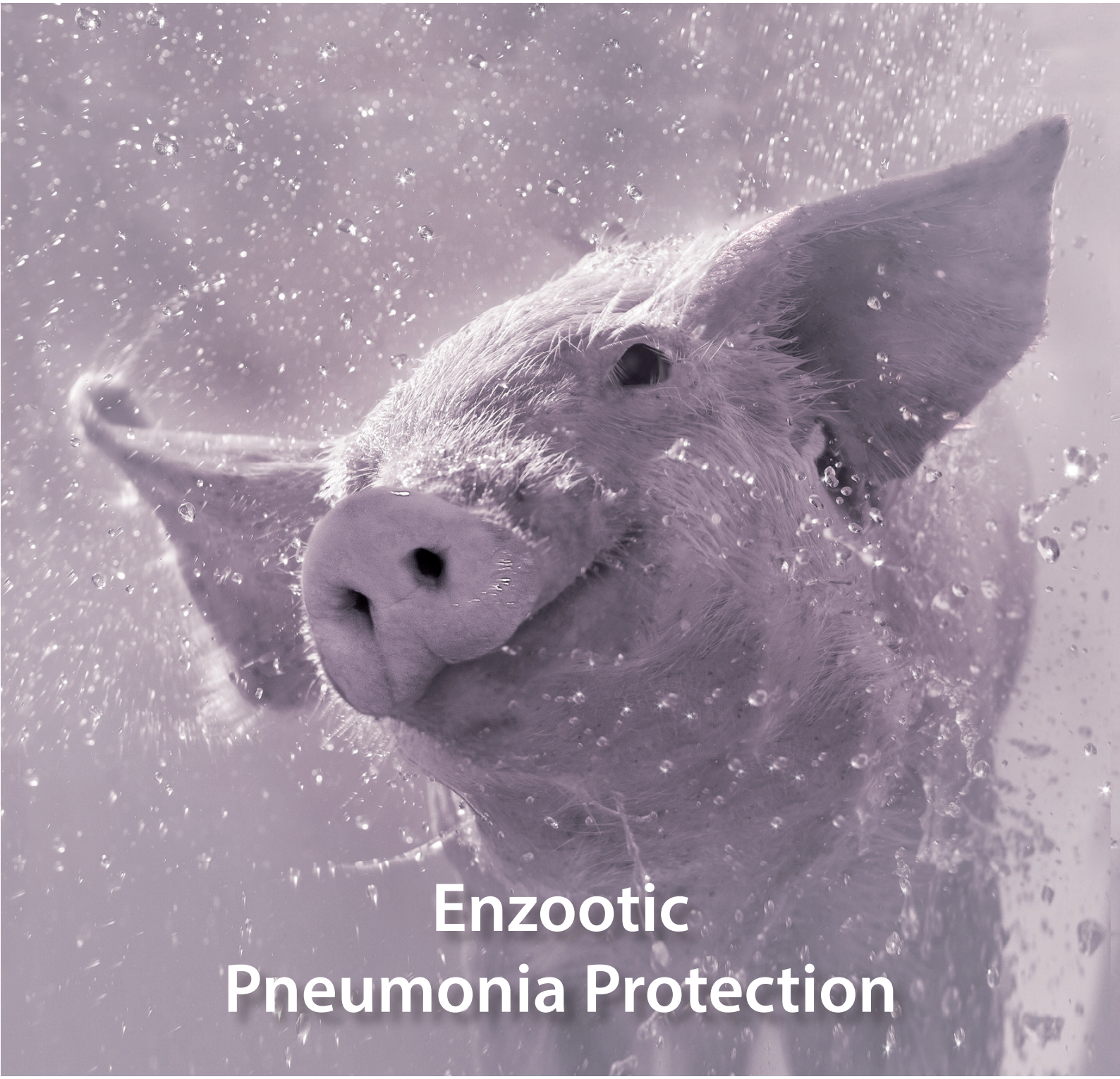
L253-0915-250

Use medicines responsibly (www.noah.co.uk/responsible)

Further information is available from:
Ceva Animal Health Ltd
Unit 3, Anglo Office Park, White Lion Road, Amersham, Bucks HP7 9FB
Tel: 01494 781510 **www.ceva.co.uk**

