$\frac{C \ B \ G}{M \ E \ B}$

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

CMDv/TEM/003-02 1/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report



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.

CMDv/TEM/003-02 2/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report



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

CMDv/TEM/003-02 3/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report



PUBLIC ASSESSMENT REPORT

Legal basis of original	Full application in accordance with Article 12(3)
application	of Directive 2001/82/EC as amended.
Date of completion of the	28 April 2016
original mutual recognition	
procedure	
Date product first authorised	15 July 2015
in the Reference Member	
State (MRP only)	
Concerned Member States for	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR,
original procedure	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.

CMDv/TEM/003-02 4/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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.

CMDv/TEM/003-02 5/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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.

CMDv/TEM/003-02 6/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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.

CMDv/TEM/003-02 7/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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)		т .	1	1
Chickens	SPF	Spray on feed	D21 of the	7 days post		
0		(day-old),	study (21	challenge (PC):		
One day old		spray on chickens (day-	days PV)	euthanasia for 10 birds in all		
Negative		old)	Strain	groups		
control		oluj	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						
				- Faecal	Both vaccinated	
Vaccinated2,				oocysts	groups had a lower	
spray on feed: 20					OPG for day 6-8 PC than the positive	
20					control group ^a (Ph. Eur.	
					compliant)	
					Compilation	
				- 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
					1.4 for spray on bird	(Ph. Eur.
					and spray on feed,	compliant)
					respectively (Not Ph.	
	<u> </u>) /==: 00.0 0.1		Eur. compliant).	
		etti (single antige			-	
Chickens	Hy-Line	Eye drop (14 days old)	21 days PV	7 days post		
14 days old	brown male	uays old)	Strain	challenge: euthanasia for		
14 uays old	(not	E. brunetti	E. brunetti	10 birds in all		
Negative	SPF)	Roybru 3+28	(AM),	groups		
control	5,	, 5, 6, 6, 5, 20	10,000	0.000		
(unvaccinated,		Dose:	oocysts per	14 days post		
unchallenged):		50 oocysts	dose by oral	challenge:		
19		Or	gavage	euthanasia		
		100 oocysts		remaining birds		

CMDv/TEM/003-02 8/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

	1	1	T	1	ı	
Positive control		Or				
(unvaccinated,		200 oocysts		- Body weight	All 3 vaccinated groups	Negative controls
challenged): 20		,		, ,	were heavier than the	higher weight
0aegea/. =0					positive control group	gain than positive
W						
Vaccinated1, 50					on both day 7 and 14	controls ^a .
oocysts/dose:					PC ^a . (Ph. Eur.	
20					compliant)	
Vaccinated2,				- Faecal	No faecal oocyst	Significantly
100				oocysts	output after challenge	higher in positive
oocysts/dose:				Oocysts	in any of the 3	control when
20					vaccinated groups	compared to
						vaccinates ^a (Ph.
Vaccinated3,						Eur. compliant)
200						
oocysts/dose:				- Intestinal	No lesions (score of 0	Positive control:
20				lesions	for 100% of the birds)	score ≥2 in 70% at
20				16310113	,	
					in all 3 vaccinated	7 days PC; no
					groups. (Ph. Eur.	lesions at day 14
					compliant)	PC (Not Ph. Eur.
						compliant)
	1	<u> </u>		I.	l	
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	
Chickeris	311	day-old) and	Day ZII V	challenge:	drinking water group	
1.4 -4			Chuna in	_		
14 days old		drinking water	Strain	euthanasia for	died (not vaccine	
			E. brunetti	_		
14 days old Negative		drinking water	E. brunetti (AM) 10,000	euthanasia for	died (not vaccine	
		drinking water	E. brunetti	euthanasia for 12 birds in all	died (not vaccine	
Negative control		drinking water (14 day-old)	E. brunetti (AM) 10,000 oocysts per	euthanasia for 12 birds in all groups	died (not vaccine	
Negative control (unvaccinated,		drinking water (14 day-old) HuveGuard NB	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post	died (not vaccine	
Negative control (unvaccinated, unchallenged):		drinking water (14 day-old) HuveGuard NB Test antigen:	E. brunetti (AM) 10,000 oocysts per	euthanasia for 12 birds in all groups 15 days post challenge:	died (not vaccine	
Negative control (unvaccinated,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia	died (not vaccine	
Negative control (unvaccinated, unchallenged): 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28,	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge:	died (not vaccine	
Negative control (unvaccinated, unchallenged): 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related)	
Negative control (unvaccinated, unchallenged): 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28,	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia	died (not vaccine related) Significantly higher for	
Negative control (unvaccinated, unchallenged): 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related)	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related) Significantly higher for	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related) Significantly higher for both vaccinated groups compared to	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds	died (not vaccine related) Significantly higher for both vaccinated groups compared to	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant)	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2,		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to	
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controls ^a (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control ^a	On day 7 PC 100%
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for 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	On day 7 PC 100%
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for 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
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for 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
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive controla (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.
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive controla (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
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controls (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive control (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 positive controls. (Ph.	of positive control birds had a lesion score of 2 (Ph.
Negative control (unvaccinated, unchallenged): 22 Positive control (unvaccinated, challenged): 22 Vaccinated1, eye drop: 22 Vaccinated2, drinking water:		drinking water (14 day-old) HuveGuard NB Test antigen: E. brunetti Roybru 3+28, 50 oocysts per	E. brunetti (AM) 10,000 oocysts per dose by oral	euthanasia for 12 birds in all groups 15 days post challenge: euthanasia remaining birds - Body weight - Faecal oocysts	died (not vaccine related) Significantly higher for both vaccinated groups compared to the positive controlsa (Ph. Eur. compliant) Significantly reduced for both vaccinated groups compared to the positive controla (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 score of 2 (Ph.

