Irish Medicines Board

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Ireland

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR AN IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT

Unistrain PRRS lyophilisate and solvent for suspension for injection for pigs

MODULE 1

PRODUCT SUMMARY

EU Procedure number	IE/V/0287/001/DC
Name, strength and pharmaceutical form	UNISTRAIN PRRS lyophilisate and solvent for suspension for injection for pigs.
Applicant	Laboratorios Hipra, S.A. Avda. la Selva, 135 17170 Amer (Girona) SPAIN
Active substance(s)	Live, attenuated Porcine reproductive and respiratory syndrome virus (PRRSV), strain VP-046 BIS
ATC Vet code	QI09AD03
Target species	Pigs
Indication for use	For active immunisation of breeding females from farms affected with European PRRS virus to reduce reproductive disorders, incidence and duration of viraemia, transplacental virus transmission, virus tissue load and clinical signs associated with infection with strains of PRRS virus. Under laboratory conditions, vaccination reduced the negative impact of PRRS virus infection on piglet performance (mortality and weight gain) within the first 28 days of life.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Article 12(3) of Directive 2001/82/EC, as amended (that is, a dossier with full administrative, quality, safety and efficacy data)
Date of completion of the original decentralised procedure	20th December 2012
Date product first authorised in the Reference Member State (MRP only)	Not applicable
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, EE, EL, ES, FR, HU, IT, LV, LT, LU, MT, NL, PL, PT, RO, SK, SI, UK

I. SCIENTIFIC OVERVIEW

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.

It has been shown that the product can be safely used in the target species; the slight reactions observed are indicated in the SPC.

The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

The efficacy of the product was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The lyophilised powder fraction contains live attenuated porcine reproductive and respiratory syndrome virus (PRRSV), strain VP-046 BIS ($10^{3.5}$ – $10^{5.5}$ $CCID_{50}$ per 2 ml dose) as the active ingredient and the excipients disodium phosphate dodecahydrate, potassium dihydrogen phosphate, gelatine, povidone, monosodium glutamate, sodium chloride, potassium chloride, sucrose and water for injections.

A phosphate buffered saline (PBS) solvent is supplied for reconstitution of the lyophilised powder fraction.

The vaccine is supplied in Type I glass vials containing lyophilised powder for 10, 25 or 50 doses while the solvent is supplied in volumes of 20, 50 or 100 ml in Type I (20 ml) or Type II (50 and 100 ml) glass vials. The particulars of the containers and controls performed are provided and conform to the regulation.

The vaccine strain originates from a European isolate PRRSV field strain. Attenuation of this strain was performed by serial passaging in cell cultures to produce the vaccine strain. The choice of the vaccine strain is satisfactorily justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

Starting materials used in production comply with the relevant Ph. Eur. monographs.

Biological starting materials are in compliance with the relevant Ph. Eur. monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the relevant Ph. Eur. monographs and guidelines; any deviation has been adequately justified.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

E. Control on intermediate products

The tests performed during production of the antigen are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

F. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified.

The demonstration of the batch to batch consistency is based on the results of data provided for 6 x lyophilised powder batches and 3 x solvent batches including production scale size batches. Other supportive data provided confirm the consistency of the production processes.

G. Stability

Stability data on batches of the lyophilised powder and solvent batches have been provided in accordance with applicable European guidelines, demonstrating the stability of the product over the 24 month shelf life when stored at 2-8°C .

The in-use shelf-life of the reconstituted vaccine is supported by the data provided.

H. Genetically Modified Organisms

None.

J. Other Information

Not applicable.

III. SAFETY ASSESSMENT

All batches used in the safety studies were representative of the production process. The dose to be used was that recommended for use and contained the maximum antigen content to be included in the finished product. Studies were performed in accordance with the requirements of Directive 2001/82/EC, as amended, and the relevant guidelines.

III. A Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of a dose in the target animal, and the special requirements for live vaccines, were investigated in several well-conducted, GLP-compliant laboratory studies. In each safety study, a suitable number of animals were used, in compliance with the general safety Ph. Eur. monograph.

The safety studies demonstrated that the administration of one dose, an overdose, and the repeated administration of a dose are considered to be safe. In all studies, safety parameters measured included the examination of reproductive performance, temperature changes, evaluation of injection site reactions and general clinical signs.

Following the administration of an overdose (10x), there were no additional adverse reactions further to that observed after a single dose.

