MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

PRIMUN GUMBORO W2512 Lyophilisate for use in drinking water for chicken

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0273/001/DC
Name, strength and pharmaceutical form	PRIMUN GUMBORO W2512 Lyophilisate for use in drinking water for chicken
Applicant	LABORATORIOS CALIER, S.A. c/o. Barcelonés 26, Pla del Ramassa 08520 LES FRANQUESES DEL VALLES, (Barcelona) SPAIN
Active substance(s)	Avian infectious bursal disease (IBD) virus, live attenuated, intermediate plus IBDV_2512 strain, 1.5 log10 - 3.0 log10 EID50* * EID50 (embryo infectious dose 50%)
ATC Vet code	ATCvet code: QI01AD09
Target species	Broiler
Indication for use	For the active immunization of broiler chickens with maternally-derived antibodies (MDA) to reduce mortality, clinical disease, weight loss and acute lesions in the bursa of Fabricius associated with infection caused by very virulent strains of Infectious Bursal Disease viruses. Onset of immunity: 14 days post-vaccination. Duration of immunity: 28 days.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	3rd July, 2019
Date product first authorised in the Reference Member State (MRP only)	-
Concerned Member States for original procedure	PT

I. SCIENTIFIC OVERVIEW

For public assessment reports for the first authorisation in a range*:*

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 product is safe for the user 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 product contains 1.5 log10 - 3.0 log10 EID50 (embryo infectious dose 50%) of Avian infectious bursal disease (IBD) virus, live attenuated, intermediate plus IBDV_2512 strain. The excipients are disodium phosphate, potassium dihydrogen phosphate, lactose monohydrate, skimmed milk powder and water highly purified.

The container for the lyophilised vaccine (containing the antigen) are type I glass vials of 10 ml, sealed with bromobutyl rubber stopper and aluminium cap with red lid.
One vial of 1000 doses presented in a cardboard box. 10 vials of 1000 doses are presented in a plastic box.

The choice of the vaccine strain and formulation are properly explained. Neither adjuvant nor preservative are included in the vaccine and it is 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 from a licensed manufacturing site.

The product is manufactured in general in accordance with the European Pharmacopoeia and relevant European guidelines and OIE texts.

C. Control of Starting Materials

The active substance is Avian infectious bursal disease (IBD) virus, live attenuated, intermediate plus IBDV_2512 strain, 1.5 log10 - 3.0 log10 EID50 (embryo infectious dose 50%), an established substance described in the European Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Starting materials of non-biological origin used in production comply with pharmacopoeia monographs or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur. and EMA Guidelines; any deviation was 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 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 tests during production

The tests performed during production 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 tests include in particular potency, freedom from extraneous agents and sterility.

The demonstration of the batch to batch consistency is based on the results of 3 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions during 2 years, when stored protected from light at a temperature of 5 ± 3 °C.

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

H. Genetically Modified Organisms

Non applicable

J. Other Information

The manufacturing of this vaccine is well described and conditions of transport and handling are also clearly indicated.

III. SAFETY ASSESSMENT

Summary of safety trials and vaccine batches used:

Code	Batch	passage	Study
GUM P 091-2A S 13	1307811	least attenuated passage level present in a batch of the vaccine. (Final product)	Safety of an overdose oral
GUM P 091-2B S 13	1307811	least attenuated passage level present in a batch of the vaccine. (Final product)	Safety of an overdose ocular
GUM P 099-2A S 13	1307811	least attenuated passage level present in a batch of the vaccine. (Final product)	Safety single dose and repeated oral
GUM P 099-2B S 13	1307811	least attenuated passage level present in a batch of the vaccine. (Final product)	Safety single dose and repeated ocular
GUM P 090-2 S 13	IBDV_2512/WSV 1205020	-WSV: least attenuated passage level present between MSV and a batch of the vaccine -	Damage to the bursa of Fabricious.
	5th passage of IBDV_2512/MSV 1201019	Passage 5th of MSV after *in vivo* passages in chicks for increase of virulence (GUM P 090-2 S 13)	
BUR P 020 S 16-CLI 0300	5th passage of IBDV_2512/WSV 1205020	Passage 5th of WSV after *in vivo* passages in chicks for increase of virulence (BUR P 019 S 16)	Damage to the bursa of Fabricious.
BUR A 019 S 14	IBDV_2512/WSV 1205020	WSV: least attenuated passage level present between MSV and a batch of the vaccine	Immunosuppression
GUM P 090-2 S 13	IBDV_2512/MSV 1201019	MSV: Master Seed Virus	Increase of virulence
BUR P 019 S 16	IBDV_2512/WSV 1205020	WSV: Working Seed Virus	Increase of virulence
GUM A 004 S 14	IBDV_2512/WSV 1205020	WSV: least attenuated passage level present between MSV and a batch of the vaccine	Spread and dissemination
BUR A 003 E 15	1412766	(Final product) batch of the vaccine.	FIELD TRIAL