Hyogen®

WITH Imuvant™



Enzootic Pneumonia Protection

LUNG PROGRAM

ceva

Mycoplasma hyopneumoniae : a real economic problem for pig farmers

***Mycoplasma hyopneumoniae*, associated with enzootic pneumonia, plays a major role in the porcine respiratory disease complex (PRDC) and can cause huge economic losses. A 17% decrease in daily weight gain and a 14% decrease in feed efficiency in herds with enzootic pneumonia has been reported[1].**

***Mycoplasma hyopneumoniae* is unable to penetrate and live within host cells but does colonise the mucosal surface of the ciliated epithelium of the respiratory system. In addition to the detrimental effect on the cilia, *Mycoplasma hyopneumoniae* infection attracts lymphocytes and macrophages into the lungs resulting in pneumonia. Protection against the infection requires complex activation of the host immune system.**

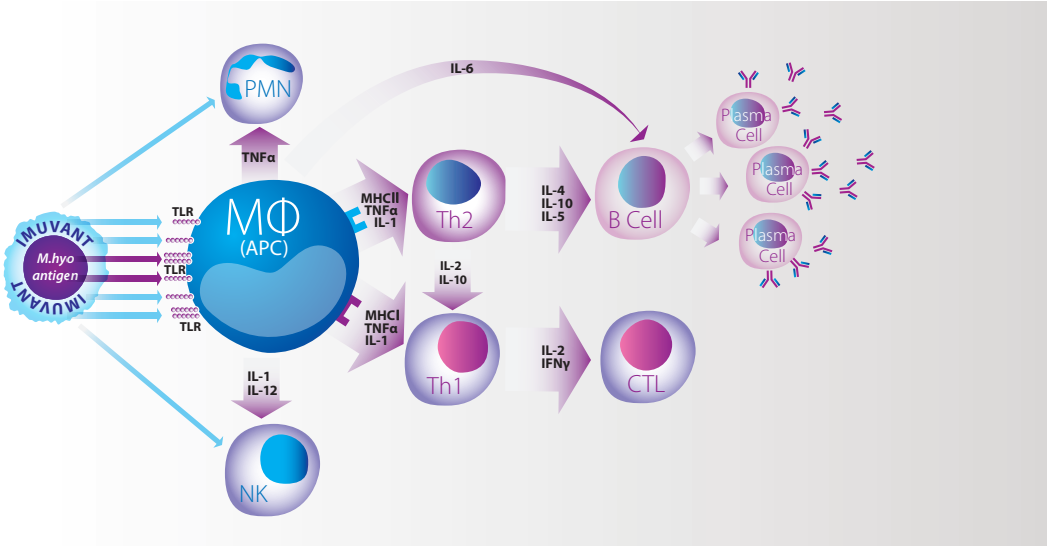
Hyogen® : protect your pigs against *Mycoplasma hyopneumoniae*

After a single injection, Hyogen® provides effective protection against *Mycoplasma hyopneumoniae* due to the potent stimulation of the immune system by the antigen originated from Ceva *Mycoplasma hyopneumoniae* strain BA 2940-99 along with the adjuvant, Imuvant™.

Ceva proprietary strain BA 2940-99: To determine the best option, for a new vaccine, Ceva has decided not to use the old J strain and undertook research to find a circulating virulent strain reflecting current field situation. The lab has also worked on proteomic and antigenic characterisation of the strain to induce high level of immunity.

Imuvant™ is a unique Ceva adjuvant composed of a non-toxic lipopolysaccharide (LPS) from J5 *E. coli* together with a mineral oil in water emulsion that forms a complex and highly efficient immunostimulant[2]. This stimulation is due to the oil in water formula acting as a direct delivery system, which promotes the uptake of antigen by Antigen Presenting Cells (APC). At the same time, the LPS component of Imuvant™ stimulates the innate immune system while simultaneously enhancing the specific response to mycoplasma antigen via B and T lymphocyte activation pathways[3,4,5].