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.

CMDv/TEM/003-02 9/19

a: significant difference b: no significant difference

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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	Follow up: Duration Endpoints*	Results:	
Study					Vaccinates	Controls
Immunogenicity	of HuveGu	ard NB by spray o	n bird, spray or	feed, drinking wate	er (EPL 2018-09)	•
Study	of HuveGu	ard NB by spray of HuveGuard NB (vaccination in day-old birds via spray on birds or spray on feed and in 3-day-old birds via drinking water)	Part A: challenge with E. necatrix at 21 days old for group 1-3 and at 24 days old for group 4-5. Part B: challenge with E. brunetti at 21 days old for group 1-3 and at 24 days old for group 1-5 and at 21 days old for group 1-3 and at 24 days old for group 1-3	Day 7, 14, 21 post vaccination and day 2, 5, 7, 8, 11, 14 post challenge - Body weight - Lesion score		Controls
				- Faecal oocysts	Part B <i>E. brunetti:</i> 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 showed oocyst cycling with the peak on day 7 PV. Total oocysts output from days 3-14	Both control groups remained free from oocysts for study part A

CMDv/TEM/003-02 10/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

						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).	
According the off	icacy of Hu	voGuard® NB vac	ing sprayed on	hirds	in protecting o	hickens against the challe	ngo with Eimoria
necatrix and Eim			lile sprayed on	Dirus	in protecting c	illickens against the challe	inge with Eilliena
Chicken, male	SPF	Group 3 and 4:	Oocyst	Stuc	ly day 7, 14,		
and female	311	HuveGuard NB	counting		25, 26, 27,		
		(vaccination in	and lesion		31, 34.		
1 positive		day-old birds	scoring was		-,		
control		via spray on	blinded.	-	Body weight	During the acute phase	
(unvaccinated,		birds)			, 0	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	
challenged with E. necatrix: 26						score was observed for	
challenged with						score was observed for <i>E. necatrix</i> for the	
challenged with E. necatrix: 26 birds						score was observed for E. necatrix for the vaccinated group 3	
challenged with E. necatrix: 26 birds 4 test groep						score was observed for E. necatrix for the vaccinated group 3 (mean score: 0)	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated,						score was observed for E. necatrix for the vaccinated group 3 (mean score: 0) compared to its	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with						score was observed for E. necatrix for the vaccinated group 3 (mean score: 0) compared to its positive control (mean	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with E. brunetti): 26						score was observed for E. necatrix for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5)a (Ph. Eur.	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with						score was observed for <i>E. necatrix</i> for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5) ^a (Ph. Eur. compliant). In both	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with E. brunetti): 26						score was observed for <i>E. necatrix</i> for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with E. brunetti): 26						score was observed for <i>E. necatrix</i> for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with E. brunetti): 26						score was observed for <i>E. necatrix</i> for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions were observed ^b (Not	
challenged with E. necatrix: 26 birds 4 test groep (vaccinated, challenged with E. brunetti): 26						score was observed for <i>E. necatrix</i> for the vaccinated group 3 (mean score: 0) compared to its positive control (mean score: 1.5) ^a (Ph. Eur. compliant). In both groups challenged with <i>E. brunetti</i> , no lesions	

CMDv/TEM/003-02 11/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

		-	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 E. brunetti 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 Groups	Antibo dy	Vaccine, dose, route of	Challenge, dose,	Follow up: Duration	Results:	
Number	status	administration	Day	Endpoints*		
Age			post-			
			vaccination			
Study					Vaccinates	Controls
Assessment of the	ne duration	of the immunity	of HuveGuard N	/IMAT and HuveGua	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		
biccaing fichs		MMAT (day-	group 3	animals per		
0		old, spray on feed)	animals remained	group culled.		
9 months old		and	unchallenge	Oocyst count:	Total OPG were not	No difference in
		HuveGuard NB	d)	Oocyst count.	different between	total OPG
Vaccinated1,		(7 days old,	a)		groups ^b .	between infected
Huveguard		drinking water)	15 animals		g.cape .	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		HuveGuard group than	scores between
90			E. tenella		in the Paracox group ^a .	infected and
			Or <i>E. maxima</i>		Odds of presenting lesions associated with	uninfected birds ^b .
			Or		Eimeria spp. were not	
			E. mitis		different between	
			Or		groups ^b .	
			E. necatrix		g. 5 3 p c .	
			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

CMDv/TEM/003-02 12/19

b: no significant difference

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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)	No difference between	
Vaccinated1, HuveGuard MMAT +		Paracox (drinking		- Body weight	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
				- Faecal oocysts	Peak at around 2 weeks PV	Peak at around 4 weeks of age
R-Huvepharma- 2011-55		HuveGuard MMAT (spray on feed, day	Comparison with PARACOX©	5 animals per house were euthanized on		
Belgium		old) and		days 7, 14, 21, 28, 35, 56 and 84		
Chickens Broiler breeder		HuveGuard NB (eye drop, 9 days old)		- Body weight	Significantly higher in the HuveGuard group	Control group was heavier at the
Day-old		Or			at all timepoints except at day 0 ^a	start of the study ^a
Vaccinated1, Huveguard MMAT + HuveGuard NB: 13898		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
Vaccinated2: 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						

