ANSES

Agence Nationale du Médicament Vétérinaire
(National Agency for Veterinary Drugs)
(Reference Member State)
BP 90203
35302 FOUGERES CEDEX
FRANCE

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

HATCHPAK IB H120

Update 14/11/2016

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/171/001/DC
Name, strength and pharmaceutical form	HATCHPAK IB H120 – Frozen vaccine
Applicant	MERIAL 29 avenue Tony Garnier 69007 LYON France
Active substances	Live Infectious Bronchitis virus, H120 strain: 3.7 to 4.7 $\log_{10}$ EID_{50}/dose
ATC Vetcode	QI01AD07
Target species	One day-old chickens
Indication for use	Active immunisation against Infectious Bronchitis in order to reduce infection with Massuchusetts serotype of Infectious Bronchitis virus.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v) website .

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 32 (3) of Directive 2001/82/EC as amended
Date of completion of the original procedure	25/07/2007
Date product first authorised in the Reference Member State (MRP only)	Not applicable (decentralised application)
Concerned Member States for original procedure	AT, BE, CZ, DE, EL, ES, FI, HU, IE, IT, LT, LU, LV, NL, PL, PT, SK, 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 product consists of 1 ampoule Hatchpak IB H120, which contains:

Hatchpack IB H120

Name of ingredients	Quantity per dose
Live Infectious Bronchitis (H120) component	3.7 to 4.7 log10 EID_{50}

The container consists of type I glass ampoules of 5 ml. The particulars of the container and controls performed are provided and conform to the regulation.

The choice of the vaccine strain and formulation are justified, as well as other points of interest in particular frozen product.

The product is a novel 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:

- Live Infectious Bronchitis (H120) component: an established active 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 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 Ph. Eur. ; 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:

- physico-chemical tests
- identification and assay of the active ingredient
- safety test in day old chickens (TABST withdrawn on 07/03/2013)
- bacterial, fungal and mycoplasmic sterility according to Ph. Eur.
- viral purity

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

G. Stability

The active substance is fully tested to ensure compliance with the specification immediately prior its use in manufacture of the product.

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

III. SAFETY ASSESSMENT

The vaccine batches used are representative of the production process. As it is a live vaccine, dilutions were adapted to perform the tests with the maximum release titer for each component.

Laboratory trials

Some of the trials were performed using HatchPak Avinew IB H120, which is a combined vaccine associating HatchPak IB H120 with HatchPak Avinew (Live Newcastle disease vaccine). Conclusions with the combined vaccine are applicable to HatchPak IB H120.
The safety of the oculo-nasal (ON) and spray administration of one dose, an overdose and the repeated administration of one dose in the target species is demonstrated in the following studies:

- **safety of 1 dose and of an overdose in day-old SPF chicks, HatchPak IB H120 by ON route**: in 3 groups of SPF day-old birds, receiving either a single dose, either 10 doses, or no vaccine. Birds were observed for 28 days, including a record of respiratory signs, weight gain, serological response and post-mortem examination
- **safety of 1 dose and of an overdose in day-old SPF chicks, combined vaccine (HatchPak Avinew IB H120) by nebulisation**: in 3 groups of SPF day-old birds, receiving either a single dose, either 10 doses, or no vaccine. Birds were observed for 21 days, including a record of respiratory signs, weight gain, serological response and post-mortem examination

- **safety of 1 dose (HatchPak Avinew IB H120) in day-old conventional chicks by ON route:** in 2 groups of day-old birds, receiving either a single dose, or no vaccine. Birds were observed for 28 days, including a record of respiratory signs, weight gain, serological response and post-mortem examination
- **safety of the repeated administration of 1 dose (HatchPak Avinew IB H120) in day-old SPF chicks**: in 2 groups of SPF day-old birds, receiving either 2 single doses with an interval of 14 days, or no vaccine. Birds were observed for 28 days, including a record of respiratory signs, weight gain, serological response and post-mortem examination

The investigations were performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. Bronchial rales not associated with any respiratory distress or any general sign were observed in up to 15% of the birds. This was attributed to the IB component. A warning is indicated in section 4.6. Adverse reactions of the SPC. The overdose did not induce more severe reactions, therefore, the section 4.10 Overdose cross refers to section 4.6.

As the vaccine is not intended for this category of animals, no specific investigation of effect on reproductive performance was conducted with HatchPak IB H120. However, the applicant has provided other studies performed with a vaccine containing the same strain as HatchPak IB H120 which are not indicative of a detrimental effect on the reproductive tract; in particular the IB strain is compliant to the specifications of the Ph. Eur. with regard to the safety for the reproductive tract. This information is provided in the SPC in section 4.7 Use during pregnancy, lactation or lay.