Stimulation of the immune system with Imuvant™



Cell Mediated and Humoral Immunity

Cellular Immunity Hyogen® vaccinated pigs had a significantly higher mean *Mycoplasma hyopneumoniae* specific, IFN γ producing, white blood cell counts as compared to the controls[6].

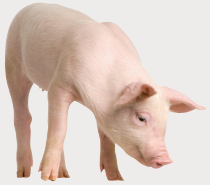
Mean Number of Antigen Specific White Blood Cells / 6 log 10 Peripheral Blood Mononuclear Cells

	Day 13 *after vaccination*	*Day 90* *after vaccination*	*Day 175* *after vaccination*
Hyogen® Vaccinated	23.75	25.31	10.38
Control	0.56	1.64	2.0

Humoral Immunity Hyogen® also elicits a significant early and long lasting antibody response after vaccination as demonstrated in both onset of immunity and duration of immunity studies[6].

Mean Antibody Titer Post Vaccination (EU/ml)

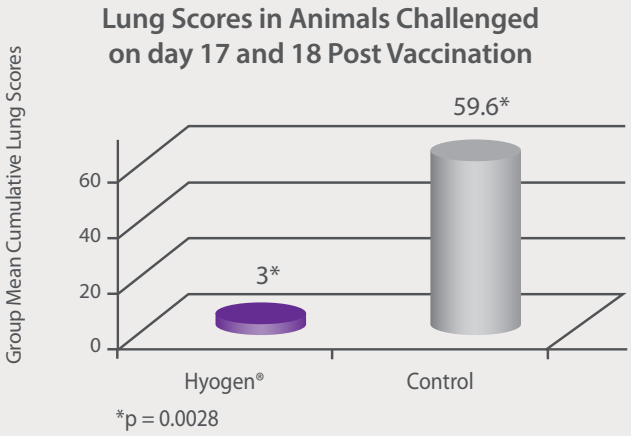
	Day 0	*Day 15* *after vaccination*	*Day 0*	*Day 175* *after vaccination*
Hyogen® Vaccinated	Negative	2.4	Negative	6.1
Control	Negative	Negative	Negative	Negative
	Study 1		**Study 2**	



IMUVANT™ INCREASES THE DEFENCE OF PIGS VACCINATED WITH HYOGEN® AGAINST *MYCOPLASMA HYOPNEUMONIAE*

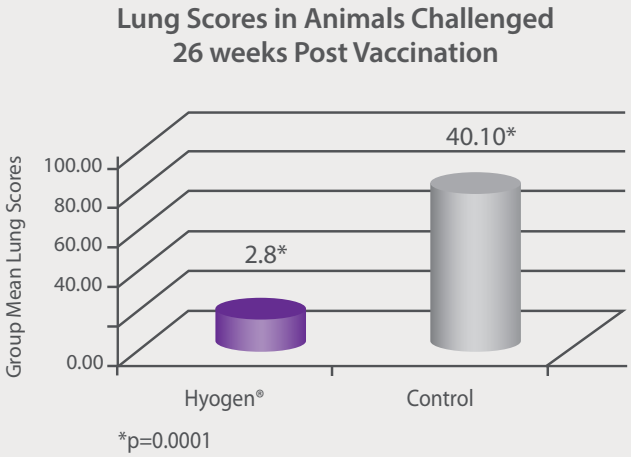
PROTECTION FROM 17 days POST VACCINATION

In a clinical trial seronegative 3 week old pigs were either vaccinated with Hyogen® or served as non-vaccinated controls. All animals were challenged with *Mycoplasma hyopneumoniae* day 17 and 18 post vaccination, and euthanised and necropsied on day 46. Hyogen® vaccinated animals had **19.9 times lower lung scores** than the non-vaccinated controls (p= 0.0028)[7].