CMDv/TEM/003-02 13/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

Newly hatched Broiler					,	
Broiler breeders Or Vaccinated 2, PARACOX-88: 10000 Broiler breeders HuveGuard NB (drinking water, 9 days old) Paracox (drinking water, 9 days old) Broiler breeders HuveGuard NB (drinking water, 9 days old) Paracox (drinking water, 9 days old) Broiler breeders HuveGuard NB (drinking water, 9 days old) Paracox (drinking wate		HuveGuard NB		 Body weight 	No difference between	
Brotler breeders Or Vaccinated1, Huveguard (Irinking water, 7 days old) Paracox 8 (Irinking water, 4 days old) Waccinated2, PARACOX-80: 19720 Paracox 8 (Irinking water, 4 days old) Paracox (Irinking water, 4 days old) Water, 9 days old) Vaccinated 1, HuveGuard Water, 9 days old) Vaccinated 2, PARACOX-80: 10000 Water, 9 days old) Vaccinated 1, HuveGuard Water, 9 days old) Vaccinated 1, HuveGuard Water, 9 days old) Vaccinated 2, PARACOX-80: 10000 Water, 9 days old) Vaccinated 3, HuveGuard Water, 9 days old) Vaccinated 4, HuveGuard Water, 9 days old) Vaccinated 5, PARACOX-80: 10000 Water, 9 days old) Vaccinated 6, HuveGuard Water, 9 days old) Vaccinated 7, PARACOX-80: 10000 Vaccinated 8, PARACOX-80: 10000 Vaccinated 9, PARACOX-80: 100000 Vaccinated 9, PARACOX-80: 1000000 Vaccinated 9, PARACOX-80: 100000000000000000000000000000000000	Newly hatched	(drinking			the groups ^b	
Vaccinated, Paracox 8 (drinking water, 9 days old) Vaccinated 1, HuveGuard Minking water, 9 days old) Vaccinated 2, Paracox (drinking water, 9 days old) Vaccinated 3, HuveGuard Minking water, 9 days old) Vaccinated 4, HuveGuard Minking water, 9 days old) Vaccinated 5, Paracox (drinking water, 9 days old) Vaccinated 6, HuveGuard Minking water, 9 days old) Vaccinated 7, Paracox (drinking water, 9 days old) Vaccinated 8, Paracox (drinking water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) Vaccin		water, 7 or 14				
Vaccinated, Paracox 8 (drinking water, 9 days old) Vaccinated 1, HuveGuard Minking water, 9 days old) Vaccinated 2, Paracox (drinking water, 9 days old) Vaccinated 3, HuveGuard Minking water, 9 days old) Vaccinated 4, HuveGuard Minking water, 9 days old) Vaccinated 5, Paracox (drinking water, 9 days old) Vaccinated 6, HuveGuard Minking water, 9 days old) Vaccinated 7, Paracox (drinking water, 9 days old) Vaccinated 8, Paracox (drinking water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) Vaccin	Broiler	days old)		- Intestinal	No difference between	
Vaccinated 1, Huveguard MMAT and HuveGuard NB: ldrinking water, 7 days old) Paracox 8 (drinking water, 7 days old) Vaccinated 2, PARACOX-88: 19720 PARACOX-88: 19720 HuveGuard MMAT (winking water, 4 days old) Paracox (drinking water, 9 days old) Vaccinated 1, HuveGuard MMAT (winking water, 9 days old) Vaccinated 2, PARACOX-88: 10000 Paracox (drinking water, 9 days old) Vaccinated 3, HuveGuard MMAT (winking water, 9 days old) Vaccinated 4, HuveGuard MMAT (winking water, 9 days old) Vaccinated 5, HuveGuard MMAT (winking water, 9 days old) Vaccinated 6, HuveGuard MMAT (winking water, 9 days old) Vaccinated 7, PARACOX-88: 10000 R-HuveGuard MMAT (winking water, 9 days old) Vaccinated 8, Paracox (drinking water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) R-HuveGuard MMAT (winking water, 9 days old) R-HuveGua	breeders	' '		lesions	the groups ^b	
Vaccinated 1, Huveguard MMAT and Huveguard MMAT and Huveguard Selegium Paracox 8 (drinking water, 7 days old) - Faccal Occysts Different OPG patterns between groups. Whether and of the rearing period for the control group. Whether and the peak at the age of 2-3 weeks in the HuveGuard groups. Whether are on the control group. Water, 7 days old) S birds/group water, 1 days old on the control group. Water, 2 days old) S birds/group water, 2 days old on the control group. Water, 3 days old on the control group. S birds/group on water, 3 days old on the control group. Significantly higher on Day 0, 83 and 119 for HuveGuard group. Signif		Or			B. c a.p.	
HuveGuard NB: 19720 Vaccinated 1, HuveGuard NB: 10d) Vaccinated 2, Paracox (drinking water, 9 days old) Vaccinated 2, Paracox (drinking water, 9 days old) Vaccinated 3, HuveGuard NB: 10000 Vaccinated 4, HuveGuard NB: 10d) Vaccinated 5, Water, 9 days old) Vaccinated 6, Water, 9 days old) Vaccinated 7, Water, 9 days old) Vaccinated 8, Water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) Vaccinated 1, HuveGuard Water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) Vaccinated 9, Paracox (drinking water, 9 days old) Vaccinated 1, HuveGuard Paracox (drinking water, 9 days old) Vaccinated 1, HuveGuard Paracox (drinking water, 9 days old) Vaccinated 9, Paracox (drinking water, 9, days old	Vaccinated1			- Faecal	Different OPG natterns	Small neaks which
MMAT and HuveGuard NB: 18760 vaccinated2, PARACOX-80: 19720 HuveGuard MMAT and HuveGuard MB: 9010 vaccinated3, PARACOX-80: 19720 HuveGuard MB: 9010 vaccinated4, PARACOX-80: 19720 Vaccinated5, PARACOX-80: 19720 Vaccinated7, Paracox (drinking water, 9 days old) value principle of the control		Daracov 9			· · · · · · · · · · · · · · · · · · ·	*
