CBG MEB

College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500 3531 AH Utrecht The Netherlands

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

HuveGuard NB

Created: July 2020

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PRODUCT SUMMARY

EU Procedure number	NL/V/0207/001/MR
Name, strength and	HuveGuard NB suspension for oral suspension
_pharmaceutical form	
Applicant	Huvepharma NV
	Uitbreidingstraat 80
	2650 Antwerp
	Belgium
Active substance(s)	Oocysts of precocious strains of coccidia species:
	- Eimeria brunetti
	- Eimeria necatrix
ATC Vetcode	QI01AN01
Target species	Chicken
Indication for use	For the active immunisation of chickens to reduce
	infection and clinical signs of
	coccidiosis caused by E. necatrix and, E. brunetti.

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

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PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	28 April 2016
Date product first authorised in the Reference Member State (MRP only)	15 July 2015
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LV, MT, NO, PL, PT, RO, SE, SI, 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 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

The product contains a minimum quantity of 100 sporulated oocysts of *Eimeria necatrix strain* mednec₃₊₈ and a minimum quantity of 50 sporulated oocysts of *Eimeria brunetti* strain roybru₃₊₂₈ during the shelf life. The excipients are: polysorbate 80, sodium chloride, potassium chloride, disodium hydrogen phosphate, potassium dihydrogen phosphate and water for injections.

The container/closure system consists of 30 ml low-density polyethylene (LDPE) vials that are closed with rubber stoppers and sealed with aluminium caps. Bottles, stoppers and caps are sterilized by gamma irradiation. The container of 30 ml is used either to hold 1,000 or 5,000 doses of in a volume of 25.2 ± 0.2 ml.

The choice of the vaccine strains and excipients are justified.

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.

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

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C. Control of Starting Materials

The active substances are sporulated oocysts of *Eimeria necatrix* strain mednec₃₊₈ and *Eimeria brunetti* strain roybru₃₊₂₈. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with Ph. Eur. monographs where these exist. For the substances where there is no such requirement the company has identified the source of the substance, explained how its quality is controlled and provided relevant certificates of analysis.

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. 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 tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified. The tests include in particular: Appearance, *In vitro* Potency test (viable oocyst count), Sterility, and Rapid Potency Test (*in vivo* potency including identity).

The demonstration of the batch to batch consistency is based on the results of 6 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 substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substances 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 in-use shelf-life of the reconstituted vaccine is supported by the data provided.

G. Other Information

None.

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III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of an overdose administration in the target animal is demonstrated in a study where a ten-fold overdose was administered via eye drop in 15 day-old chicks and 14-day-old birds using HuveGuard NB batch E2P140442 and E2P140781, respectively. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. The vaccine was found to be safe (at ten times the maximum release titre) as no vaccinated chicks showed notable signs of coccidiosis or died from causes attributable to the vaccine. The safety of repeated administration of one dose has not been tested, as the vaccination schedule is for one single dose (no booster dose required) for the life of a broiler, breeder or layer chicken as coccidiosis vaccines rely on natural cycling of the vaccine antigens via the litter for continued stimulation of the immune system.

No investigation of effect on reproductive performance was conducted because the active substances contained in the product are not considered a potential risk factor. No studies have been performed in birds during lay, a relevant warning is included in the SPC.

No studies towards the immunological functions have been performed. Based on a study performed with HuveGuard MMAT (NL/V/0206/001/MR), it may however be assumed that this product will not adversely affect the immune system of the vaccinated animal or its progeny, therefore a specific study was not carried out.

For each 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. *E. necatrix* and *E. brunetti* showed no indication of a change in virulence.

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 safety of the product has been monitored in 6 field trials. The product has been tested under field conditions in The Netherlands, Belgium and France. Different routes of administration (drinking water, eye drop, spray on birds) have been investigated in these trials. The efficacy and safety of HuveGuard NB under field conditions has been investigated following a vaccination with HuveGuard NB and HuveGuard MMAT. Results of the field studies generally conform the safety profile as established in the laboratory studies.

User Safety

A user safety risk assessment was conducted in accordance with the appropriate Guideline. The overall risk associated with exposure of users to the product is considered negligible. Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users.

Environmental Risk Assessment

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

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

Residue Studies

The excipients used are considered as not falling within the scope of the MRL regulation. Based on this information, no withdrawal period is proposed.

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IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements. Tests for immunogenicity of the *E. necatrix* mednec₃₊₈ and *E. brunetti* (roybru₃₊₂₈) antigens within HuveGuard NB vaccine and dose determination (immunogenicity) of *E. brunetti* (roybru₃₊₂₈) single antigen are described below:.