PROTECTION UNTIL 26 weeks POST VACCINATION

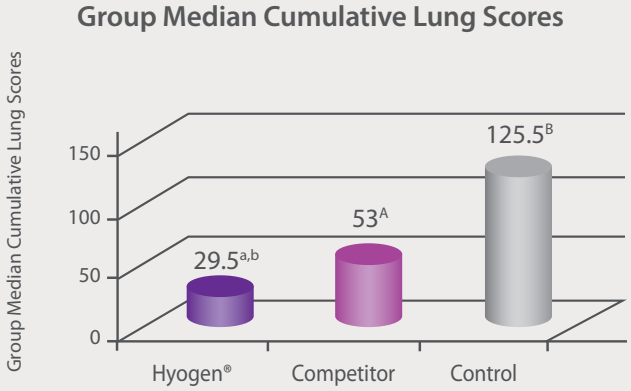
Seronegative pigs were vaccinated with Hyogen® at three weeks of age or served as non-vaccinated controls. 26 weeks after vaccination both groups were challenged with a virulent strain of *Mycoplasma hyopneumoniae* and 4 weeks later were euthanised and necropsied. Hyogen® vaccinated animals had **14.32 times lower lung scores** than the non-vaccinated controls (p=0.0001)[8].



IN THE FIELD Hyogen: Visible Difference

Protection of lungs

In a field study involving a sample of piglets on a farm where *Mycoplasma hyopneumoniae* was present, pigs were vaccinated at three weeks of age with either Hyogen®, a competitor *Mycoplasma hyopneumoniae* bacterin or a placebo. Hyogen® vaccinated pigs had statistically significant lower lung scores at slaughter. Hyogen® is both efficacious in the face of *Mycoplasma hyopneumoniae* challenge in the field and provides significantly better protection than a competitor vaccine[9].



a, A are statistically significant (p=0.00002);
b, B are statistically significant (p<0.005)

Hyogen® is part of the Ceva Lung Program. The Ceva Lung Program provides an overview of the diseases associated with *Actinobacillus pleuropeumoniae* and *Mycoplasma hyopneumoniae*.

It offers the methodology and guidelines on how to correctly evaluate the presence, incidence and circulation patterns of these diseases. Looking at the impact of these infections using serological investigation and an adapted lung scoring of slaughter pigs, it is used to determine the appropriate vaccination protocol and monitor the results of vaccination with Coglapix® and Hyogen®. The program is supported by key opinion leaders and is an asset for building Ceva's reputation as experts in respiratory health.

An iPad and Android application to aid effective lung scoring at the slaughterhouse.

The CLP App is available from:

Download on the App Store

ANDROID APP ON Google play

or by scanning:

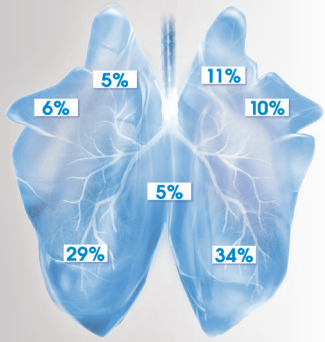
Evaluation of pneumonia and pleurisy

Pneumonia and pleurisy can be evaluated in a qualitative and quantitative manner. In the Ceva Lung Program, pneumonia is scored based on the Madec method, which has been modified considering the contribution of each lobe to the overall capacity of the lungs. Quantification of scarring is included. Pleurisy is scored using the Slaughterhouse Pleurisy Evaluation System (SPES) method, although in the Ceva Lung Program only cranial pleurisy is recorded separately as Cranial Pleurisy Scoring. Dorso-causal pleurisy (associated with *Actinobacillus pleuropneumoniae* infection) is assessed separately and this score is used to calculate the APPI (*Actinobacillus Pleuropneumoniae* Index).

Modified Madec Scoring

For the modified Madec score, the enzootic pneumonia-like lung lesions of each lobe are quantified according to the following:

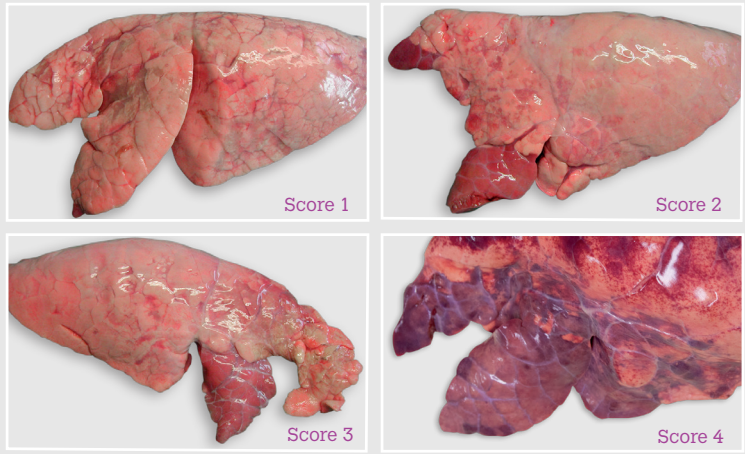
Since each lobe does not represent an equal proportion of the lung, the following weightings were assigned according to Christensen (1999)[10].