While vaccination of naïve animals during pregnancy under the recommended conditions of use has been shown to be safe, negative effects in reproductive parameters could not be excluded following administration of a 10x overdose to naïve pregnant females. Therefore, appropriate warnings have been included in the SPC to instruct the user to take particular care to avoid accidental overdose when vaccinating pregnant females that have not already been vaccinated or exposed to a field pathogen. The applicant has investigated the special requirements to be taken into account for live vaccines, such as dissemination in the target animal, spread of the vaccine strain and reversion to virulence. It was concluded that:

- Vaccinated females may excrete the vaccine strain for up to nine days following vaccination by nasal secretions. In some cases, faecal excretion can also occur.

- The vaccine strain can spread to non-vaccinated cohabitant animals (horizontal transmission) without any clinical consequence.

- There is no reversion to virulence of the vaccine strain under laboratory conditions.

- The recombination of the vaccine strain with field strains would not be expected to result in any worse consequences then what may occur following natural recombination of field strains.

Study of residues

All excipients included in the composition of this vaccine are listed in Annex 1 of Commission Regulation (EU) 37/2010 (not being necessary for the protection of public health to establish MRLs). Consequently, there is no need to perform residue studies for the vaccine and no withdrawal period is proposed.

User Safety

The main risk concerning user safety is accidental self-injection. However, although the vaccine is live, it is not known to infect humans, and no other components are present in the vaccine that would present a risk to the user. It is accepted that use of the vaccine does not pose an unacceptable risk to the user. Advice is included in the SPC to seek medical advice in the event that an adverse reaction was to occur following accidental self-injection.

Interactions

A compatibility claim for the use of Unistrain PRRS with another veterinary medicinal product has not been established. Therefore the standard warning when no information is available concerning the use of this product with any other veterinary medicinal product is included in the SPC.

III.B Field studies

One multicentric, positively-controlled field trial was performed, which was conducted in two EU Member States in commercial pig farms known to be affected by the presence of the PRRS virus. A total number of 869 female pigs were included, approximately half of which

were vaccinated with a positive control (a different commercially available live PRRS virus vaccine). The results obtained reflected those observed in the laboratory safety studies (slight increases in temperature and mild injection site reactions were observed) and the reproductive parameters of animals vaccinated with Unistrain PRRS were not inferior to the reproductive parameters of animals in the positive control group.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The conclusions of the environmental risk assessment, that there is a very low risk to the environment associated with use of the vaccine, were accepted. The applicant has included the standard disposal statement for live vaccines on the product literature.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV. A General requirements

The applicant justified that the vaccine strain included in Unistrain PRRS is relevant to the current epidemiological situation in the EU. Two different heterologous challenge strains were employed in the laboratory efficacy trials. A multicentric field trial was conducted in two EU member states, for which data concerning the circulating strains prior to conduct of the trial confirmed that the PRRS virus strains in each country had different geographic origin and were non-contemporaneous with the vaccine strain.

IV. B Laboratory Trials

The claimed indications for Unistrain PRRS are supported by different laboratory efficacy studies, which included either naïve gestating sows vaccinated at 8 – 9 weeks of gestation or naïve gilts vaccinated four weeks prior to mating, i.e. in accordance with the recommended vaccination schedule. The vaccine was administered at the minimum dose recommended for vaccination ($10^{3.5}$ $CCID_{50}$/dose), via the recommended route of administration (intramuscular). Challenge of study animals at 30 days post-vaccination was conducted with a heterologous PRRS virus isolate in two studies, and with another heterologous isolate in one study. In each efficacy study, a suitable number of vaccinated and control animals were included.

The efficacy of the product has been demonstrated in the laboratory studies in accordance with the relevant requirements which show the efficacy of the vaccine with regard to the following claims:

- Reduction in reproductive disorders.
- Reduction in the incidence and duration of viraemia.
- Reduction in transplacental virus transmission.
- Reduction in tissue virus load and clinical signs associated with infection with strains of PRRS virus.
- Reduction in the detrimental impact of PRRS virus infection on piglet performance (mortality and weight gain) within the first 28 days of life.

Although seroconversion was shown to occur by 15 days post-vaccination, protection from challenge has been demonstrated at 30 days post-vaccination, therefore the onset of immunity is 30 days post-vaccination.

The duration of protection is demonstrated at 16 weeks.

IV.C Field Trials

The applicant conducted one multicentric, positively-controlled field trial including farms from two EU member states which were known to be affected by the PRRS virus. Efficacy parameters evaluated in the field trial included the Reproductive Index, which took into account the number of live born piglets per sow corrected by the farrowing rate, percentage of abortions, conception at 1st service, gestation length, lactation length and weaning to breeding interval. The results of the field trial demonstrated that Unistrain PRRS was as effective as a different commercially available live PRRS virus vaccine in farms which are known to be affected by the PRRS virus.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Heads of Veterinary Medicines Agencies website (www.HMA.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

None.