Animals	Antibo	Vaccine, dose,	Challenge,	Follow up:	Results:	
Groups	dy	route of	dose,	Duration		
Number	status	administration	Day	Endpoints*		
Age			post-			
			vaccination			1
Study					Vaccinates	Controls
		rix (single antigen)		Τ	T	Γ
Chickens	SPF	Spray on feed	D21 of the	7 days post		
		(day-old),	study (21	challenge (PC):		
One day old		spray on	days PV)	euthanasia for 10 birds in all		
Nogativo		chickens (day- old)	Strain			
Negative control		olu)	E. necatrix	groups		
(unvaccinated,		E. necatrix	Gronec, 2.5	14 days post		
unchallenged):		(mednec 3+8)	x 10 ³	challenge:		
20		at passage	oocysts per	euthanasia		
		level X+8, 100	bird by oral	remaining birds		
Positive control		oocysts/dose	gavage			
(unvaccinated,				- Body weight	Only higher than the	Negative control
challenged): 20					positive control for the	group had a
					spray on chicks group	higher weight
Vaccinated1,					for day 0-7 PC ^a .	gain than positive
spray on bird:						control group ^a .
20				Faces	Dath was instead	
Vaccinated2,				- Faecal oocysts	Both vaccinated groups had a lower	
spray on feed:				oocysts	OPG for day 6-8 PC	
20					than the positive	
					control group ^a (Ph. Eur.	
					compliant)	
					, ,	
				- Intestinal	Significantly lower for	90% of positive
				lesions	both vaccinate groups	control birds at
					compared to positive	day 7 PC had a
					control at day 7 PCa,	lesion score of 2
					although mean lesion	or 3, with a mean
					scores were 1.2 and	lesion score of 2.1 (Ph. Eur.
					1.4 for spray on bird and spray on feed,	compliant)
					respectively (Not Ph.	compliant
					Eur. compliant).	
Dose Determinat	ion <i>E. brur</i>	netti (single antige	n) (EPL2010-01))	1 - 7	L
Chickens	Hy-Line	Eye drop (14	21 days PV	7 days post		
	brown	days old)		challenge:		
14 days old	male		Strain	euthanasia for		
	(not	E. brunetti	E. brunetti	10 birds in all		
Negative	SPF)	Roybru 3+28	(AM),	groups		
control			10,000			
(unvaccinated,		Dose:	oocysts per	14 days post		
unchallenged):		50 oocysts	dose by oral	challenge:		
19		Or	gavage	euthanasia		
		100 oocysts		remaining birds		

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Positive control		Or				
(unvaccinated,		200 oocysts		- Body weight	All 3 vaccinated groups	Negative controls
challenged): 20					were heavier than the	higher weight
					positive control group	gain than positive
Vaccinated1, 50					on both day 7 and 14	controls ^a .
oocysts/dose:					PC ^a . (Ph. Eur.	
20					compliant)	
Vaccinated?				- Faecal	No faecal oocyst	Significantly
Vaccinated2, 100				oocysts	output after challenge	higher in positive
oocysts/dose:				OUCYSIS	in any of the 3	control when
20					vaccinated groups	compared to
20					vacematea Broaps	vaccinates ^a (Ph.
Vaccinated3,						Eur. compliant)
200						24.1 00.11.01.11.1
oocysts/dose:				- Intestinal	No lesions (score of 0	Positive control:
20				lesions	for 100% of the birds)	score ≥2 in 70% at
					in all 3 vaccinated	7 days PC; no
					groups. (Ph. Eur.	lesions at day 14
					compliant)	PC (Not Ph. Eur.
						compliant)
Dose Confirmation	on (immun	ogenicity) E. brune	etti in the Huve	Guard® NB product ((EPL2011-03)	
Chickens	SPF	Eye drop (14	Day 21 PV	7 days post	1 bird from the	
		day-old) and		challenge:	drinking water group	
14 days old		drinking water	Strain	euthanasia for	died (not vaccine	
		(14 day-old)	E. brunetti	12 birds in all	related)	
Negative			(AM) 10,000	groups		
control		HuveGuard NB	oocysts per			
(unvaccinated,			dose by oral	15 days post		
unchallenged):			gavage	ala all anasas		
		Test antigen:	gavage	challenge:		
22		E. brunetti	gavage	euthanasia		
22		E. brunetti Roybru 3+28,	gavage	_		
22 Positive control		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds	6: 16 11 11 6	
Positive control (unvaccinated,		E. brunetti Roybru 3+28,	gavage	euthanasia	Significantly higher for	
22 Positive control		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds	both vaccinated	
Positive control (unvaccinated, challenged): 22		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds	both vaccinated groups compared to	
Positive control (unvaccinated, challenged): 22 Vaccinated1,		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds	both vaccinated groups compared to the positive controls ^a	
Positive control (unvaccinated, challenged): 22		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds	both vaccinated groups compared to	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant)	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2,		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant)	
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts - Intestinal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant)	On day 7 PC 100%
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant) 100% of vaccinated birds had a lesion	of positive control
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts - Intestinal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant) 100% of vaccinated birds had a lesion score of 0 on day 7 and	of positive control birds had a lesion
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts - Intestinal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant) 100% of vaccinated birds had a lesion score of 0 on day 7 and day 15 PC, which was	of positive control birds had a lesion score of 2 (Ph.
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts - Intestinal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant) 100% of vaccinated birds had a lesion score of 0 on day 7 and day 15 PC, which was different from the	of positive control birds had a lesion
Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		E. brunetti Roybru 3+28, 50 oocysts per	gavage	euthanasia remaining birds - Body weight - Faecal oocysts - Intestinal	both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a (Ph. Eur. compliant) 100% of vaccinated birds had a lesion score of 0 on day 7 and day 15 PC, which was	of positive control birds had a lesion score of 2 (Ph.