Laboratory trials

The safety of the administration of one dose and an overdose in the target animal is demonstrated in laboratory studies using the administration by the oral route. Also the age of the animals was set according to the vaccination schedule. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. As stated in section 4.10, from studies involving a 10 fold overdose of PRIMUN GUMBORO W2512 administered to 7 day old broiler chickens without MDAs (SPF chickens) no adverse reactions different from those mentioned under section 4.6.of the SPC were detected

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals.
Immunosupression was tested in accordance with the European Pharmacopoeia and relevant European guidelines.

For the live strain included in the vaccine:

Specific studies were carried out to describe the spread, dissemination, reversion to virulence, biological properties, of the vaccine strain as they are required by Directive 2001/82 as amended. According to the results of these studies, the following is included in the SPC:

"*It is not recommended to vaccinate birds younger than 7 days of age, regardless of the level of maternally derived antibodies (see section 4.9).*

The vaccine contains an "intermediate-plus" virus strain, causing significant immunosuppression and bursal damage when inoculated into birds without MDA. Vaccinated birds may excrete the vaccine virus up to 21 days. Appropriate veterinary and husbandry measures should be taken to avoid spreading of the vaccine strains to other birds. Especially, spread to chickens without MDAs, laying hens, birds approaching lay and young birds below 7 days of age should be prevented.

The product should be only used after it has been demonstrated that very virulent IBDV strains are epidemiologically relevant in the area of vaccination.

Vaccinate all susceptible birds on the premises at the same time."

There is not adjuvant included in the vaccine. The excipients used are according to Commission Regulation (EU) No 37/2010. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

One combined field safety and efficacy study was conducted. After administration, the vaccine was found to be safe based on the main and secondary safety parameters: weekly mortality, feed conversion ratios, age at slaughter and weight, and down grading and rejects at the processing plant.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.B Clinical Studies

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements which show that the vaccine can be used for active immunisation of broilers to reduce mortality, clinical disease, weight loss and acute lesions in the bursa of Fabricius associated with infection caused by very virulent strains of Infectious Bursal Disease viruses. 14 days after vaccination, the onset of immunity is established and vaccinated birds are protected during 28 days.

Vaccine batch: 1211821 (Immunogenicity study of the live infectious bursal disease vaccine PRIMUN GUMBORO W2512 against challenge with a vvIBDV field strain in SPF chickens) and nº: 1412766 (Study of antibody response against a Gumboro Vaccine - GUMBORO W2512 - in birds of different origins), were chosen to demonstrate the efficacy during the laboratory trials. Minimum potency of the vaccine for the efficacy trials was used at is required by Ph. Eur. and EMA Guidelines.

The challenge strain (vvIBDV strain, AV-213/09) used in these laboratory studies can be considered as virulent and a control non-vaccinated group was included. The recommended dose was administered per animal by drinking water from the age of 7 days onwards.. All studies were conducted to comply with the recommended volume and more than 15 chickens per group were used. The minimum recommended dose for vaccination is 1.5 log10 EID50. Clinical signs and mortality during post-challenge period were observed and samples were taken for histological examination.

Validity criteria were achieved and the relative protection percentage showed that the vaccine is efficacious against Gumboro disease virus challenge in SPF chickens under laboratory circumstances.

