College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
3531 AH Utrecht
The Netherlands

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR AN IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT

Avishield IB QX
lyophilisate for oculonasal suspension/use in drinking water for chickens

NL/V/0429/001/DC

July 2025

PRODUCT SUMMARY

EU procedure number	NL/V/0429/001/DC
Name and pharmaceutical form	Avishield IB QX lyophilisate for oculonasal suspension/use in drinking water for chickens
Applicant	Genera d.d. Svetonedeljska cesta 2, Kalinovica 10436 Rakov Potok Croatia
Active substance(s)	Avian infectious bronchitis virus, type QX, strain 1285, Live
ATC vetcode	QI01AD07
Target species	Chickens
Indication for use	For the active immunisation of chickens (broilers, future layers and future breeders) in order to reduce respiratory signs of avian infectious bronchitis caused by QX-like variants of infectious bronchitis virus (IBV). Onset of immunity: 3 weeks after vaccination. Duration of immunity: 10 weeks after vaccination.

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).

SUMMARY OF ASSESSMENT

Legal basis of original application	Full application in accordance with Article 8 of Regulation (EC) 2019/6 as amended.
Date of completion of the original decentralised>procedure	30 April 2025
Date immunological veterinary medicinal product first authorised in the Reference Member State (MRP only)	-
Concerned Member States (CMS) for original procedure	AT, BE, CZ, DK, DE, EE, EL, ES, FR, HR, HU, IE, IT, LT, LV, PL, PT, RO, SI, SK, UK(NI)
CMS for subsequent use procedure	-
Withdrawn CMS during original decentralised procedure	-

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 slight reactions observed 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.

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

2.A. Product description

The IVMP contains live attenuated avian infectious bronchitis virus, strain QX 1285: $10^{3.7}$ – $10^{5.3}$ EID_{50}

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

The product is packed in hydrolytic type I glass vials closed with bromobutyl rubber stoppers and sealed with aluminium caps.

The origin and characteristics of the strain are described and the strain is considered to be appropriate for the current epidemiological situation in the EU. The manufacturing process, including the stabiliser, is a an established process at Genera.

2.B. Description of the manufacturing method

The IVMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

The product is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

2.C. Production and control of starting materials

The active substance is live attenuated avian infectious bronchitis virus, strain QX 1285, an established active substance.

The active substance specification is 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.

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

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

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

2.D. Control tests during the manufacturing process

The tests performed during production are described and the results of three consecutive runs, conforming to the specifications, are provided.

In-process control tests are carried out on intermediate stages of manufacture in order to verify the consistency of the manufacturing process and the final IVMP.

A specification was set for each intermediate and the analytical methods are described and validated, if applicable.

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 methods 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 3 batches produced according to the method described in the dossier.

2.F. Batch-to-batch consistency

Full protocols of three 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. One batch was manufactured at commercial scale. Further data on commercial scale batches will be provided post-authorisation.

2.G. Stability tests

Stability data on the active substance(s) 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 claim of a 3-hour stability after reconstitution is based on the demonstration of stability for two batches broached and stored for 3 hours at +20-25°C.

The in-use shelf life of 3 hours of the mixed vaccines (Avishield IB H120, Avishield IB GI-13 and Avishield IB QX) is supported by the data provided. The recommendations in the product leaflet should be followed.

3. SAFETY DOCUMENTATION (safety and residues tests)

3.A. General requirements

The safety of the IVMP when administered to the target species, the potential harmful effects (residues in IVMP, substance in foodstuff), the potential serious risk for human beings during product administration and to the environment are adequately described.

3.B. Pre-clinical studies

The safety of the administration of a single dose to the target animal was not tested. Instead, the safety of a ten-fold overdose was demonstrated in one GLP study in SPF chicks that were vaccinated either at one day of age by spray or oculonasal or at 7 days of age via drinking water. No clinical signs were observed during the 14 days follow-up and no mortality occurred. The results are considered to support the safety of the single dose and overdose when applied via spray, oculonasal route or drinking water.