a: significant difference

The data provided on pivotal laboratory efficacy trials of HuveGuard NB vaccine against *E. necatrix* and *E. brunetti* in SPF chicks are satisfactory and in accordance with the requirements of specific Ph.Eur. monograph 2326 for this type of vaccine.

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b: no significant difference

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During a post-authorisation variation, additional laboratory studies were provided supporting the administration of the vaccine from 1 day of age when administered via spray on feed or spray on birds, and from 3 days of age when administered via the drinking water. Two post-authorisation laboratory trials were submitted, and these are summarized below.

Animals Groups Number Age	Antibo dy status	Vaccine, dose, route of administration	Study design	Dur	low up: ration lpoints*	Results:	
Study						Vaccinates	Controls
	of HuveGu	ard NB by spray o	n bird, spray or	ı feed	, drinking wate	r (EPL 2018-09)	
219 Chickens,	SPF	HuveGuard NB	Part A:		7, 14, 21	,	
Mixed gender		(vaccination in	challenge	pos	t vaccination		
		day-old birds	with	and	l day 2, 5, 7,		
1 Day-old		via spray on	E. necatrix	8, 1	1, 14 post		
positive control		birds or spray	at 21 days	cha	llenge		
(unvaccinated,		on feed and in	old for				
challenged):		3-day-old birds	group 1-3	-	Body weight	Part A E. necatrix:	
Part A ≥ 20		via drinking	and at 24			Significantly greater	
Part B ≥ 20		water)	days old for			weight gain for the	
2.6			group 4-5.			drinking water	
2 Spray on			Dowt D.			vaccinated group on	
birds vaccinated:			Part B: challenge			day 7 PC compared to	
Part A ≥ 20			with			positive control ^a (Ph. Eur. compliant), spray	
Part B ≥ 20			E. brunetti			on bird and spray on	
1 417 5 2 20			at 21 days			feed not different ^b	
3 Spray on feed			old for			(not Ph. Eur.	
vaccinated:			group 1-3			compliant)	
Part A ≥ 20			and at 24			Part B <i>E. brunetti</i> : all 3	
Part B ≥ 20			days old for			vaccinated groups	
			group 4-5.			showed greater weight	
4 3-day-old						gain compared to	
positive control						positive control at day	
(unvaccinated,						7 and 14 PC ^a (Ph. Eur.	
challenged):						compliant)	
Part A ≥ 20						D . A 5	
Part B ≥ 20				_	Lesion score	Part A E. necatrix: All 3	
5 Drinking					Lesion score	vaccinated groups had reduced lesion scores	
water						compared to the	
vaccinated:						positive controls on	
Part A ≥ 20						day 7 PC ^a (Ph. Eur.	
Part B ≥ 20						compliant).	
						,	
						Part B E. brunetti: All 3	
						vaccinated groups had	
						reduced lesion scores	
						compared to the	
						positive controls on	
						day 7 PC ^a (Ph. Eur.	
						compliant).	
						Part A <i>E. necatrix</i> : the	
						3 vaccinated groups	
				-	Faecal	showed oocyst cycling	Both control
					oocysts	with the peak on day 7	groups remained
					•	PV. Total oocysts	free from oocysts
						output from days 3-14	for study part A
						PC was lower for all 3	and B.

