



**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR THE
IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT**

AviPro IB - ND C131

AviPro IB - ND C131	DE/V/0291/001/DC
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PRODUCT SUMMARY

EU procedure number	DE/V/0291/001/DC
Name and pharmaceutical form	AviPro IB – ND C131 Lyophilisate for ocular/nasal suspension/use in drinking water for chicken
Applicant	Elanco GmbH Heinz-Lohmann-Straße 4 27472 Cuxhaven Germany
Active substance(s)	Infectious Bronchitis virus, live attenuated strain Massachusetts H120 Newcastle Disease virus, live attenuated strain clone 13-1
ATC vetcode	QI01AD11
Target species	Chickens
Indication for use	For active immunisation of chicken (broiler, future layer) against Newcastle Disease to reduce clinical signs and mortality. For active immunisation of chicken (broiler, future layer) against Infectious Bronchitis in order to reduce the detrimental effect resulting from the infection by avian infectious bronchitis virus, serotype Massachusetts on the ciliary activity, which may be manifested in respiratory clinical signs.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this immunological veterinary medicinal product (IVMP) are available in the Union Product Database (UPD).

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

SUMMARY OF ASSESSMENT

Legal basis of original application	Full application in accordance with Article 12 (3) of Regulation (EC) 2019/6 as amended
Date of completion of the original decentralised procedure	03.05.2023
Concerned Member States (CMS) for original procedure	AT, CZ, ES, FR, HU, IT, NL, PL, PT, RO
CMS for subsequent use procedure	Not applicable
Withdrawn CMS during original decentralised procedure	None

1. SCIENTIFIC OVERVIEW

The IVMP is manufactured and controlled using validated methods and tests that ensure the consistency of the IVMP released on the market.

The IVMP can be safely used in the target species; the reactions observed during clinical studies are indicated in the SPC.

The IVMP is also 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 IVMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation for this IVMP.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

2.A. Product description

The IVMP contains the live attenuated NDV strain clone 13-1 and the live attenuated IBV strain Massachusetts H120. NDV clone 13-1 is a LaSota strain with a low pathogenicity and good immunogenicity.

Further components are disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate, gelatin, sucrose and sorbitol. The final product is presented as lyophilisate for reconstitution in water and administration by spray or use in drinking water. The product is delivered without a specific solvent. All components comply with the respective Ph. Eur. monographs.

The IVMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

The vaccine is filled in colourless transparent EP Type I glass vials with a 6 ml or 10 ml filling volume (which are closed with type I rubber stoppers. Sterilization before use of the vials is performed by hot air, rubber stoppers are autoclaved. The vials are finally closed with aluminium crimp caps.

The choice of the vaccine strains and the formulation is justified.

The selection of the manufacturing process of the active substances and the finished product is explained.

Characterisation of the active substances including the determination of biological properties, biological activity, immuno-chemical properties, purity and impurities of the active substances is provided in order to allow suitable specifications to be established.

2.B. Description of the manufacturing method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site and in accordance with the European Pharmacopoeia and relevant European guidelines.

2.C. Production and control of starting materials

The active substances are live attenuated Infectious Bronchitis virus, strain Massachusetts H120 and live attenuated Newcastle Disease virus, strain clone 13-1. Both strains are already in use in currently authorised monovalent products of the same manufacturer.

The specifications of the active substances are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification are provided.

Scientific data and/or certificates of suitability issued by the EDQM are provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products was satisfactorily demonstrated.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

Starting materials of non-biological origin used in production comply with relevant pharmacopoeia monographs or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. monographs and guidelines and are appropriately assessed for the absence of extraneous agents according to the Ph. Eur. and other guidelines.

The master and working seeds were produced according to the seed lot system as described in the relevant guidelines.

2.D. Control tests during the manufacturing process

The test performed during production is described and the results of six consecutive runs, conforming to the specifications, are provided.

A shelf life and storage conditions for the intermediate IVMP are defined based on data resulting from stability studies.

2.E. Control tests on the finished product

For all tests, a short description of the techniques for analysing the finished product is provided. The tests and their specifications and limits are justified and are considered appropriate to adequately control the quality of the IVMP.

Satisfactory validation data for each analytical method are provided, if appropriate.

The tests performed on the final product conform to the relevant requirements and monographs, if applicable; any deviation from these requirements is justified.

Batch analytical data from the proposed production site are provided demonstrating compliance with the determined specification.