HuveGuard NB: 19720 Paracox (drinking water, 9 days old) Paracox (drinking and batter)	_			oucysis		
Vaccinated2, PARACOX-80: 10720 R-Huvepharma-10720 R-Huvepharma-10720 Religium Water, 4 days old) Broiler HuveGuard NB (drinking water, 9 days old) Vaccinated 1, Water, 9 days old) PARACOX-80: 10000 Water, 9 days old) Paracox (drinking and HuveGuard NB (drinking and HuveGuard NB: 9722 Vaccinated 2, Paracox (drinking and HuveGuard NB: 9722 Vaccinated 3, Water, 9 days old) R-Huvepharma-2012-74 R-Huvepharma-2012-75 Rearing pullets Vaccinated 1, HuveGuard NB (drinking and HuveGuard NB: 972) R-HuveGuard NB: 972 R-HuveGuard NB: 973 R-HuveGuar		۱ ,				
Vaccinated2, PARACOX-8®: 19720 PARACOX-8®: 19720 PARACOX-8®: 19720 Belglum Or Vaccinated 1, HuveGuard MMAT and HuveGuard N8: 10000 R-Huvepharma-2012-74 PARACOX-8®: 10000 R-Huvepharma-2012-75 Name and MAT (eyed for po, day-old) and HuveGuard N8: (spray on birds, 7 days old) Selglum R-HuveGuard N8: (spray on birds, 7 days old) Vaccinated2, Paracox (drinking and HuveGuard N8: (spray on birds, 7 days old) Vaccinated2, Paracox (drinking and HuveGuard N8: (spray on birds, 7 days old) Vaccinated2, Paracox (drinking and HuveGuard N8: (spray on birds, 7 days old) Vaccinated2, Paracox (drinking and HuveGuard N8: (spray on birds, 7 days old) Vaccinated2, Paracox (drinking and HuveGuard N8: (drin						
Vaccinated2, PARACOX-80: 19720 HuveGuard MMAT (drinking water, 9 days old) Comparison with Author (drinking water, 9 days old) S birds/group water were euthanized on D6, 13, 20, 27, 34, 55, 83 and 131 Higher at D83° Over whole study period not difference in daily weight gain? Higher on D13 an D20° in the HuveGuard on difference in daily weight gain? Higher on D13 an D20° in the HuveGuard group, although still below ILS score 1 Higher on D3 an D20° in the HuveGuard group, although still below ILS score 1 Different OPG patterns between groups. Consecutive small peaks which were decreasing towards the end of the rearing period. Different OPG patterns between groups. Consecutive small peaks which were decreasing towards the end of the rearing period. Different OPG patterns between groups. Two high peaks at the age of 41 and 83 days. R-Huvepharma-2012-74 HuveGuard MB (spray on birds, 7 days old) S birds/group on with period. Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control? Although and Paracox (drinking water, 7 days old) S birds/group on D8, 15, 22, 29, 36, 57 and 85 Significantly higher on D85 for Huveguard group compared to control? Birds, 7 days old) Significantly higher on D85 for Huveguard group compared to control? Birds, 7 days old) Similar OPG pattern in both groups, peak at around age of 7-8 weeks Vaccinated2, PARACOX-80: 20260 MMAT (spray on birds or eye drop, day-old) S birds/group on D7, 14, 21, 28, 35, 56 and 85 Similar OPG pattern in both groups, peak at around age of 7-8 weeks	18760	old)			HuveGuard groups	· ·
PARACOX-8®: 19720 19720 R-Huvepharma- 2012-11 (drinking water, 4 days old) Broiler breeders (drinking water, 9 days old) Paracox (drinking water, 9 days old) PARACOX-8®: 10000 R-HuveGuard MMAT and HuveGuard ADDO R-HuveGuard MBC Glark (Ped drop, day-old) R-HuveGuard MBC Spray on birds, 7 days old) Paracox (drinking water, 9 days old) R-HuveGuard MBC Spray on birds, 7 days old) Paracox (drinking water, 9 days old) R-HuveGuard MBC Spray on birds, 7 days old) Paracox (drinking water, 9 days old) R-HuveGuard MBC Spray on birds, 7 days old) Paracox (drinking water, 9 days old) R-HuveGuard MBC Spray on birds, 7 days old) Paracox (drinking water, 9 days old) R-HuveGuard MBC Spray on birds, 7 days old) R-Rearing pullets Vaccinated1, Paracox (drinking water, 7 days old) Vaccinated2, Paracox (drinking water, 7 days old) Vaccinated3, Paracox (drinking water, 7 days old) Vaccinated4, Paracox (drinking water, 7 days old) Vaccinated2, Paracox (drinking water, 7 days old) Vaccinated3, Paracox (drinking water, 7 days old) Vaccinated4, Paracox (drinking water, 7 days old) Vaccinated4, Paracox (drinking water, 7 days old) Vaccinated4, Paracox (drinking water, 7 days old) Vaccinated6, Paracox (drinking water, 7 days old) Vaccinated6, Paracox (drinking water, 7 days old) Vaccinated6, Paracox (drinking water						control group.
19720 HuveGuard MMAT (drinking water, 9 days old) Marter, 9	Vaccinated2,					
R-Huvepharma- 2012-11 Belgium Grinking water, 4 days old) Broiler breeders HuveGuard NB (drinking water, 9 days old) Vaccinated 2, PARACOX-8©: 10000 R-Huvepharma- 2012-74 R-Huvepharma- 2012-74 R-HuveGuard NB (spray on birds, 7 days old) Vaccinated 1, HuveGuard NB (spray on birds, 7 days old) Vaccinated 1, HuveGuard NB (spray on birds, 7 days old) Vaccinated 1, HuveGuard NB (spray on birds, 7 days old) Vaccinated 1, HuveGuard NB (spray on birds, 7 days old) Vaccinated 2, Paracox MMAT and HuveGuard NB (spray on birds, 7 days old) Vaccinated 3, HuveGuard NB (spray on birds, 7 days old) Vaccinated 4, HuveGuard NB (spray on birds, 7 days old) Vaccinated 5, HuveGuard NB (spray on birds, 7 days old) Vaccinated 6, HuveGuard NB (drinking water, 7 days old) Vaccinated 7, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 7, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 7, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 80, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 7 days old) Vaccinated 9, HuveGuard NB (drinking water, 9 days on birds or eye drinking drinking water, 9 days on birds or eye drinking drinking drinking water, 9 days on birds or eye drinking drinking drinking drinking water, 9 days on birds or eye drinking drinking drinking water, 9 days on birds or eye d	PARACOX-8©:					