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.

For the IB live strain included in the vaccine:
Specific studies were carried out to describe the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strain.
The vaccine strain was demonstrated as compliant to the Ph. Eur. requirements. The vaccine virus can spread to unvaccinated birds. Infection of unvaccinated chickens with the vaccine virus from vaccinated birds does not cause any sign of disease. Reversion to virulence trials carried out in the laboratory have shown that the vaccine virus does not acquire any pathogenic characteristics after at least 5 passages in chickens. This is transcribed in the SPC section 4.4. Special warning for target species

The excipients used are included in annex II of MRL regulation. Based on this information, a withdrawal period is not justified. The withdrawal period is therefore set at zero days.

The interaction of the combined vaccine (HatchPak Avinew IB H120) with a recombinant HVT+IBD vaccine was studied by administration of both vaccines in day-old SPF chickens. Concerning the association with the recombinant HVT

expressing the protective antigen of the Infectious Bursal disease virus, the safety has been established and the efficacy has been demonstrated by challenge for the Newcastle, Infectious Bronchitis and Gumboro strains. The interaction with HatchPak Avinew was also studied (see previously the demonstration of the safety of a single dose, overdose and repeated dose). Taking into account the safety and efficacy demonstration of the association, the following statement is given in the SPC section 4.8. Interaction:

No information is available on the safety and efficacy from the concurrent use of this vaccine with any other except with a frozen live vaccine against Newcastle disease containing VG/GA strain and with a recombinant HVT vaccine expressing the protective antigen of the Infectious Bursal disease virus. It is therefore recommended that no other vaccines than these should be administered within 14 days before or after vaccination with the product.
Concerning the association with the recombinant HVT vaccine expressing the protective antigen of the Infectious Bursal disease virus, the safety has been established and the efficacy has been demonstrated by challenge for the Infectious Bronchitis and Gumboro strains.

Field studies

A field trial was conducted in 44,000 newly-hatched conventional broiler chickens, half of them vaccinated with Hatchpak Avinew IB H120, and the other birds receiving AVINEW and BIORAL H120. The birds were followed during 58 days; records of coughing and individual examinations of 50 birds per groups were performed during 26 days; zootechnical performances were recorded as well as serological response. Both groups had similar results.

Ecotoxicity

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

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

It is reminded that the vaccine strain contained in this vaccine has already been registered in another live vaccine (BIORAL H120) which has been used for years in the field with no record of ecotoxicity problems.

IV CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

Some of the trials were performed using HatchPak Avinew IB H120, which is a combined vaccine associating HatchPak IB H120 with HatchPak Avinew (Live Newcastle disease vaccine). Conclusions with the combined vaccine are applicable to HatchPak IB H120.

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

- **Efficacy of HATCHPAK IB H120 by means of an IBV 91-1 challenge**: in day-old SPF birds. The vaccine is compliant to the potency test of the Ph. Eur. monograph 442.
- **efficacy against a virulent IBV 91-1 challenge in conventional broilers 6 weeks after vaccination with the combined vaccine (HatchPak Avinew IB H120)**: Day-old birds were either vaccinated, either kept as controls. All the birds were challenged at the age of 6 weeks. 5 days after challenge, the challenge virus was reisolated in 5% of the vaccinates and in 100% of the controls.
- **efficacy against a virulent IBV 91-1 challenge in conventional broilers 3 weeks after vaccination with the combined vaccine (HatchPak Avinew IB H120)**: Day-old birds were either vaccinated, either kept as controls. All the birds were challenged at the age of 3 weeks. 5 days after challenge, the challenge virus was reisolated in 10% of the vaccinates and in 100% of the controls.

Field Trials

The applicant has conducted field studies including challenges under controlled conditions (birds vaccinated under field conditions, removed from the farms and challenged under laboratory conditions); other groups or birds are included (unvaccinated, vaccinated under laboratory conditions). IB challenges were conducted at different ages. It was shown that despite in some challenges the level of protection was reduced in birds vaccinated and reared under field conditions compared to birds vaccinated and reared under laboratory conditions, the vaccine induced a significant protection in birds under field conditions.

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 Medicines Agencies (veterinary) (HMA(v)) website.

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:

1. Compatibility with a recombinant HVT vaccine expressing the protective antigen of the IBD virus (vaxxitek HVT+IBD) authorised on 6/10/2008
2. New Manufacturing Sites authorised in 2009
3. Extension of shelf-life from 2 to 3 years authorised on 21/11/2012
4. Repeat-use including new CMS: AT BE BG CY IE NL RO SI UK (2013)
5. Change in the freezing steps, authorised on 03/12/2015