The demonstration of the batch-to-batch consistency is based on the results of six batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

2.F. Batch-to-batch consistency

Full protocols of six consecutive batches of the product, representative of the routine production and giving the results for all tests performed during production and on the finished product, are provided in order to ensure that quality is consistent from batch to batch and to demonstrate conformity with the predefined specifications.

2.G. Stability tests

Stability data on the active substances are provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product are 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 2 hours of the reconstituted product is supported by the data provided. The recommendations in the product leaflet should be followed.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

3. SAFETY DOCUMENTATION (safety and residues tests)

3.A. General requirements

The safety of AviPro IB – ND C131 when administered to the target species at the minimum age recommended in the SPC for vaccination was evaluated in several preclinical studies and one clinical study, which were performed according to the current legislation and guidance documents.

The pre-clinical studies performed in SPF chicken are considered applicable to both broilers and future layers. Observations made in the clinical study that was performed in broilers can be considered applicable to layers kept under field-conditions as well since commercial broilers are immunologically more vulnerable than layers and technically represent the “worst-case scenario”.

The vaccine batches used for these studies were manufactured according to the description of the manufacturing process in the quality part of the product dossier.

3.B. Pre-clinical studies

The **safety of the administration of one dose** administered by spray on the day of hatch and orally at seven or 14 days of age to SPF (specific pathogen free) chickens was demonstrated in one dedicated study:

Animals and application scheme (study groups)	Group	Age in days	Route	Vaccine	Dose
	1	1	spray	AviPro IB – ND C131, low passage level	1
	2	7	oral		
	3	14	oral		
	4	1	spray	AviPro IB – ND C131, higher passage level	1
	5	7	oral		
	6	14	oral		
	7	1	spray	Placebo (water)	-
	8	7	oral		
9	14	oral			
Follow-up	- Check for specific antibodies against IBV or NDV before the start of the study - Presence of clinical abnormalities and mortality. Pathological examination in case of mortalities. - Ciliary activity of tracheal explants - Histological examination of kidney samples - Presence of IBV in the kidneys and ureters with an IBV specific immunohistochemical staining				
Results	- No specific antibodies were detected confirming the SPF status of the chickens. - No clinical signs were noted. However, 4 chickens were found dead or were euthanised for reasons unrelated to the vaccination. Additionally, 1 chicken from a group with higher passage level exhibited respiratory symptoms related to vaccination, therefore the passage level of the virus present in a commercial batch was restricted. - Complete ciliostasis was noted after spray vaccination after vaccination, but respiratory epithelia recovered in the following week. In group vaccinated orally ciliostasis scores were initially also high after vaccination, but respiratory epithelia recovered as well. - In histological kidney samples, only mild lesions were found after vaccination.				

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

	- No virus was detected in the kidneys, but was found in two cases in the ureter.
Conclusion	The study complied with the requirements of Ph. Eur. monographs 0442 (live IBV vaccines) and 0450 (live NDV vaccines). The results of this study indicate that vaccination of a single maximum dose via spray to 1-day-old chicks is safe or oral vaccination of a single maximum dose to 7/14-day-old chickens is safe, when the passage level of the vaccine virus is restricted to a lower level.

The **safety of a tenfold overdose** to the target animal was also investigated as required:

Animals and application scheme (study groups)	Group	Age in days	Route	Vaccine	Dose
	1	1	spray	AviPro IB – ND C131	10
	2	7	oral	AviPro IB – ND C131	10
	3	1	eye drop	Placebo (water)	-
Follow-up	- Check for specific antibodies against IBV or NDV before the start of the study - Presence of clinical abnormalities, mortality, and pathological examination - Ciliary activity of tracheal explants - Histological examination of kidney samples - Presence of IBV in the kidneys and ureters with an IBV specific immunohistochemical staining				
Results	- No specific antibodies were detected confirming the SPF status of the chickens. - 7 chickens developed respiratory symptoms related to vaccination. - Complete ciliostasis was noted after spray vaccination, but respiratory epithelia recovered in the following week. A slightly lower ciliostasis score was noted after oral vaccination and also a recovery of the epithelia. - Histological evaluation of kidney samples revealed mild to moderate lesions in some of the birds after vaccination. - No virus was detected in the kidneys, but was found in one case in the ureter.				
Conclusion	The study complied with the requirements of Ph. Eur. monograph 0442 (live IBV vaccines) and 0450 (live NDV vaccines). The administration of an overdose may lead to clinical signs reflected in sections 3.6 and 3.10 of the SPC and sections 6 and 7 of the package leaflet. The recommended dose regime described in the SPC and the package leaflet should be followed.				