### ARACOX® Belgium Water, 4 days old) Broiler	19720					
### ARACOX® Belgium Water, 4 days old) Broiler	R-Huvepharma-	HuveGuard	Comparison	5 birds/group		
Belgium Garinking water, 4 days old) Seroller Se						
Belgium Broiler Broile	2012-11		PARACOX©			
Broiler breeders Comparison with Group Agroup on birds, 7 days old) Comparison with MAT and HuveGuard MB (Begium And And HuveGuard MB (Brain pullets) Comparison with MAT	Dalaium	, ,				
Broller breeders And HuveGuard NB (drinking water, 9 days old) Accinated 1, HuveGuard NB (drinking water, 9 days old) Accinated 2, PARACOX-8®: 10000 Paracox (drinking water, 9 days old) Accinated 2, Paracox (drinking water, 9 days old) Accinated 1, HuveGuard Mariand Mariand HuveGuard National Mariand HuveGuard Mariand HuveGuard Mariand HuveGuard Mariand Mariand HuveGuard Mariand Mariand HuveGuard Mariand HuveGuard Mariand Mariand HuveGuard Mariand Ma	Beigium	-				
HuveGuard NB (drinking water, 9 days old) Paracox (drinking water, 7 days old) Paracox (drinking water, 9 days old) Paracox (dr		· ·		and 131		
Vaccinated 1, HuveGuard MMAT and HuveGuard Qrinking water, 9 days old) R-Huvepharma-2012-74 Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard MAT and HuveGuard MAT and HuveGuard MBE water, 9 days old) Vaccinated2, PARACOX-8©: 10000 R-Huvepharma-2012-75 Rearing pullets Vaccinated2, Paracox (drinking water, 9 days old) R-HuveGuard MMAT (eye drop, day-old) and MAT and HuveGuard MMAT and HuveGuard						
Vaccinated 1, HuveGuard MMAT and HuveGuard NB: 9722 Paracox (drinking water, 9 days old) - Intestinal lesions Higher on D13 an D20° in the HuveGuard group, although still below ILS score 1 oocysts Higher on B3° Different OPG patterns between groups. Two high peaks at the age of 41 and 83 days Different OPG patterns between groups. Two high peaks at the age of 41 and 83 days Paracox (Mithar) Significantly higher on Day 0, 85 and 119 for Day 0, 85 for HuveGuard group compared to control² Paracox (drinking water, 7 days old) Faecal oocysts Significantly higher on Day 0, 85 for HuveGuard group control² Faecal oocysts Significantly higher on Day 0, 85 for HuveGuard group contr	breeders			 Body weight 	_	U
HuveGuard MBMAT and HuveGuard NB: 9722 Vaccinated2, PARACOX-8©: 10000 R-Huvepharma- 2012-74 Rearing pullets Vaccinated1, HuveGuard MB: 45015 Vaccinated2, Paracox (drinking water, 7 days old) Vaccinated2, PARACOX-8®: 20260 Vaccinated2, PARACOX-8®: 20260 Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MBMAT and HuveGuard MBMAT and HuveGuard MBMAT and Racox (drinking water, 7 days on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MBMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye Belgium Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) Vaccinated2, PARACOX-8®: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) Vaccinated2, PARACOX-8®: 20260		(drinking			whole study period not	D27a. Over whole
MMAT and HuveGuard NB: 9722	Vaccinated 1,	water, 9 days			difference in daily	study period not
MMAT and HuveGuard NB: 9722	HuveGuard	old)			weight gain ^b	difference in daily
HuveGuard NB: 9722 Vaccinated2, PARACOX-8©: 10000 R-Huvepharma- 2012-74 Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard MMAT and HuveGuard MMAT and HuveGuard MMAT spray on birds, 7 days old) Vaccinated2, PARACOX-8©: 20360 R-Huvepharma- 2012-75 R-HuveGuard MB (drinking water, 2 days old) R-HuveGuard MB (spray on birds, 7 days old) R-HuveGuard MB (drinking water, 2 days old) R-HuveGuard MB (spray on birds, 7 days old) R-HuveGuard MB (drinking water, 2 days old) R-HuveGuard MMAT (spray on birds or eye drop, day-old) R-HuveGuard MB (drinking water, 2 days old) R-HuveGuard MB: 45015 R-Huvepharma- 2012-75 R-Huvepharma- 2012-75 R-Huvepharma- 2012-75 R-HuveGuard MMAT (spray on birds or eye drop, day-old) R-HuveGuard MMAT (spray on birds or eye drop, day-old) R-HuveGuard MMAT (spray on birds or eye drop, day-old) R-HuveGuard MMAT (spray on birds or eye drop, day-old) R-HuveGuard MMAT (spray on birds or eye drop, day-old)	MMAT and	,			8 8	•
9722 Vaccinated2, PARACOX-8©: 10000 R-Huvepharma- 2012-74 Belgium Chickens Comparison with PARACOX® Charactor Comparison with PhareCoX® Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control® Comparied to		Or				
Vaccinated2, PARACOX-8©: 10000 R-Huvepharma- 2012-74		01		- Intectinal	Higher on D13 an D20a	Higher on 83b
