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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

GALLIVAC IB88 NEO

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0450/001/MR
Name, strength and pharmaceutical form	GALLIVAC IB88 NEO effervescent tablet for suspension for nebulisation (France, Bulgaria, Cyprus, Greece, Croatia, Slovenia), GALLIVAC IB88 NEO effervescent tablet for suspension for nebulisation for chicken (Austria) Gallivac IB88 (working name for Sweden, Denmark, Finland, Iceland)
Applicant	Boehringer Ingelheim Animal Health France 29 avenue Tony Garnier 69007 Lyon – France
Active substances	Each dose contains: Attenuated Infectious Bronchitis coronavirus, CR88121 strain ≥ 4.0 log10 EID50* * EID50: egg infective dose 50%
ATC Vetcode	QI01AD07.Live viral vaccines, avian infectious bronchitis virus.
Target species	Broiler chickens.
Indication for use	In broiler chickens, from 1 day of age: active immunisation against coronavirus variant strain CR88, to reduce the tracheal ciliostase related to the development of clinical signs.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.ircp.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 32 (3) of Directive 2001/82/EC as amended.
Date of completion of the original procedure	2 March 2022
Date product first authorised in the Reference Member State (MRP only)	18 May 2015
Concerned Member States for original procedure	Austria, Bulgaria, Croatia, Cyprus, Denmark, Finland, France, Greece, Iceland, Slovenia, Sweden,

I. SCIENTIFIC OVERVIEW

The vaccine is a live attenuated infectious bronchitis virus which is indicated for the immunisation of broiler chickens from one day of age and presented in effervescent tablet in blister to be reconstituted with water and administered by nebulisation.
The vaccine was first developed under a freeze-dried pellet presentation for suspension and was first authorized in 1998 (in France) under the name of GALLIVAC IB88. Then, the presentation of the vaccine was improved and an effervescent tablet form was developed (GALLIVAC IB88 NEO). The formulation of the tablet form was also improved by the addition of mannitol to reduce foaming. The tablet form contains the same CR88 strain at the same dose.
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 reactions observed are indicated in the SPC (Summary of Product Characteristics).
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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

Each dose of reconstituted vaccine contains:

Active substance :
Attenuated Infectious Bronchitis coronavirus, CR88121 strain ≥ 4.0 log10 EID50*

* EID50: egg infective dose 50%

The tablets are packed in aluminium blisters. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strains 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 practices in a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with European pharmacopoeia monographs where these exist, 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 “Guideline on requirements for the production and control of immunological veterinary medicinal products” (EMA/CVMP/IWP/206555/2010-Rev02).

Seed lots and cell banks have been produced 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 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 are in line with the relevant requirements; any deviation from these requirements is justified. The tests performed are as follows:
- Appearance
- Disintegration time
- pH
- Titration and identity test
- Total viable aerobic germs
- Mycoplasma
- Viral purity
- Determination of residual humidity

G. Stability

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 (2 years for the tablet) when stored under the approved conditions (at 2-8° C).

The vaccine must be used within 2 hours after reconstitution.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of oculo-nasal and nebulisation administrations of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated in different laboratory studies. The initial safety trials were made by using the freeze-dried GALLIVAC IB88 vaccine. Afterwards, when the effervescent tablet form of the vaccine GALLIVAC IB88 NEO was developed and when the day-old claim was introduced, new safety studies were performed. The investigations were done according to the recommendations of Directive 2001/82/EC as amended by Directive 92/18/EC and Directive 2009/9/EC respectively as well as the relevant guidelines.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals.
Specific studies were carried out to describe the spread, dissemination, reversion to virulence. Biological properties, recombination or genetic reassortment of the vaccine strain were also assessed.
The excipients used are covered by MRL regulation and 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.
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.

Overall, the vaccine proved to be well tolerated in the target species. The local and systemic reactions observed are described in the SPC (Summary of Product Characteristics) and package leaflet under “adverse reactions”.

Details are given in the Summary of Product Characteristics (SPC) as follows:

3.5 Special precautions for use

Special precautions for safe use in the target species:
The vaccinal virus can spread to non-vaccinated birds, with no virulence for the hen species and apathogenic to other birds species.
Appropriate veterinary and husbandry measures should be taken to avoid spread of the vaccine strain to unvaccinated chickens and wildlife avian populations.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
. Care should be taken when dissolving and administering the vaccine.
Wear respiratory and eye protection conforming to current European standards.
Hands should be washed with soap and disinfected after vaccinating.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Common *(1 to 10 animals / 100 animals treated):*	*Vaccination may induce mild respiratory signs that may persist for up to 21 days.*

3.7 Use during pregnancy, lactation or lay

Do not vaccinate during laying period

3.8 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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

No undesirable effect other than those mentioned in section "adverse events" was observed after the administration of ten doses of vaccine.

Field studies

Three field trials were performed. Two were conducted with the freeze-dried form of the vaccine (GALLIVAC IB88) in two weeks old chickens either associated with a vaccine against swollen head syndrome or during a year within the frame of the Temporary Authorization for Use. One study was done with the tablet form of the vaccine (current formulation of GALLIVAC IB88 NEO) in day-old chicks.
In the first field trial, approximately 400,000-day-old chicks received a standard vaccination program. At 14 days of age, chickens were vaccinated against swollen head syndrome and with GALLIVAC IB88.
Results were also obtained in industrial chicken farms vaccinated with GALLIVAC IB88 vaccine between July 1997 and March 1998 in the context of the Temporary Authorization for Use of this vaccine in France. Approximately 2.6 million of 14 days old chicks were vaccinated with commercial batches of vaccine.
The third field safety study was designed for collecting safety data in three flocks of at least 18000 newly hatched chicks vaccinated with GALLIVAC IB88 NEO associated with the vaccine HATCHPAK IB H120.