No dedicated study to examine **application of a repeated dose** was provided. The vaccine is intended for broilers with a relatively short lifespan and future layers, and is recommended only to be administered once; therefore, this approach was considered acceptable.

Effects on the reproductive performance were examined in the following study:

Animals and application scheme (study groups)	Group	Age in days	Route	Vaccine	Dose
	1	1	spray	AviPro IB – ND C131	1
	2	1	spray	Placebo (water)	-
Follow-up	- Check for specific antibodies against IBV or NDV before the start of the study - Presence of clinical abnormalities and mortality - Necropsies with focus on the reproductive tract				
Results	- No specific antibodies were detected. - No clinical signs or deaths related to the vaccination were noted.				

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

	- No abnormalities were detected.
Conclusion	The study complied with the requirements of Ph. Eur. monograph 0442 (live IBV vaccines) and 0450 (live NDV vaccines). Administration of the vaccine at the maximum dose does not induce abnormalities in the oviduct of female SPF chickens.

There are no data suggesting that this product might adversely **affect the immune system** of the vaccinated animal or its progeny. Therefore, no specific study was carried out.

For each live virus strain included in the vaccine specific studies were carried out to evaluate their characteristics regarding **spreading** to unvaccinated target species and non-target species, **dissemination** of the vaccine strains in the birds' body and a possible **reversion to virulence**:

Excretion of IBV in oropharyngeal and cloacal swabs was detected at least until day 21 after vaccination. The virus disseminated to all evaluated organs. Spread of IBV from vaccinated to unvaccinated in-contact chickens was confirmed. In some of the vaccinated and in one of the in-contact chicken minor transient respiratory signs were noted, indicating the activation of the immune system after vaccination or contact with the vaccine strains.

Excretion of NDV in faeces was detected until day 12 after vaccination. The virus disseminated to all evaluated organs. Spread to in-contact chickens was demonstrated but caused no clinical signs.

IBV is in first line relevant for chickens; therefore, no spread to non-target species was investigated. The safety of the NDV vaccine strain was evaluated in the following non-target species: Peking ducks, geese, turkeys, and pigeons. The vaccine strain was safe in ducks, geese and turkeys, but caused slight pathological findings in pigeons. In general, spread to other susceptible species should be avoided. In SPC section 3.5 and section 6 of product leaflet adequate information is included.

No reversion to virulence was detected for both virus strains included in AviPro IB – ND C131.

No specific studies were carried out concerning the **biological properties** or a possible **recombination or genetic reassortment** of the vaccine strains because both virus strains were extensively investigated over the last decades and have been used in authorised vaccines for many years in the EU.

The **user safety risk** has been adequately addressed in accordance with the Guideline on user safety for IVMPs (EMA/CVMP/IWP/54533/2006). The excipients can be considered as not to pose a user safety risk. Live IBV is not zoonotic, whereas live NDV may cause conjunctivitis in humans. However, if the vaccine is used as recommended it is highly improbable that the dose and routes of administration of the vaccine would have significant adverse effects on the health and safety of the user. Appropriate warnings and risk management measures are proposed for section 3.5 of the SPC and section 6 of product leaflet.

Regarding **residues**, the excipients used are standard ingredients, which do not require an MRL as food additives or do not fall under the scope of Commission Regulation (EU) No 37/2010. An antibiotic is added to the harvest to avoid bacterial contamination in an amount far below the acceptable MRL limits. Based on this information, no withdrawal period is necessary.

No specific assessment of the **interaction** of this product with another veterinary medicinal product was made. Therefore, an appropriate warning in the SPC is included.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

3.C. Clinical trials

The safety of AviPro IB – ND C131 was evaluated when administered by spray to one-day-old commercial broilers under field conditions:

Animals and application scheme (study groups)	Group	Age [d]	Number	Route	Vaccine	Dose
	1	1	30,621	spray	Comparator vaccine	1
	2	1	30,626	spray	AviPro IB – ND C131	1
Follow-up	- Test for presence of maternal derived antibodies (MDA) against NDV and IBV prior to vaccination - Clinical signs and mortality - Performance parameters: Body weight/ average daily weight gain (ADWG), feed conversion ratio (FCR), European Efficiency Factor (EEF)					
Results	- Presence of MDA was confirmed for in both groups for both virus strains. - No clinical signs related to the vaccination were observed in the test group. In the comparator group slight respiratory signs were noted as reflected in the SPC of this product. The mortality threshold of the farm of 4% was not exceeded in both groups. - The performance data of the flock vaccinated with AviPro IB – ND C131 did not differ significantly from the results of broilers vaccinated with the comparator product.					
Conclusion	The results of this study indicate that AviPro IB – ND C131 is safe when administered on the day of hatch to broilers with MDA against NDV and IBV kept under field conditions.					