Field Trials

One combined field safety and efficacy study was conducted. After administration, the vaccine was found to be safe based on the main and secondary safety parameters: weekly mortality, feed conversion ratios, age at slaughter and weight, and down grading and rejects at the processing plant.

PRIMUN GUMBORO W2512 vaccine was evaluated performing an efficacy test described in OIE Manual. Three parameters were measured to evaluate efficacy:

Primary parameters:

- microscopic lesions in the bursa of Fabricius

Secondary parameters:

- clinical signs; or
- mortality

Serology was also assessed.

Summary of efficacy trials/studies included in the application:

STUDY/CENTRE	TITLE/CODE	BATCH /DOSE	RESULT
Immunogenicity **CReSA**	**CReSA Code:** **C-402/13-B** **Calier Code: GUM A 029 E 12 BURSABAX**	1211821 1 mínimum dose: $10^{1.5}$ EID_{50}/animal	The vaccine complies with OIE requirements because at least 96% of the vaccinated chickens survive without showing either clinical signs or severe lesions in the Bursa of Fabricius at the end of the observation period.
Study of antibody response against a Gumboro vaccine, Primun Gumboro W2512, in birds of different origins. **ANIMALIA**	**BUR A 047 E 15**	1412766 $10^{2.9}$ EID_{50}/animal	Chickens with MDA* responded to vaccination only when vaccinated at 21 and 28 days of age. Chickens without MDA responded to vaccination at all ages tested: 7, 14, 21 and 28 days of age.
Study of duration of immunity of Primun Gumboro W2512 (former called Calier Bursabax) vaccine in broilers	**BUR A 036 E 18**	1808782 $10^{2.1}$ EID_{50}/animal	The efficacy of the vaccine was demonstrated in chickens with MDA after challenge at 28 days post vaccination.
FIELD TRIAL **CReSA**	**BUR A 003 E 15**	1412766 $10^{2.9}$ EID_{50}/animal	The efficacy of the vaccine was demonstrated because after experimental challenge with vvIBDV strain the presence of microscopic lesions of the bursa of Fabricius was significantly lower than in the non-vaccinated group

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 veterinary Heads of 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>

or

Complete this section for extensions to the same VPA range or defined, significant variations, using the table shown below.

Some examples of significant changes in safety or efficacy data are:

- *Changes to pharmacokinetic data leading to a change in the SPC*
- *Changes to toxicological data leading to a change in the SPC*
- *Changes to user safety warnings*
- *Changes to ecotoxicological information as given in the SPC or changes to disposal warnings*
- *New residue studies in new target species or tissues*
- *Reassessment of residue data or new studies resulting from changes to MRL*
- *Changes to withdrawal period*
- *Changes to target species*
- *Changes to target species tolerance data leading to change in warnings/precautions for target species*
- *New or changed indications*

Significant changes in administrative or quality data include any Type II change, which affects the initial report. The following Type IA or IB changes may also apply:

- *Name of product [Type IA: 2]*
- *Name of active substance [Type IA: 3}*
- *MAH [Type IA: 1]*
- *Composition of the medicinal product [Type IB: 18, Type IA/B: 25, 34, 35, 39]*
- *Container/closure system [Type 1/B: 26, 28, 29, 36, 41, 43]*
- *Method of preparation [Type 1B: 33]*
- *Active substance specification [Type IB: 25]*
- *CEP [Type IA/B: 15]*
- *Re-test period or storage conditions of active substance [Type IB: 17]*
- *Excipient specifications [Type 1A/B: 25]*
- *Packaging materials[Type 1A/B: 28, 29, 36, 41, 43]*
- *TSE [Type 1A: 16, 22]*
- *Shelf-life or storage conditions of the finished product [Type 1B: 42]*

Quality changes

Summary of change **(Application number)**	**Section updated in Module 3**	**Approval date**
<Example: Change to active substance specification> (MS/V/XXX/X/IB/XX)	N/A	

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated in Module 3**	**Approval date**
<Example: Addition of target species - pigs> (MS/V/XXX/X/II/XX)	<IIIA> <IIIB> <IV>	