The safety of the overdose to the respiratory tract and the kidney when applied via oculonasal route and via spray was demonstrated in two GLP safety studies in day old SPF chicks. The results show moderate to high ciliary scores, mild respiratory signs (sneezing) and mild to moderate inflammatory kidney lesions.

A further study was provided as supportive data. In this GLP study in SPF chicks, the safety for the respiratory tract and the kidney after application of an 8-fold overdose applied by spray was determined. Ciliary scores were high, mild to moderate kidney lesions were observed at necropsy. Mild clinical signs (sneezing) were observed in few animals.

The safety of an overdose of mixed Avishield IB QX, Avishield IB GI-13 and Avishield IB H120 was tested in a GLP study in day-old SPF chicks vaccinated via spray application. No clinical signs or mortality were observed.

For the virus strain included in the vaccine specific studies were carried out to describe the spread, dissemination and reversion to virulence. The studies were performed according to the recommendations of Regulation (EC) 2019/6 and the relevant guidelines. No increase in virulence was observed. The vaccine disseminates in the body of the vaccinated animal and was shown to persist for at least 28 days. The strain may spread to non-vaccinated in-contact chickens and may spread to other species. Safety aspects for non-target species and the environment is addressed in the dossier. Appropriate warnings are included in the SPC.

The biological properties and risk of recombination or genetic reassortment of the vaccine strain were analysed based on bibliographic data. It was concluded that although the theoretical risk of recombination cannot be excluded, due to the established safety record of attenuated vaccines, controlled attenuation of the vaccine strains, ongoing surveillance and the economic benefits derived from disease prevention vaccination outweighs this risk.

Safety for the developing reproductive tract was shown when the vaccine is administered on the 1st day of life. The vaccine is not intended for use during lay therefore no investigation of effects on the reproductive performance was conducted. Appropriate warnings are included in the SPC.

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.

3.C. Clinical trials

Two controlled, blinded, GCP clinical trials were performed in broilers in order to study safety and efficacy, the vaccine was applied via spray or drinking water. The results of the studies confirm the safety of the vaccine. A further clinical trial in broilers was performed to study the safety of associated (mixed) use of three IBV vaccines. No significant negative effects of the treatment were observed, the results support the safety of the associated (mixed) use of Avishield IB QX, Avishield IB H120 and Avishield IB GI-13.

Study 1/2022:

Quality statement	Blinded, controled GCP study (performed by U. of Ljubljana, vet.faculty, Slovenia)
Test system	1-day old broiler chicks hybrid Ross 308, in two different houses on the same farm,
Test item	IVMP: Avishield IB QX (batch 5008072/PE) CVMP: Poulvac IB QX (zoetis)
Study set up	1: 20.033 Chicks, vaccination IVMP on D1 by coarse spray at the hatchery. 2: 25.024 Chicks, vaccination control item on D1 by coarse spray at the hatchery.
Method	Safety parameters; Clinical signs, mortality (incl. culling), weekly bodyweight (n=50), serological response (by ELISA on Day 1, 22, 40) and virus detection (PCR on cloacal and orapharyngeal

	swabs on Day 9, 16 and 40). At the end of the fattening period total animal loss, rejects, down grades, feed conversion and PI were calculated and compared. At SD1 and SD15 40 birds were taken randomly from the IVP group for challenge study, 40 birds were taken form the CVP group to retain blinding.
Results	The overall mortality was 2.52% and 3.41% for IVP and CVP respectively. Overall chickens in both groups were in good health during the trial. In the IVP group on D9 dirty cloaca was noticed in some chickens, in the CVP group on D18 some coughing was noticed. No serious adverse events were reported. Overall production results were comparable in both flocks. PI was 409.10 in the IVP group and 402.30 in the CVP group. Based on statistical analysis body weights on SD 29 were considered significantly higher in the CVP group compared to the IVP group (P = 0.0007). Body weights did not differ significantly between groups on all other SDs. IBV antibodies did not differ between the groups on D0 or D22 but on D40 were significantly higher in the IVP group (p=0.0002)
Conclusion	Differences were small and not considered significant at clinical or commercial level. The vaccine was safe for commercial broilers in the field.