3.D. Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline (EMA/CVMP/074/95), which showed that no further assessment is required. Both virus strains included in this vaccine are used in the EU since many years. The assessment concluded that the overall risk to the environment is estimated as effectively zero when AviPro IB – ND C131 is used according to the SPC/package leaflet.

A Phase II assessment therefore was not considered to be necessary and no warnings are required.

4. EFFICACY DOCUMENTATION

4.A. General requirements

Eleven laboratory studies in total were performed to support the efficacy of the vaccine. Among these are three dose finding studies for the IB component and two for the ND component. Based on results of these studies, the minimum titre for IB was set as $10^{3.4}$ EID₅₀ and for ND as $10^{5.5}$ EID₅₀. These minimum titres were used in all following efficacy studies. In addition, the onset of immunity (OOI) as claimed for the two components was examined by these studies.

To support the duration of immunity (DOI), one study for IB and one for ND was carried out with challenges at 8 weeks p.v.

To evaluate the influence of maternally derived antibodies (MDA) on the efficacy of the vaccine, two studies for IB and two studies for ND were carried out.

Both routes of administration (spray and oral ingestion) have been used in the studies.

Efficacy studies were performed under controlled laboratory conditions using batches produced as detailed in Part 2.B of the dossier.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

The preclinical studies conducted in both SPF chickens and broilers are applicable to future layers as well, based on the aforementioned rationale.

Efficacy IBV

For IBV, studies were set up according to requirements of Ph. Eur. 0442. The IBV component of the vaccine was applied at the most attenuated passage level that will be present in a batch of the vaccine. Challenges were carried out with IB challenge strain M41 by eye drop.

Examination parameters in IB challenge studies were clinical observations including mortality recording as well as ciliary activity of tracheal explants. The examination parameters and their follow up, the validity criteria and pass criteria are in accordance with what is mentioned in the corresponding monograph.

Efficacy NDV

Studies on the efficacy of the NDV component follow the requirements of Ph. Eur. 0450. The ND vaccine virus used in the study was at the most attenuated passage level that will be present in a batch of the vaccine.

For challenges, the avian Newcastle Disease virus challenge strain Herts (Weybridge 33/56) is used at a dose of $10^{5.0}$ EID₅₀ per animal by i.m. route at 14 or 21 days p.v. as requested in the corresponding monograph.

In ND challenge studies, animals are clinically observed and the mortality is recorded after challenge.

The examination parameters and its follow up, the validity criteria and pass criteria are in accordance with what is mentioned in the corresponding monograph.

4.B. Pre-Clinical Studies

The efficacy of the product was demonstrated in laboratory studies under well-controlled conditions in accordance with the relevant requirements, which show that the vaccine is efficacious in protection against infection with virulent ND virus as well as virulent IB virus.

Dose finding and onset of immunity (Ool) for IBV

Three studies are presented to establish a suitable minimum efficacious dose. Since an initial IBV dose of $10^{3.0}$ EID₅₀ was not sufficiently efficacious in the first study, two further studies with increasing doses were performed. The Ool of the IBV component of AviPro IB – ND C131 could be confirmed in the third study with the determined minimum dose of $10^{3.4}$ EID₅₀. This relevant study for onset of immunity with the claimed minimum titre of $10^{3.4}$ EID₅₀ is summarised in the following table.