Vaccinated2, PARACOX-8©: 10000 R-Huvepharma-2012-74 Belgium Rearing pullets Chickens Rearing pullets Cormparison Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 5 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla Significantly higher on Day 6 for Huveguard group compared to controla	3722	Daragov			_	riigilei oli 65
PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 10000 PARACOX-8©: 100000 PARACOX-8©: 10000 PARACOX-8©: 100000 PARACOX-8©: 10000 PAR	Manada at a d2			iesions		
10000 Comparison with HuveGuard NB (spray on birds, 7 days old) Vaccinated1, HuveGuard MMAT and HuveGuard NB (drinking 45015	,	, ,				
R-Huvepharma- 2012-74 Belgium HuveGuard NB (spray on birds, 7 days old) HuveGuard MMAT and HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX® Old) Vaccinated2, PARACOX® Old) R-Huvepharma- 2012-75 R-Huvepharma- 2012-75 R-Huvepharma- 2012-76 R-Huvepharma- 2012-77 Different OPG patterns between groups. Two high peaks at the age of 41 and 83 days Different OPG patterns between groups. Two high peaks with were decreasing towards the end of the rearing period S birds/group on D8, 15, 22, 29, 36, 57 and 85 Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Paracox (drinking water, 7 days old) Vaccinated2, PARACOX-8®: 20260 R-Huvepharma- 2012-75 MMAT (spray on birds or eye Belgium Paracox HuveGuard MMAT (spray on birds or eye Belgium Paracox Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to control® Significantly higher on D85 for Huveguard group compared to co					below ILS score 1	
R-Huvepharma- 2012-74 Belgium Chickens Comparison With PARACOX® 36, 57 and 85 Body weight Chickens Cignificantly higher on Day 0, 85 and 119 for HuveGuard group Compared to controla D85 for Huveguard group compared to Controla Paracox (drinking water, 7 days old) Vaccinated2, PARACOX-8®: 20260 R-Huvepharma- 2012-75 MMAT (spray on birds or eye Belgium Document Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on Day 0, 85 or Huveguard group compared to controla Similar OPG pattern in both groups, peak at around age of 7-8 weeks S birds/group on D7, 14, 21, 28, on birds or eye Belgium Document Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Paracox (drinking water, 7 days old) Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher On D85 for Huveguard group compared to controla	10000	old)				
R-Huvepharma- 2012-74 HuveGuard MMAT (eye drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX® (drinking water, 7 days old) Vaccinated2, PARACOX® (drinking water, 7 days on birds or eye Belgium drop, day-old) Who is a control and belay to be decreasing towards the end of the rearing period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to control and period period period Significantly higher on Day 0, 85 and 85 an				- Faecal	Different OPG patterns	Different OPG
R-Huvepharma- 2012-74 Belgium Chickens Comparison Das, 15, 22, 29, 36, 57 and 85 Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Das for Huveguard group compared to controla Controla Chickens				oocysts	between groups.	patterns between
R-Huvepharma- 2012-74 Belgium Chickens Comparison Das, 15, 22, 29, 36, 57 and 85 Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Das for Huveguard group compared to controla Feacal Oocysts Ooth Tiple Chickens					Consecutive small	groups. Two high
R-Huvepharma- 2012-74 Belgium Chickens Chic					peaks which were	peaks at the age
R-Huvepharma- 2012-74					decreasing towards	
R-Huvepharma- 2012-74 Belgium Belgium Chickens Comparison Wall, 15, 22, 29, 36, 57 and 85 Body weight Significantly higher on Day 0, 85 and 119 for HuveGuard group compared to controla Significantly higher on D85 for Huveguard group compared to controla The paracox (drinking water, 7 days old) Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Comparison With PARACOX® Figure Significantly higher on D85 for Huveguard group compared to controla Similar OPG pattern in both groups, peak at around age of 7-8 weeks Figure PARACOX® Similar OPG pattern in both groups, peak at around age of 7-8 weeks Figure PARACOX® Similar OPG pattern in both groups, peak at around age of 7-8 weeks Figure PARACOX® Similar OPG pattern in both groups, peak at around age of 7-8 weeks Figure PARACOX® Similar OPG pattern in both groups, peak at around age of 7-8 weeks						,
R-Huvepharma- 2012-74					_	
2012-74	R-Huvenharma-	HuveGuard	Comparison	5 birds/group on	p	
Belgium drop, day-old) and HuveGuard NB (spray on birds, 7 days old) Vaccinated1, HuveGuard MB: 45015 Vaccinated2, PARACOX® old) Vaccinated3, HuveGuard MB: 45015 Vaccinated4, HuveGuard NB: (drinking water, 7 days old) Vaccinated2, PARACOX® old) Vaccinated3, HuveGuard NB: (drinking water, 7 days old) Vaccinated4, Faecal Similar OPG pattern in oocysts both groups, peak at around age of 7-8 weeks Vaccinated5, PARACOX on birds or eye or on birds or eye or op, day-old) Belgium Vaccinated5, PARACOX on birds or eye or op, day-old)	'		•			