Surface of the lobe affected	
Score 0	No lesions
Score 1	1-25 %
Score 2	26-50 %
Score 3	51-75 %
Score 4	76-100 %

< Fig 3: Percentage of total lung capacity representated by each lobe

> Fig 4: Scoring of bronchopneumonia lesions typical for EP on the cardiac lobe



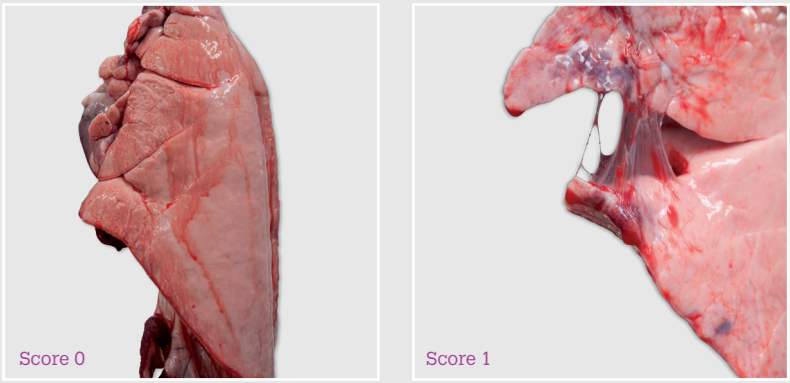
Courtesy of IZSLER Inst. Reggio Emilia, Italy

Cranial Pleurisy Scoring

Cranial pleurisy can be attributed to pathological processes in this area which are likely related to *Mycoplasma hyopneumoniae* and other respiratory pathogens such as SIV, *Pasteurella multocida* and other bacteria. This cranial pleurisy should be recorded separately from the dorso-caudal pleurisy to allow the appropriate differential diagnosis. These lesions include pleurisy on the surface of the lung lobes or between lobes as interlobar pleurisy. Pleurisy in the apical and cardiac lung lobes are scored as follows:

Score 0 : No pleurisy in apical and cardiac lung lobes
Score 1 : Pleurisy in apical and cardiac lung lobes

> **Fig. 5 : Scoring of pleurisy in the apical and cardiac lung lobes**

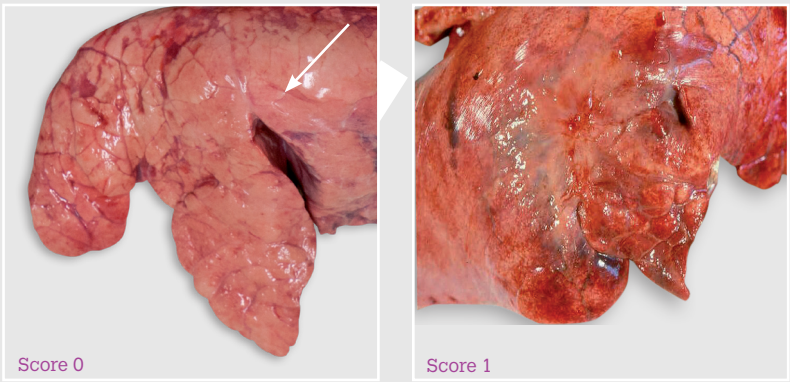


Quantification of Scarring

The presence of fissures or scarring is recorded. Fissures are evidence of old infections likely due to *Mycoplasma hyopneumoniae*

Score 0 : Absence of fissures (scarring)
Score 1 : Presence of fissures (scarring)

> **Fig 6 : Prevalence of fissures in pig lungs**



Courtesy of Pig Research Centre, Denmark