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					vaccinated groups	
					compared to the	
					control groups ^a (Ph.	
					Eur. compliant).	
					Part B <i>E. brunetti</i> : the	
					drinking water and	
					spray on bird	
					vaccinated groups	
					showed oocyst cycling	
					with the peak on day 7	
					PV, the spray on feed	
					group only had oocysts	
					observed on day 21	
					PV. Total oocyst	
					output from days 3-14	
					PC was lower for spray on bird and drinking	
					water vaccinates	
					compared to the	
					· ·	
					control groups ^a (Ph. Eur. compliant), the	
					spray on feed group	
					failed to show	
					protection ^b (not Ph.	
					Eur. compliant).	
Assessing the off	icacy of Hu	veGuard® NB vac	ine snraved on	hirds in protecting (chickens against the challe	nge with Fimeria
necatrix and Eim			e sprayea on	birds iii protectiiig t	mercens against the chanc	inge with Emileria
Chicken, male	SPF	Group 3 and 4:	Oocyst	Study day 7, 14,		
and female		HuveGuard NB	counting	20, 25, 26, 27,		
		(vaccination in	and lesion	28, 31, 34.		
1 positive		day-old birds	scoring was	-, - , -		
control		via spray on	blinded.	- Body weight	During the acute phase	
(unvaccinated,		birds)		, -	of infection (day 20-	
challenged with			Challenge		26) both vaccinated	
E. necatrix): 26			on day 20:		groups had higher	
birds			all groups		weight gain compared	
			were		to their respective	
2 positive			inoculated		control groups ^a . For	
control			orally with		the groups challenged	
(unvaccinated,			challenge		with E. brunetti,	
challenged with			strains of		overall weigh gain (day	
E. brunetti): 26			E. acervulin		20-34) was also higher	
birds			a combined		in the vaccinated	
			with either		group ^a (Ph. Eur.	
			E. necatrix		compliant).	
3 test group			or			
(vaccinated,			E. brunetti	- Lesion score	On day 26 and 27, a	
challenged with					reduction in lesion	
E. necatrix: 26					score was observed for	
birds					E. necatrix for the	
4 4 4					vaccinated group 3	
4 test groep					(mean score: 0)	
(vaccinated,					compared to its positive control (mean	
aballan and other						
challenged with						
E. brunetti): 26					score: 1.5) ^a (Ph. Eur.	
					score: 1.5) ^a (Ph. Eur. compliant). In both	
E. brunetti): 26					score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with	
E. brunetti): 26					score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions	
E. brunetti): 26					score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions were observed ^b (Not	
E. brunetti): 26					score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions	

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		-	Faecal	On day 7, 14 and 20	On day 7, 14 and
			oocysts	oocyst cycling is	20 the OPG of
				observed in vaccinated	unvaccinated
				groups (Ph. Eur.	controls is 0 (Ph.
				compliant).	Eur. compliant)
				OPG countings on day	
				25, 28, 31 and 34	
				showed a high	
				shedding pattern for	
				E. acervulina and only	
				minor OPG countings	
				for <i>E. brunetti</i> and	
				E. nectatrix and was	
				therefore inconclusive	
				(Not Ph. Eur.	
				compliant).	

Duration of immunity at 9 months was investigated in broiler breeding hens, Ross 308 of 9 months old.

Animals	Antibo	Vaccine, dose,	Challenge,	Follow up:	Results:	
Groups	dy	route of	dose,	Duration		
Number	status	administration	Day	Endpoints*		
Age			post-			
			vaccination			
Study					Vaccinates	Controls
Assessment of th	ne duration	of the immunity	of HuveGuard N	MMAT and HuveGu	ard NB in breeders (R-Huve	pharma-2012-102)
Chickens	Com-	Before start of	At day 14 of	Day 6 PC: 30	One bird died on D21,	
	mercial	trial:	trial (9	animals per	vaccine-unrelated.	
Broiler			month old	group culled		
breeding hens		HuveGuard	hens). (per	Day 12 PC: 30		
biccamig fichs		MMAT (day-	group 3	animals per		
9 months old		old, spray on	animals remained	group culled.		
9 months old		feed) and	unchallenge	Oocyst count:	Total OPG were not	No difference in
		HuveGuard NB	d)	Oocyst count.	different between	total OPG
Vaccinated1,		(7 days old,	۵)		groups ^b .	between infected
Huveguard		drinking water)	15 animals		" '	and uninfected
MMAT and NB:		,	per group			birds ^b .
90		Or	were			
			challenged			
Vaccinated2,		Paracox (7 day	with either:	Gut lesion	Total gut lesion scores	No differences in
PARACOX-8©:		old, drinking	E. acervulin	scores:	were higher in the	total gut lesion
90		water)	a and E. tenella		HuveGuard group than	scores between infected and
50			Or		in the Paracox group ^a . Odds of presenting	uninfected birds ^b .
			E. maxima		lesions associated with	uninected bilds .
			Or		Eimeria spp. were not	
			E. mitis		different between	
			Or		groups ^b .	
			E. necatrix			
			Or			
			E. brunetti			

a: significant difference

There were no significant differences between HuveGuard NB and positive control groups for total lesion scores and *E. brunetti* and *E. necatrix* OPGs. Nevertheless, duration of immunity past 21 days after vaccination has not been established.