Objective of the studies	Determination of the onset of immunity
Animals, age, vaccination scheme	day-old SPF chicks 22 SPF chicks vaccinated by spray 22 SPF chicks vaccinated orally 6 SPF chicks as controls sham vaccinated by oral route 6 SPF chicks as controls (untreated)
Challenge	IB challenge strain M41 21 days post vaccination

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

Follow-up	Clinical observations including mortality recording for 5 days after challenge Ciliary activity of tracheal explants explants taken at day 5 after challenge
Results	Clinical observations No clinical signs or mortality during the whole study. Ciliary activity of tracheal explants Non-vaccinated and challenged control group: 0% protection Non-vaccinated and non-challenged group: (1/5) minor loss of ciliary activity. Group vaccinated by spray, 18/20 (90%) protection Group vaccinated by oral route, 18/18 (100%) protection

The onset of immunity of 21 days after vaccination at a minimum titre of $10^{3.4}$ EID₅₀ for IBV can be regarded as demonstrated. Even if the applicant increased the minimum age for oral use to 7 days, the study is relevant since performed in chickens of younger age.

Dose finding and onset of immunity for NDV

One study with three different NDV titres was performed to determine the minimum efficacious titre for the ND antigen. The lowest chosen titre of $10^{5.5}$ EID₅₀ provided adequate protection according to requirements of Ph. Eur 0450 in vaccinated animals after challenge at 21 days post vaccination.

The claimed onset of immunity (14 days after vaccination) against NDV is supported in a further study which is summarized in the following table:

Objective of the studies	Onset of immunity of a combined attenuated NDV/IBV live vaccine against a Newcastle Disease challenge infection in SPF chicken
Animals, age, vaccination scheme	day-old SPF chicks 22 SPF chicks vaccinated by spray 22 SPF chicks vaccinated orally 11 SPF chicks as controls sham vaccinated by oral route
Challenge	ND challenge strain Herts Weybridge 33/56, $10^{5.0}$ EID ₅₀ per animal, i.m., 14 days p.v.
Follow-up	Clinical observations including mortality recording for 14 days after challenge
Results	Clinical observations Non-vaccinated and challenged control group: 0% protection Group vaccinated by spray, 19/20 (95%) protection Group vaccinated by oral route, 19/20 (95%) protection

The onset of immunity of 14 days after vaccination at a minimum titre of $10^{3.4}$ EID₅₀ for IBV can be regarded as demonstrated.

Duration of immunity

For both NDV and IBV, a study with SPF animals was performed according to special monographs to demonstrate the claimed duration of immunity of 8 weeks.

IBV

To demonstrate the duration of immunity for IB, the vaccine was administrated to day-old chicks either by spray or via oral route with a minimum titre of IB vaccine virus ($10^{3.4}$ EID₅₀).

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

The study is summarized in the following table:

Objective of the studies	Duration of immunity of a combined attenuated NDV/IBV live vaccine (spray and oral) against an Infectious Bronchitis challenge infection in SPF chickens
Animals, age, vaccination scheme	day-old SPF chicks 24 SPF chicks vaccinated by spray 24 SPF chicks vaccinated orally 8 SPF chicks as controls sham vaccinated by oral route 8 SPF chicks as controls (untreated)
Challenge	IB challenge strain M41 56 days post vaccination
Follow-up	Clinical observations including mortality recording for 5 days after challenge Ciliary activity of tracheal explants explants taken at day 5 after challenge
Results	Clinical observations No clinical signs or mortality that was related to challenge. Ciliary activity of tracheal explants Non-vaccinated and challenged control group: 20% protection Non-vaccinated and non-challenged group: normal ciliary activity Group vaccinated by spray, 18/19 (95%) protection Group vaccinated by oral route, 17/20 (85%) protection

The DOI of 8 weeks as claimed could be demonstrated accordingly for the IB component of the vaccine after vaccination at day-old by either route.

NDV

To demonstrate the duration of immunity for ND, the vaccine was administrated to day-old chicks either by spray or via oral route with a minimum titre of ND vaccine virus ($10^{5.5}$ EID₅₀).

The study is summarized in the following table:

Objective of the studies	Duration of immunity of a combined attenuated NDV/IBV live vaccine against a Newcastle Disease challenge infection in SPF chicken
Animals, age, vaccination scheme	day-old SPF chicks 23 SPF chicks vaccinated by spray 23 SPF chicks vaccinated orally 12 SPF chicks as controls sham vaccinated by oral route
Challenge	ND challenge strain Herts Weybridge 33/56, $10^{5.0}$ EID ₅₀ per animal, i.m., 56 days p.v.
Follow-up	Clinical observations including mortality recording for 14 days after challenge
Results	Clinical observations Non-vaccinated and challenged control group: 0% protection Group vaccinated by spray, 18/20 (90%) protection Group vaccinated by oral route, 19/20 (95%) protection

The DOI of 8 weeks as claimed could be demonstrated accordingly for the ND component of the vaccine after vaccination at day-old by either route.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

Immunogenicity in the presence of maternally derived antibodies

The influence of MDA on the efficacy of AviPro IB – ND C131 was examined in two studies for each component. The studies were performed considering the two relevant special monographs of Ph. Eur. (requirements in general do not have to apply for commercial animals) as well as the reflection paper on the demonstration of a possible impact of maternally derived antibodies on vaccine efficacy in young animals (EMA/CVMP/IWP/439467/2007).

