MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios

DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

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España
(Reference Member State)

ES/V/0295/001/DC

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

PRIMUN BRONCHITIS H120

CORREO ELECTRÓNICO

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0295/001/DC
Name, strength and pharmaceutical form	Primun Bronchitis H120
Applicant	LABORATORIOS CALIER, S.A. Calle Barcelones, 26 Pla de Ramassar 08520 Les Franqueses del Vallés (Barcelona) SPAIN
Active substance(s)	Live attenuated Avian Infectious Bronchitis Virus (IBV), Massachusetts IBV_H120 strain: 3.0 - 4.0 log_{10} EID_{50}* * EID_{50} = 50% embryo-infective dose.
ATC Vet code	QI01AD07
Target species	Chickens
Indication for use	For the active immunization of broilers and future layers against avian infectious bronchitis, produced by strains of the Massachusetts serotype. Onset of immunity: 3 weeks after 1st vaccination. Duration of immunity in broilers: up to 6 weeks of age (after 2 vaccinations at day 1 and day 21). Duration of immunity in future layers: up to 10 weeks of age (after 3 vaccinations at days 1, 21 and 49).

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 Art/icle 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Day 210: 13/03/2019
Date product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States for original procedure	DE, IT, PL and PT

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. Qualitative and quantitative particulars

Composition

Each dose of reconstituted vaccine contains:

Active substances:

Live attenuated Avian Infectious Bronchitis Virus (IBV), Massachusetts IBV_H120 strain: 3.0 - 4.0 $\log_{10}$ EID_{50}*
* EID_{50} = 50% embryo-infective dose.

Excipients:

Disodium phosphate
Potassium dihydrogen phosphate
Lactose monohydrate
Skimmed milk powder
Water, highly purified

The container/closure system is transparent glass vials type I, which are closed with bromobutyl rubber stoppers and sealed with aluminum caps.The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strain and the absence of preservatives are 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 accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substance is a live attenuated Avian Infectious Bronchitis Virus (IBV), Massachusetts IBV_H120 strain, an established substance described in the European Veterinary 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 indicate 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 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. Control tests during production

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

E. Control Tests on the Finished Product

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.

F. 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.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The claim of 2 hours stability after reconstitution is based on the demonstration of stability for a batch broached and stored as indicated.

G. Other Information

Non applicable

III. SAFETY ASSESSMENT

Primun Bronchitis H120 is a live attenuated vaccine. It is claimed for the active immunization of broiler and future layers against avian infectious bronchitis produced by strains of the Massachusetts serotype.

Laboratory trials

The safety of the administration of an overdose and the repeated administration of one dose in the target animal is demonstrated. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. Results of adverse reactions were included in the SPC: “Slight respiratory signs may be noted commonly in vaccinated birds 3-10 days after vaccination. All clinical signs subside within about 5 days” as well as overdose results “complete ciliostasis was detected after the application of an overdose”.

Safety studies results for the respiratory tract and kidney of chicken complies with the requirements of section 2-4-1-1 of the monograph 0442 *“Avian infectious bronchitis vaccine (live)”*

Safety studies results for the reproductive tract of chicken complies with the requirements of section 2-4-1-2 of the monograph 0442 *“Avian infectious bronchitis vaccine (live)”*

The safety of the veterinary medicinal product has not been established during lay. An advertisement is included in the SPC: “Do not use in birds in lay and within 4 weeks before the start of the laying period”.

The vaccine virus complies with the test “increase in virulence” (section 2-4-2, monograph 442) as no indication of increasing virulence of the virus recovered for the final passage compared with the material used for the 1st passage was observed.

Specific studies were carried out to describe the spread, dissemination and reversion to virulence. Results are included in the SPC: “Vaccinated chickens may excrete the vaccine strain up to 18 days following vaccination. During this time, the contact of unvaccinated chickens with vaccinated chickens should be avoided. To prevent spread of vaccine virus vaccinating equipment and chicken houses should be disinfected between flocks. All the chickens on the site should be vaccinated at the same time”

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.

Excipients used are out of scope with reference to MRL regulation. 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

The applicant has performed a study to evaluate the efficacy and safety of the vaccine in pullets under field conditions and another one in broilers, both of them in compliance with the principles of Good laboratory Practice (GLP) and Good clinical Practice (GCP).

Environmental Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The product is safe to the environment.

IV. CLINICAL ASSESSMENT (EFFICACY)

Primun Bronchitis H120 is a live freeze-dried vaccine claimed for the active immunization of broiler and future layers against avian infectious bronchitis produced by strains of the Massachusetts serotype.

It is administered by drinking water, nebulisation or oculo-nasal route.

Vaccination scheme:
Broilers: first vaccination on the 1st day of life and revaccination at 3 weeks after first vaccination.

Future layers: first vaccination on the 1st day of life and revaccination at 3 weeks and 7 weeks after first vaccination.

IV.B Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements.

Immunogenicity assay was performed after vaccination for each route and method of administration (oral, oculo-nasal and spray) according to the European Pharmacopoeia 0442: "*Avian infectious bronchitis vaccine (live)*". Ciliary activity in tracheal explants has been recorded.

The challenge was performed on day 22 post-vaccination by eye-drop with IBV M41-CK strain. Onset of immunity was established at 3 weeks after first vaccination.

The following table shows a summary of the laboratory trials provided in the dossier:

	Laboratory studies	Nº animals	Batch
1	Inmunogenicity test by oral route SPF chickens one day old One vaccination	25/8 (vaccinated/control)	1209810 Minimum dose ($10^{3.0}$ EID_{50}/animal)
2	Inmunogenicity test by oculonasal route SPF chickens one day old One vaccination	25/15 (vaccinated/control)	1308756 Minimum dose ($10^{3.0}$ EID_{50}/animal)
3	Inmunogenicity test by spray route SPF chickens one day old One vaccination	25/15 (vaccinated/control)	1308756 Minimum dose ($10^{3.0}$ EID_{50}/animal)

Field Trials

	Field study	Nº animals	Follow up	Results
1	Field efficacy trial of live infectious bronchitis virus vaccine administered to broilers in a commercial farm (spray route)	T1 (Vaccinated): 8000 T2 (vaccinated with Bronhipra): 10000 Challenged at 21 days post second vaccination T1 (vaccinated): 20 T2 (vaccinated with Bronhipra): 20 T3 (SPF unvaccinated): 10	Ciliary activity Mortality Clinical signs	T1: 100% protection T2:100% T3: 0% 0% No clinical signs
2	Evaluation of the efficacy of Primun IB-ND DUO against bronchitis disease in pullets under field conditions (first vaccination by spray route and booster doses by drinking water)	Challenged at 10 weeks of age by oculo-nasal route T1 (vaccinated): 20 T3 (untreated): 20	Virus recovery Ciliary activity Mortality Clinical signs	T1: 30% T3: 90% T1: 70% T3: 10% 0% ----

According to the results:

- Duration of immunity in broilers is established up to 6 weeks of age (after 2 vaccinations at day 1 and day 21).
- Duration of immunity in future layers is established up to 10 weeks of age (after 3 vaccinations at days 1, 21 and 49).

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