Field Trials

Initially the applicant conducted 6 field studies. In total, 9 flocks been have vaccinated with HuveGuard NB. All studies have been executed in accordance with the same protocol. On each trial site, at least one house has been vaccinated with HuveGuard NB and at least one house has been vaccinated with a positive control vaccine. Different routes of administration

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b: no significant difference

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have been investigated: 6 flocks were vaccinated via drinking water, 2 flocks were vaccinated via eye drop, 1 flock was vaccinated by spray on chick (supportive evidence only). In the field studies birds were vaccinated at ages between 7 and 14 days. The results of the 6 studies have been statistically analysed for each study separately and a meta-analysis has been performed for 3 studies to confirm efficacy when administered via the proposed routes of application.

Animals Groups Number Age	Antibo dy status	Vaccine, dose, route of administration	Study design	Follow up: Duration Endpoints*	Results:	
Study					Vaccinates	Controls
R-Huvepharma- 2011-54		HuveGuard MMAT (spray on feed, day	Comparison with PARACOX©	5 animals of the 4 houses used were euthanized		
Netherlands		old) and		on days 7, 14, 21, 28, 35, 56		
Chickens		HuveGuard NB (drinking		and 84. Trial ended at day 140		
Broiler breeder		water, 7 or 13 days old)		(last animals moved to		
Day-old		Or		production farm)		
Vaccinated1, HuveGuard MMAT +		Paracox (drinking		- Body weight	No difference between groups	
HuveGuard NB: 48216		water, 6 or 7 days old)		- Intestinal lesions	No differences overall; significantly higher on D14 and 56;	Significantly higher on D21
Vaccinated2, PARACOX-8©: 47500					significantly lower on D21 and 28 ^a	and D28 ^a
47300				- Faecal oocysts	Peak at around 2 weeks PV	Peak at around 4 weeks of age
R-Huvepharma- 2011-55		HuveGuard MMAT (spray	Comparison with PARACOX©	5 animals per house were euthanized on		
Belgium		on feed, day old) and		days 7, 14, 21, 28, 35, 56 and 84		
Chickens		HuveGuard NB (eye drop, 9		- Body weight	Significantly higher in	Control group was
Broiler breeder Day-old		days old) Or			the HuveGuard group at all timepoints except at day 0 ^a	heavier at the start of the study ^a
Vaccinated1, Huveguard MMAT + HuveGuard NB: 13898 Vaccinated2:		Paracox (drinking water, 7 days old)		- Lesion scores	No scores above 1 in both groups; significantly higher ILS scores on D35 in the HuveGuard group ^a	No scores above 1 in both groups; Significantly higher ILS scores on D56 in the control groups ^a
PARACOX-8©: 13342			_	- Faecal oocysts	Similar patterns in both groups ^b	
R-Huvepharma- 2011-96		HuveGuard MMAT (spray on feed, day	Comparison with PARACOX©	5 birds/group were euthanized on D7, 14, 21,		
France		old) and		28, 35, 56 and 84		
Chickens						