The efficacy of a vaccination with AviPro IB – ND C131 in SPF chickens was examined in corresponding laboratory studies based on the immunogenicity test in Ph. Eur. already. Accordingly, no separate group of vaccinated SPF chickens was included in the following studies. As unvaccinated broilers are expected to be less affected in challenge than SPF animals, an additional control group of non-vaccinated SPF chicken was added to the studies in order to assess the validity of the challenge infection.

IBV

To demonstrate the efficacy of the IB component of AviPro IB – ND C131 in presence of MDA, two separate studies were provided in which the vaccine was administrated to day-old broiler chicks either by spray or via oral route with a minimum titre of IB vaccine virus ($10^{3.4}$ EID₅₀).

The studies are summarized in the following table

Spray vaccination:

Objective of the studies	Determination of the efficacy of a combined attenuated ND/IB live vaccine (spray) against an Infectious Bronchitis Virus (IBV) challenge infection in one-day-old broiler chickens having maternally derived antibodies against IBV.
Animals, age, vaccination scheme	1-day-old SPF chicks 22 broiler chicks vaccinated by spray 6 broiler chicks as controls sham vaccinated by spray 6 SPF chicks as controls sham vaccinated by spray 6 broiler chicks (untreated) for ciliary activity, serology day 21 10 broiler chicks, serology day 0
Challenge 7	IB challenge strain M41 21 days post vaccination
Follow-up	Serology Day 0 and day 21 Clinical observations including mortality recording for 5 days after challenge Ciliary activity of tracheal explants explants taken at day 5 after challenge
Results	Serology (ELISA): Day 0: 9/10 MDAs against IBV. All chicken MDAs against NDV. Day 21: None of the chickens had MDA against IBV. 2/5 MDA against NDV. Clinical observations No clinical signs or mortality that was related to challenge. Ciliary activity of tracheal explants Non-vaccinated and challenged SPF control group: 0% protection Non-vaccinated and challenged broiler control group: 0% protection Group vaccinated by spray, 19/20 (95%) protection

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

Based on the results of the study, it can be concluded that MDAs do not interfere with the IB efficacy after spray vaccination at day-old.

Oral administration:

Objective of the studies	Determination of the efficacy of a combined attenuated ND/IB live vaccine (oral administration) against an Infectious Bronchitis Virus (IBV) challenge infection in one-day-old broiler chickens having maternally derived antibodies against IBV.
Animals, age, vaccination scheme	7-day-old SPF chicks 22 broiler chicks vaccinated orally 6 broiler chicks as controls sham vaccinated orally 6 SPF chicks as controls sham vaccinated orally 6 broiler chicks (untreated) for ciliary activity, serology day 28 10 broiler chicks, serology day 0, 7
Challenge	IB challenge strain M41 21 days post vaccination
Follow-up	Serology Day 0, day 7 and day 28 Clinical observations including mortality recording for 5 days after challenge Ciliary activity of tracheal explants explants taken at day 5 after challenge
Results	Serology (ELISA): Day 0: 10/10 MDA against IBV; 9/10 MDAs against NDV. Day 7: 8/10 MDA against IBV and NDV. Day 28: None of the chickens had MDA against IBV and NDV. Clinical observations No clinical signs or mortality that was related to challenge. Ciliary activity of tracheal explants Non-vaccinated and challenged SPF control group: 0% protection Non-vaccinated and challenged broiler control group: 0% protection Group vaccinated by spray, 20/20 (100%) protection

Based on the results of the study, it can be concluded that MDAs do not interfere with the IB efficacy after vaccination by oral route at 7-day-old.