The results confirm the observations made in the laboratory studies. The reactions observed are described in the SPC and package leaflet under "adverse events".

Environmental risk assessment

The applicant provided an environmental risk assessment which showed that the risk for the environment and other animals and species posed by this vaccine can be considered as very low.

Warnings and precautions as listed in the product literature for its disposal are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the vaccine has been established in laboratory studies that have been performed in accordance with Ph. Eur. requirements: performed on the target species at the minimum age recommended for vaccination and at minimum dose. Onset and duration of immunity have been set in relation to the claim proposed which is also consistent with the claim usually set for such vaccine against the Infectious Bronchitis disease. Efficacy in presence of Maternal Derived Antibodies has also been shown.
The efficacy of the product has been demonstrated after challenge of vaccinates and control birds in laboratory studies in accordance with the relevant requirements which indicate that the vaccine is satisfactory if not fewer than 80 per cent of the vaccinated chickens show normal ciliary activity or if the challenge virus is detected in not more than 20 per cent of the vaccinated chickens after challenge.

Summary table of challenge studies

Animals Treatment Number	**Antibody status**	**Vaccine: Age Route of administration**	**Challenge: Day post-vaccination**	**Follow up**	**Results: Cases/total**		**Conclusion**
					Vaccinates	Controls	
20 birds vaccinated 10 controls	Sero negative	Freeze dried One dose at 1 day of age nebulization	D21	Virus isolation in trachea	3/20	7/10	Significant difference
20 birds vaccinated with 4 log10 EID50 20 birds vaccinated 3.7 log10 EID50 10 controls	Sero negative	Freeze dried One dose at 2 weeks of age nebulization	D21	Virus isolation in trachea	4/20 15/20	9/9	Significant difference
20 birds vaccinated 10 controls	Sero negative	Effervescent tablet One dose at 2 weeks of age nebulization	D21	Virus isolation in trachea	4/20	9/10	Significant difference
20 birds vaccinated 10 controls	Sero negative	Effervescent tablet One dose at 1 day of age nebulization	D21	Clinical signs: tracheal rales Ciliary activity: score $\geq$ 2	0/20 1/20	7/10 at D26 10/10	Conform to European Pharmacopeia requirements

20 birds vaccinated 10 controls	Sero positive	Effervescent tablet One dose at 1 day of age nebulization	D35	Ciliary activity at D5 post challenge: score ≥ 2	0/20	10/10	Conform to European Pharmacopeia requirements
20 birds vaccinated 10 controls	Sero positive	Effervescent tablet One dose at 1 day of age nebulization	D42	Ciliary activity at D5 post challenge: score ≥ 2	0/20	8/10	Conform to European Pharmacopeia requirements
39 birds vaccinated 20 controls	Sero positive	Effervescent tablet One dose at 1 day of age nebulization	D30-31	Virus detection in trachea	0/39	11/20	Significant difference

Three additional laboratory studies performed with the freeze dried vaccine were provided in which only a serological follow up was performed. No correlation between antibodies and protection is demonstrated and therefore these studies are considered as supportive of the challenge results.

Based on the observations made in laboratory efficacy studies, it can be concluded that vaccination reduces the tracheal ciliostase related to the development of clinical signs caused by coronavirus variant strain CR88. An onset of immunity of 3 weeks and duration of immunity of 6 weeks after vaccination was observed in these laboratory studies.

Field Trials

Efficacy of vaccination was also demonstrated under field conditions in three field trials described above in the safety part. Two were conducted with the freeze-dried form of the vaccine (GALLIVAC IB88) and one study was done with the tablet form of the vaccine (current formulation of GALLIVAC IB88 NEO) in day-old chicks.
The data obtained from the field studies confirm the results obtained from the laboratory studies.

The following conclusions can be drawn from the results of the efficacy studies concerning onset and duration of immunity, indications for use and immunisation scheme:

3.2 Indications for use for each target species

In broiler chickens, from 1 day of age: active immunization against coronavirus variant strain CR88, to reduce the tracheal ciliostase related to the development of clinical signs.

Onset of immunity: 3 weeks
Duration of immunity: 6 weeks

3.9 Administration routes and dosage

One dose of vaccine to be administered by nebulisation from 1 day old.
Use clean equipment, free from any antiseptic and/or disinfectant for the preparation and administration of the vaccine.
Dissolve the tablets in an appropriate volume of non-chlorinated drinking water for the number of animals to be vaccinated (adapt the volume of necessary water to suit the type of nebulizer to be used, for example, use 10 litres of water to vaccinate around 20,000 animals). Wait until complete dissolution of the tablets before using the vaccine solution.
Do not use "fogger"-type sprayer.
The ventilation system of the poultry house should be inoperative during the spray administration and appropriate protective mask must be worn.
The vaccine should be sprayed over the animals, using a spray equipment capable of producing microdroplets (average diameter 80 to 150 µm).

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 benefit risk 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 (http://www.hma.eu/vmriproductindex.html).

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.