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	HuveGuard NB		- Body weight	No difference between	
Newly hatched	(drinking			the groups ^b	
	water, 7 or 14				
Broiler	days old)		- Intestinal	No difference between	
breeders			lesions	the groups ^b	
	Or				
Vaccinated1,			- Faecal	Different OPG patterns	Small peaks which
Huveguard	Paracox 8		oocysts	between groups.	were decreasing
MMAT and	(drinking			Higher peak at the age	towards the end
HuveGuard NB:	water, 7 days			of 2-3 weeks in the	of the rearing
18760	old)			HuveGuard groups	period for the
					control group.
Vaccinated2,					
PARACOX-8©:					
19720					
R-Huvepharma-	HuveGuard	Comparison	5 birds/group		
2012-11	MMAT	with	were euthanized		
	(drinking	PARACOX©	on D6, 13, 20,		
Belgium	water, 4 days		27, 34, 55, 83		
20.8.0	old)		and 131		
Broiler	and				
breeders	HuveGuard NB		- Body weight	Higher at D83 ^{a.} Over	Higher in D20 and
breeders	(drinking		Body Weight	whole study period not	D27 ^a . Over whole
Vaccinated 1,	water, 9 days			difference in daily	study period not
HuveGuard	old)			weight gain ^b	difference in daily
MMAT and	0.07			Weight gam	weight gain ^b
HuveGuard NB:	Or				weight gain
9722	01		- Intestinal	Higher on D13 an D20a	Higher on 83 ^b
3722	Paracox		lesions	in the HuveGuard	riighter on 65
Vaccinated2,	(drinking		16310113	group, although still	
PARACOX-8©:	water, 9 days			below ILS score 1	
10000	old)			Delow IL3 Score 1	
10000	old)		- Faecal	Different ODC netterns	Different OPG
				Different OPG patterns	patterns between
			oocysts	between groups. Consecutive small	'
				peaks which were	groups. Two high peaks at the age
				'	of 41 and 83 days
				decreasing towards	OI 41 allu 65 uays
				the end of the rearing	
R-Huvepharma-					
	HuveGuard	Comparison	5 hirds/group on	period	
2012-74	HuveGuard	Comparison with	5 birds/group on	period	
2012-74	MMAT (eye		D8, 15, 22, 29,	period	
	MMAT (eye drop, day-old)	with		period	
2012-74 Belgium	MMAT (eye drop, day-old) and	with	D8, 15, 22, 29, 36, 57 and 85		
Belgium	MMAT (eye drop, day-old) and HuveGuard NB	with	D8, 15, 22, 29,	Significantly higher on	
	MMAT (eye drop, day-old) and HuveGuard NB (spray on	with	D8, 15, 22, 29, 36, 57 and 85	Significantly higher on Day 0, 85 and 119 for	
Belgium Chickens	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days	with	D8, 15, 22, 29, 36, 57 and 85	Significantly higher on Day 0, 85 and 119 for HuveGuard group	
Belgium	MMAT (eye drop, day-old) and HuveGuard NB (spray on	with	D8, 15, 22, 29, 36, 57 and 85	Significantly higher on Day 0, 85 and 119 for	
Belgium Chickens Rearing pullets	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old)	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a	
Belgium Chickens Rearing pullets Vaccinated1,	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old)	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on D85 for Huveguard group compared to	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB:	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on D85 for Huveguard group compared to controla	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Similar OPG pattern in	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2,	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©:	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at around age of 7-8	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days old)	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal oocysts	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma-	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days old) HuveGuard	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal oocysts 5 birds/group on	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at around age of 7-8	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days old) HuveGuard MMAT (spray	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal oocysts 5 birds/group on D7, 14, 21, 28,	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at around age of 7-8	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days old) HuveGuard MMAT (spray on birds or eye	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal oocysts 5 birds/group on	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at around age of 7-8	
Belgium Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma-	MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Or Paracox (drinking water, 7 days old) HuveGuard MMAT (spray	with	D8, 15, 22, 29, 36, 57 and 85 - Body weight - Intestinal lesions - Faecal oocysts 5 birds/group on D7, 14, 21, 28,	Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a Similar OPG pattern in both groups, peak at around age of 7-8	

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Chickens	HuveGuard NB		Significantly higher in	Significantly
	(eye drop or		D85 ^{a,} although no	higher on D28
Rearing pullets	drinking water,		difference at the end	and D56 ^a
– bio layers	7 days old)		of the study compared	
			to control ^b	
Vaccinated1,	Or	- Intes	tinal	
Huveguard:		lesio	ns	Higher on D14
14430	Paracox			and D28, D35,
	(drinking			D56 in the control
Vaccinated2,	water, 9 days			groupa
PARACOX-8©:	old)	- Faec	al	
12726		оосу	sts Different OPG patterns	Different OPG
			between groups. Peaks	patterns between
			appeared at younger	groups. Lower
			age (2 weeks and 7	peaks at age of 3,
			weeks) and were	7 and 10 weeks
			higher	

a: significant difference

The efficacy is confirmed by appropriate performance parameters in field trials in Europe in breeder chickens. Based on the efficacy data above, the vaccine is considered to be suitable for the active immunisation of chickens from 14 days of age to reduce infection and clinical signs of coccidiosis caused by E. necatrix and E. brunetti with an Onset of Immunity at 21 days post vaccination.

During a post-authorisation variation, additional field studies were provided supporting the administration of the vaccine from 1 day of age when administered via spray on feed or spray on birds, and from 3 days of age when administered via the drinking water. These post-authorisation field trials are summarized below.

Animals Groups Number Age	Antibo dy status	Vaccine, dose, route of administration	Study design	Follow up: Duration Endpoints*	Results:			
Study					Vaccinates	Controls		
Efficacy and Saf	Efficacy and Safety of HuveGuard NB under commercial conditions when applied at first day of age by course spray							
(R-Huvepharma	-2016-12)							
Chickens,		House 1	Controlled,	Study days 7, 14,				
females, Ross		(positive	non-blinded	21, 28, 35, 42,				
308		control): day-	study	49, 56, 63, 70,				
		old chicks	(oocyst	77, 84, 91, 98,				
House 1		vaccinated on	counting	105, 112, 118,				
(positive		day 0 with	and	126 and 136				
control): 9484		HuveGuard	differenciati					
birds		MMAT (spray	on was	- Faecal	No differences were			
		on bird) and on	blinded)	oocysts	detected in OPG			
House 2 (test		day 14 (15 day			between the houses			
group): 8862		old) with	Field study		for all <i>Eimeria</i> species			
birds		HuveGuard NB			in the vaccine ^b .			
		(via drinking						
		water).		- Lesion	No differences in total			
				scores	mean lesion score			
		House 2: day-			were observed			
		old chicks			between the groups ^b .			
		vaccinated on			No differences were			
		day 0 with			detected in species			
		HuveGuard			specific lesion scores ^b .			
		MMAT and						