NDV

Spray vaccination:

Objective of the studies	Determination of the efficacy of a combined attenuated ND/IB live vaccine against a Newcastle Disease (ND) challenge infection in day-old broiler chicken having maternally derived antibodies against ND
Animals, age, vaccination scheme	1-day-old broiler chicken 22 broiler chicken vaccinated by spray 11 broiler chicken as controls sham vaccinated 11 SPF chicken as controls -sham vaccinated 10 broiler chicken-serology
Challenge	ND challenge strain Herts Weybridge 33/56, 10 ^{5.0} EID ₅₀ per animal, i.m., 21 days p.v.
Follow-up	Serology Day 0 and day 19 Clinical observations including mortality recording for 14 days after challenge
Results	Serology Day 0 : 10/10 MDA against IBV, 9/10 MDA against NDV Day 19: 0/11 MDA against IBV, 4/11 still MDA against NDV

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

	Clinical observations Non-vaccinated and challenged broiler control group: 40% protection Non-vaccinated and challenged SPF control group: 0% protection Group vaccinated by spray: 18/20 (90%) protection
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Based on the results of the study, it can be concluded that MDAs do not interfere with the ND efficacy after spray vaccination at 1-day-old.

Oral administration:

Objective of the studies	Determination of the efficacy of a combined attenuated ND/IB live vaccine against a Newcastle Disease (ND) challenge infection in day-old broiler chicken having maternally derived antibodies against ND
Animals, age, vaccination scheme	7-day-old broiler chicken 22 broiler chicken vaccinated orally 11 broiler chicken as controls orally 11 SPF chicken as controls -sham vaccinated 10 broiler chicken-serology (day old) 10 broiler chicken-serology (7-day old)
Challenge	ND challenge strain Herts Weybridge 33/56, 10 ^{5.0} EID ₅₀ per animal, i.m., 21 days p.v.
Follow-up	Serology Day 0, day 7 and day 26 Clinical observations including mortality recording for 14 days after challenge
Results	Serology Day 0 : 10/10 MDA against IBV and NDV Day 7: 5/10 MDA against IBV, 9/10 still MDA against NDV Day 26: 0/10 MDA against IBV and NDV Clinical observations Non-vaccinated and challenged broiler control group: 10% protection Non-vaccinated and challenged SPF control group: 100% protection Group vaccinated orally: 19/20 (95%) protection

Based on the results of the study, it can be concluded that MDA do not interfere with the ND efficacy after spray vaccination at 7-day-old.

4.C. Clinical trials

No efficacy field study was performed to support the results from the laboratory trials.

This omission has been justified:

- Several laboratory efficacy studies were performed with commercial broilers with confirmed MDA levels as target animals.
- As prophylactic vaccination is a common measure to control the outbreak of IB and ND, the occurrence of a natural challenge with IB and ND field strains is unlikely. To demonstrate the efficacy of the vaccination under field conditions by challenge, the transport of a limited number of animals to laboratory for a challenge under laboratory conditions would be required. To avoid unnecessary suffering of the birds of the non-vaccinated control groups, especially in case of an ND challenge, and in absence of any obvious additional benefit of expected data, the study was omitted.
- It should be noted that the ND and IB components of AviPro IB-ND C131 are each licensed as monovalent vaccines. Both vaccines are indicated for spray or drinking

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

water administration in chicken from 1-day-old. Since no major adverse events were reported via pharmacovigilance signal detection, the safety and efficacy of the monovalent vaccines is substantiated in the field and the same can be expected for the bivalent vaccine. Based on this information and with respect to the 3R principles, the applicant refrained from carrying out additional field trials to demonstrate efficacy of the bivalent vaccine in chicken.

- For Newcastle Disease as well as for Infectious Bronchitis, well-established challenge models exist (e.g. strains representative of the EU epidemiological situation causing reproducible signs of the diseases). Therefore, a field efficacy trial is not considered to provide significant further value in addition to the available laboratory challenge trials.
- The SPC of AviPro IB – ND C131 does not mention a production-related claim like e.g. weight gain.

5. 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 are acceptable.

AviPro IB - ND C131	DE/V/0291/001/DC
Elanco GmbH	DCP
Publicly available assessment report	

POST-AUTHORISATION PROCEDURES

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/labelling/package leaflet is/are available in the Union Product Database (UPD).

Sequence of significant variations

Summary of change (Application number)	Approval date
DE/V/0291/001/A/001: VRA G.I.4 - Change in the summary of product characteristics, labelling or package leaflet due to new quality, preclinical, clinical or pharmacovigilance data - "Future layer" as additional target species category	22.11.2023
DE/V/0291/001/A/001: VNRA 11834 – Classification A.4 - Change in ATCvet Code	27.11.2023