Belgium Chickens Chickens Rearing pullets Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Body weight Significantly higher on Day 0, 85 and 119 for HuveGuard For HuveGuard Significantly higher on D85 for Huveguard group compared to control ^a Significantly higher on D85 for Huveguard group compared to control ^a - Faecal Similar OPG pattern in oocysts both groups, peak at around age of 7-8 weeks Significantly higher on D85 for Huveguard group compared to control ^a - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks	2012 74		PARACOX©			
Chickens Chickens (spray on birds, 7 days old) Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-HuveGuard MMAT (spray on birds or eye drop, day-old) HuveGuard R-HuveGuard	Dalaium			50, 57 allu 65		
Chickens (spray on birds, 7 days old) Rearing pullets old) Vaccinated1, HuveGuard MAT and HuveGuard NB: 45015 (drinking water, 7 days old) Vaccinated2, PARACOX-8©: 20260 R-Huvepharma-2012-75 HuveGuard MMAT (spray on birds or eye Belgium down and the state of th	Beigium			D-3 * * * *	Cincificantly 1111	
Rearing pullets birds, 7 days old) Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-HuveGuard R-HuveGuard MMAT (spray on birds or eye drop, day-old) birds, 7 days old) - Intestinal lesions - Intestinal group compared to controla group compared to controla - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Similar OPG pattern in both groups, peak at around age of 7-8 weeks				- Body weight		
Rearing pullets Old) Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Or Intestinal lesions - Intestinal lesions OB5 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - S birds/group on D7, 14, 21, 28, 35, 56 and 85 Belgium compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Significantly higher on D85 for Huveguard group compared to controla Similar OPG pattern in both groups, peak at around age of 7-8 weeks	Chickens					
Vaccinated1, HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Paracox (drinking water, 7 days old) - Intestinal lesions Significantly higher on D85 for Huveguard group compared to control ^a - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85 Belgium		-				
HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Paracox (drinking water, 7 days old) Paracox (drinking water, 7 days old) - Faecal oocysts both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85 Belgium D85 for Huveguard group compared to control³ Similar OPG pattern in both groups, peak at around age of 7-8 weeks	Rearing pullets	old)			compared to control ^a	
HuveGuard MMAT and HuveGuard NB: 45015 Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Paracox (drinking water, 7 days old) Paracox (drinking water, 7 days old) - Faecal oocysts both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85 Belgium D85 for Huveguard group compared to control³ Similar OPG pattern in both groups, peak at around age of 7-8 weeks						
MMAT and HuveGuard NB: 45015 Water, 7 days old) - Faecal oocysts PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Paracox (drinking water, 7 days old) - Faecal oocysts both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, on birds or eye drop, day-old) Belgium group compared to controla - Faecal both groups, peak at around age of 7-8 weeks	Vaccinated1,	Or		 Intestinal 	Significantly higher on	
MMAT and HuveGuard NB: 45015 Water, 7 days old) - Faecal oocysts PARACOX-8©: 20260 R-Huvepharma- 2012-75 Belgium Paracox (drinking water, 7 days old) - Faecal oocysts both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, on birds or eye drop, day-old) Belgium group compared to controla - Faecal both groups, peak at around age of 7-8 weeks	HuveGuard			lesions	D85 for Huveguard	
HuveGuard NB: 45015 Water, 7 days old) - Faecal oocysts Similar OPG pattern in both groups, peak at around age of 7-8 weeks R-Huvepharma- 2012-75 MMAT (spray on birds or eye drop, day-old) Similar OPG pattern in both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85	MMAT and	Paracox			_	
45015 water, 7 days old) - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks R-Huvepharma- 2012-75 MMAT (spray on birds or eye drop, day-old) - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks						
Old) - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks R-Huvepharma-2012-75 MMAT (spray on birds or eye drop, day-old) - Faecal Similar OPG pattern in both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85		, ,				
Vaccinated2, PARACOX-8©: 20260 R-Huvepharma- 2012-75 MMAT (spray on birds or eye drop, day-old) Belgium Doctysts both groups, peak at around age of 7-8 weeks 5 birds/group on D7, 14, 21, 28, 35, 56 and 85	.5015	-		- Faecal	Similar OPG nattern in	
PARACOX-8©: around age of 7-8 weeks 20260 HuveGuard R-Huvepharma- 5 birds/group on D7, 14, 21, 28, on birds or eye drop, day-old) Belgium drop, day-old)	Vaccinated?	olu)				
20260 weeks R-Huvepharma- 2012-75 HuveGuard MMAT (spray on birds or eye drop, day-old) 5 birds/group on D7, 14, 21, 28, 35, 56 and 85 Belgium drop, day-old)				oucysts		
R-Huvepharma-					_	
2012-75 MMAT (spray on birds or eye drop, day-old) D7, 14, 21, 28, 35, 56 and 85					weeks	
on birds or eye drop, day-old) 35, 56 and 85						
Belgium drop, day-old)	2012-75					
				35, 56 and 85		
and - Body weight	Belgium	drop, day-old)				
		and		- Body weight		