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b: no significant difference

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			T		
	HuveGuard NB		- Body weight	At D0 and D84 birds	
	(both: course			that were vaccinated	
	spray on bird).			with HuveGuard NB on	
				day 0 (house 2)	
				weighed more ^a , on	
				other test days there	
				was no difference ^b .	
Efficacy and Safety	of HuveGuard NB under co	mmoreial cone	litions when applied		so spray on food
(R-huvepharma-20		mmerciai conc	iltions when applied	at first day of age by cour	se spray on reed
Chickens,	House 1	Controlled,	Study days 7, 14,		
females, Ross	(positive	non-blinded	21, 28, 35, 42,		
308	control): 8	study	49, 56, 63, 70,		
	days old chicks	(oocyst	77, 84, 91, 98,		
House 1	vaccinated (on	counting	105, 112, 118,		
(positive	study day 7)	and	126 and 136		
••	with Paracox®	differentiati	120 and 130		
control):24,500					
birds	8 via drinking	on was	- Faecal	No differences in total	
	water.	blinded)	oocysts	or species-specific OPG	
House 2 (test				between houses ^b .	
group): 11,200	House 2: day-	Field study			
birds	old chicks	-	- Lesion	The HuveGuard group	
	vaccinated on		scores	had a higher total	
	day 0 (arrival			lesion score on day 14	
	on farm) with			(2.8 vs. 1.4) and day 56	
	· · · · · · · · · · · · · · · · · · ·			(1.8 vs. 0.4) ^a . On day	
	HuveGuard			, , ,	
	MMAT and			28, the HuveGuard	
	HuveGuard NB			group had a	
	(both: course			significantly lower	
	spray on feed).			total lesion score (1.6	
				vs. 3.8) ^a . There was no	
				difference in lesion	
				score on day 7, 21,	
				35,and 85. Species	
				specific lesion scoring	
				was only different for	
				E. tenella (higher score	
				for HuveGuard	
				group) ^a .	
			- Body weight	At the start of the	
				study birds from the	
				HuveGuard group	
				weight less ^a . At day 56,	
				85, and 135 no	
				difference in weight	
Efficacy and Cafat	of HuveGuard NB under co	mmoreial as :-	litions when and!ad	was observed ^b .	ro carav
(R-Huvepharma-20		ommerciai conc	iitions when applied	at first day of age by cour	se spray
Chickens, H&N	House 1	Controlled,	Study days 7, 14,		
Super Nick,	(positive	non-blinded	21, 28, 35, 42,		
H&N Nick	control)	study	49, 56/57, 63,		
Chick, H&N	treatment 1:	(oocyst			
			70, 77, 84, 91,		
Brown Nick, LB	Paracox® 8 via	counting	98, 105, 112, 116		
Classic	spray on birds	and	and 119.		
House1	at 1 day of age	differentiati			
	in the hatchery	on was	- Faecal	Total and species	
(positive		blinded)	oocysts	specific oocyst	
control): 85,649	House 1	,		shedding was not	
animals	(positive	Field study		different between	
		. icia stady		houses ^b .	
House 2 /test					
House 2 (test	control)			nouses .	
House 2 (test group): 63,240 animals	treatment 2: Evalon® via			nouses.	

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	spray on birds		- Lesion	No differences were	
	at 1 day of age		scores	observed in lesion	
	in the hatchery		555.55	scores for all study	
	, , , , , , , , , , , , , , , , , , , ,			days. E. acervulina	
	House 2 (test			lesion scores were	
	group):			lowest for Evalon®	
	HuveGuard			vaccinated birds ^a .	
	MMAT and			vaccinated birds :	
	HuveGuard NB		- Body weight	At set-up and day 28,	
			- Body weight	bird vaccinated with	
	via spray on			HuveGuard weighed	
	birds at 1 day			less than birs from	
	of age in the				
	hatchery			house 1 ^a . At day 116	
				birds vaccinated with	
				HuveGuard were	
				heavier than birds	
				from house 1a.	
-	_	coccidiosis i	n slow growing b	roilers under field conditions	in Belgiui
(R-Huvepharma-201		Combinell	Carration of the Carration	Г	
Chickens, Sasso	House 1:	Controlled,	Study days 0, 7,		
broilers.	vaccinated at	non-blinded	14, 21, 28, 35, 56		
	day of arrival	trial (oocyst	and 70.		
House 1 (test	on study site	counting	Slaughter after		
group): 5000	(day-old) with	and	70 days.		
birds	HuveGuard	differentiati			
	MMAT and	on was	- Faecal	No statistical analysis	
House 2	HuveGuard NB	blinded)	oocysts	performed.	
(vaccinated	via spray on				
positive	birds.	Field study	 Lesion score 	No differences in total	
control): 5000				intestinal lesion scores	
birds	House 2			were observed	
	(control):			between the	
	vaccinated on			HuveGuard group and	
	day of arrival			the control group ^b .	
	on study site			, , , , , , , , , , , , , , , , , , ,	
	(day-old) with		- Body weight	No difference in weight	
	Paracox® via		2007 110.8.10	gain between the	
	spray on birds.			HuveGuard groups and	
	spray on birds.			the control group ^b .	
Efficacy of HuyeGua	rd® NR in controlling cocc	idiosis in slow (rowing broilers und	er field conditions in Belgium	
(R-Huvepharma-201		iulosis ili siow į	growing broners und	er field conditions in beigidin	
	House 1:	Controlled	Study days 0. 7		
Chickens, Sasso broilers.		Controlled,	Study days 0, 7,		
טוטוופוג.	vaccinated at	non-blinded	14, 21, 28, 35, 56 and 70.		
	day of arrival	trial (oocyst			
House 1 (test	on study site	counting	Slaughter after		
group): 5035	(day-old) with	and	70 days.		
birds	HuveGuard	differentiati		[<u></u>	
	MMAT and	on was	- Faecal	No statistical analysis	
House 2	HuveGuard NB	blinded)	oocysts	performed.	
(vaccinated	via spray on				
positive	feed.	Field study	- Lesion score	No differences in total	
control): 5035				intestinal lesion scores	
birds	House 2			wer observed between	
	(control):			the HuveGuard group	
	vaccinated on			and the control group ^b .	
	day of arrival				
			- Body weight	No difference in bird	
	on study site		, , , , , , , , , , , , , , , , , , , ,		
	on study site (day-old) with			weight between the	
	(day-old) with			weight between the HuveGuard groups and	
				weight between the HuveGuard groups and the control groupb.	

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Chickens, Sasso	House 1:	Controlled,	Stud	dy days 0,		
broilers.	vaccinated at 5	non-blinded	5/6,	14, 21, 28,		
	days of age	trial (oocyst	35,	56 and 70.		
House 1 (test	with	counting	Slau	ghter after		
group): 4955	HuveGuard	and	70 c	lays.		
birds	MMAT and	differentiati				
	HuveGuard NB	on was	-	Faecal	No statistical analysis	
House 2	via drinking	blinded)		oocysts	performed.	
(vaccinated	water.					
positive		Field study	-	Lesion score	No differences in total	
control): 5000	House 2				intestinal lesion scores	
birds	(control):				wer observed between	
	vaccinated on				the HuveGuard group	
	day of arrival				and the control group ^b .	
	on study site					
	(day-old) with		-	Body weight	Bird body weight was	
	Paracox® via				lower for the	
	spray on birds.				HuveGuard group	
					(mean 1,358 kg)	
					compared to the	
					control group (mean	
3::::::::::::::::::::::::::::::::::					1,423 kg) ^a .	

a: significant difference

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.

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b: no significant difference

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Huvepharma NV	MRP	
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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.

Summary of change	Section updated	Approval date
Increase batch size (NL/V/0207/001/IB/002)	N/A	01 October 2016
Change in rapid potency test: from testing in dayold SPF chicks to testing in 1-14 days old SPF chicks (NL/V/0207/001/II/001)		07 April 2017
Change in the description of the manufacturing process and deletion of the autoclaving process in the production of saturated salt (NL/V/xxxx/WS/010)	N/A	31 July 2017
Deletion of eye drops as route of administration and and subsequent changes to the pharmaceutical form and product name (NL/V/xxxx/WS/009)	Module 1(Name of the veterinary medicinal product)	11 October 2017
Addition of secondary packaging site. (NL/V/xxxx/IA/024/G)	N/A	01 November 2017
Change in the name of the sterility and Campylobacter testing site (NL/V/xxxx/IA/026/G)	N/A	28 March 2018
Reduction minimum age for vaccination to 1 day of age for administration via spray onto feed or spray on birds and to 3 days of age for administration via drinking water (NL/V/0207/001/II/007)	Module 3, section IV	27 November 2019
Addition of site for batch release sterility testing, removal <i>Campylobacter</i> batch release test and inclusion of Rapid Potency Test as an alternative test for the end of shelf life potency (NL/V/0207/II/008/G)	Module 3, section II.E	13 March 2020

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