CMDv/TEM/003-02 14/19

HuveGuard NB	NL/V/0207/001/MR
Huvepharma NV	MRP
	Publicly available assessment report

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	- Intestinal		
Huveguard:		lesions		Higher on D14
14430	Paracox			and D28, D35,
	(drinking			D56 in the control
Vaccinated2,	water, 9 days			groupa
PARACOX-8©:	old)	- Faecal		
12726		oocysts	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 Safe	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			
- 4		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			N. 1:00			
		water).		- Lesion	No differences in total			
		Haves 2. day.		scores	mean lesion score			
		House 2: day- old chicks			were observed			
		vaccinated on			between the groups ^b . No differences were			
		day 0 with			detected in species			
		HuveGuard			specific lesion scores ^b .			
		MMAT and			specific lesion scores.			

CMDv/TEM/003-02 15/19

b: no significant difference

HuveGuard NB	NL/V/0207/001/MR	
Huvepharma NV	MRP	
	Publicly available assessment report	

		I	Τ		
	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 (R-huvepharma-201		ommercial cond	ditions when applied	at first day of age by cour	rse spray on feed
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		
control):24,500	with Paracox®	differentiati	120 and 130		
birds	8 via drinking	on was	- Faecal	No differences in total	
bii us					
27	water.	blinded)	oocysts	or species-specific OPG	
House 2 (test		ends - 1		between houses ^b .	
group): 11,200	House 2: day-	Field study	1		
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	
	HuveGuard			(1.8 vs. 0.4) ^a . On day	
	MMAT and			28, the HuveGuard	
	HuveGuard NB			group had a	
	(both: course			significantly lower	
	spray on feed).			total lesion score (1.6	
	spray on recay.			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	
			, = 5	study birds from the	
				HuveGuard group	
				weight less ^a . At day 56,	
				85, and 135 no	
				difference in weight	
				_	
Ffficacy and Safety	of HuveGuard NR under co	mmercial cond	litions when applied	was observed ^b . at first day of age by cour	rse snrav
(R-Huvepharma-201	6-83)			at mist day of age by coul	эсэргау
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.		
	at 1 day of age	differentiati			
House1	in the hatchery	on was	- Faecal	Total and species	
(positive	in the natchery	blinded)		specific oocyst	
control): 85,649	House 4	billided)	oocysts	1	
animals	House 1	e		shedding was not	
	(positive	Field study		different between	
House 2 (test	control)			houses ^b .	
group): 63,240	treatment 2:				
animals	Evalon® via				

CMDv/TEM/003-02 16/19

HuveGuard NB	NL/V/0207/001/MR	
Huvepharma NV	MRP	
	Publicly available assessment report	

	spray on bir	ds	- Lesion	No differences were	
	at 1 day of a		scores	observed in lesion	
	in the hatch	ery		scores for all study	
				days. E. acervulina	
	House 2 (tes	st		lesion scores were	
	group):			lowest for Evalon®	
	HuveGuard			vaccinated birds ^a .	
	MMAT and				
	HuveGuard	NR	- Body weight	At set-up and day 28,	
	via spray on		Body Weight	bird vaccinated with	
	birds at 1 da			HuveGuard weighed	
	of age in the	•		less than birs from	
	hatchery	•		house 1 ^a . At day 116	
	Hatchery			birds vaccinated with	
				HuveGuard were	
				heavier than birds	
	- 10 1		<u> </u>	from house 1 ^a .	
-		olling coccidiosis i	n slow growing b	roilers under field cond	litions in Belgiu
(R-Huvepharma-2			Ta. 1 1 a =		
Chickens, Sasso	House 1:	Controlled,	Study days 0, 7,		
broilers.	vaccinated a		14, 21, 28, 35, 56		
	day of arriva	` '	and 70.		
House 1 (test	on study site	_	Slaughter after		
group): 5000	(day-old) wi		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 o	on		HuveGuard group and	
	day of arriva			the control group ^b .	
	on study site			the control group .	
	(day-old) wi		- Body weight	No difference in weight	
	Paracox® via		Body Weight	gain between the	
				HuveGuard groups and	
	spray on bir	us.			
rff:	 			the control group ^b .	
		coccidiosis in slow	growing proliers und	ler field conditions in Belgi	lum
(R-Huvepharma-2		Cantuallad	Charles described	<u> </u>	
Chickens, Sasso	House 1:	Controlled,	Study days 0, 7,		
broilers.	vaccinated a		14, 21, 28, 35, 56		
	day of arriva		and 70.		
House 1 (test	on study site	_	Slaughter after		
group): 5035	(day-old) wi		70 days.		
birds	HuveGuard	differentiati			
	MMAT and	on was	- Faecal	No statistical analysis	
House 2	HuveGuard	NB blinded)	oocysts	performed.	
(vaccinated	via spray on				
	feed.	Field study	- Lesion score	No differences in total	
positive		, i		intestinal lesion scores	
'	House 2			wer observed between	
control): 5035				the HuveGuard group	
control): 5035	(control):			and the control groupb.	
control): 5035	, , ,	on			
control): 5035	vaccinated o				
control): 5035	vaccinated of day of arriva	ıl	- Rody weight		
control): 5035	vaccinated of day of arriva on study site	ıl 2	- Body weight	No difference in bird	
positive control): 5035 birds	vaccinated of day of arriva on study site (day-old) wi	ıl e th	- Body weight	No difference in bird weight between the	
control): 5035	vaccinated of day of arriva on study site	al e th	- Body weight	No difference in bird	

CMDv/TEM/003-02 17/19

HuveGuard NB	NL/V/0207/001/MR	
Huvepharma NV	MRP	
	Publicly available assessment report	

Chickens, Sasso	House 1:	Controlled,	Stu	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	ughter after		
group): 4955	HuveGuard	and	70 (days.		
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	
3iifi					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.

CMDv/TEM/003-02 18/19

b: no significant difference

HuveGuard NB	NL/V/0207/001/MR	
Huvepharma NV	MRP	
	Publicly available assessment report	



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 day- old 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

CMDv/TEM/003-02 19/19