Study 1/2023:

Quality statement	Blinded, controled GCP study (performed by U. of Ljubljana, vet.faculty, Slovenia)
Test system	1-day old broiler chicks (hybrid Ross 308). Two groups housed on the same farm
Test item	IVMP: Avishield IB QX CVMP: Avishield IB H120
Study set up	1: 19,519 Chicks, vaccination IVMP on D7 via drinking water. 2: 22,896 Chicks, vaccination control item on D7 via drinking water.
Method	Safety parameters; Clinical signs, mortality (incl. culling), weekly bodyweight (n=50), serological response (by ELISA on Day 8, 29, 41/42) and virus detection (PCR on cloacal and orapharyngeal swabs on Day 8, 16 and 23). At the end of the fattening period total animal loss, rejects, downgrades, feed conversion and PI were calculated and compared. At SD8 and SD23 15 and 25 birds were taken randomly from the IVP group for challenge study, birds were taken form the CVP group to retain blinding.
Results	The overall mortality was 3.74% and 7.94% for IVP and CVP respectively. In weeks 2 and 3 in the CVP group the weekly total animal loss exceeded the historical average + 2SD. Overall chickens in both groups were in good health during the trial. In the CVP group on D9 E.coli infection was detected and treatment with a.b. was initiated. On D23 respiratory problems and up to D26 some coughing was noticed. Overall production results were comparable in both flocks. PI was 388.13 in the IVP group and 382.16 in the CVP group. Rejects and downgrades were lower in the IVP group. Based on statistical analysis body weights on SD 8, 15, 22 and 36 were significantly higher in the CVP group compared to the IVP group. IBV antibodies did not differ between the groups on D0 or D29 but on D41 were significantly higher in the CVP group (p=0.0015)
Conclusion	The vaccine was safe for broiler chicks in the field after administration via drinking water.

Study 2/2023

Quality statement	Blinded, controled GCP study (performed by U. of Ljubljana, vet.faculty, Slovenia)
Test system	1-day old broiler chicks (hybrid Ross 308). Three groups housed on the same farm
Test item	IVMP 1: Avishield IB QX (5008072/PE) + Avishield IB H120 + Avishield IB GI-13 (mixed) IVMP 2: Avishield IB H120 + Avishield IB GI-13 (mixed) CVP: Avishield IB H120
Study set up	1: 19,000 Chicks, vaccination IVMP 1 on D1 via coarse spray at the hatchery 2: 19,000 Chicks, vaccination IVMP 2 on D1 via coarse spray at the hatchery

	3: 18,500 chicks, vaccination CVMP on D1 via coarse spray at the hatchery Oropharyngeal swabs taken at D1, D10 and before slaughter, cloacal swabs at D10 and before slaughter, blood samples taken on D1, D22 and before slaughter.
Method	Safety parameters; Clinical signs, mortality (incl. culling), weekly bodyweight (n=50), serological response (by ELISA) and virus detection (PCR on cloacal and orapharyngeal swabs). At the end of the fattening period total animal loss, rejects, down grades, feed conversion and PI are calculated and compared.
Results	Mild respiratory disorders were observed in individual chickens in all groups during the third and fourth week and were resolved spontaneously within maximum of five days. Such mild disorders are quite often seen in commercial broiler flocks and could be associated with sub-optimal environmental conditions such as ventilation, dust etc. Furthermore, no elevated mortality or culling was recorded in any of the groups during the mentioned periods, consequently these incidences were not considered as adverse events. Total animal loss calculated at slaughter in the IVP 1 group was 2.56%, in IVP 2 group it was 2.01%, while in the CVP group it was 2.39%. Based on statistical analysis significantly higher body weights were achieved in the CVP group in comparison to the IVP 1 group on SD 8 ($p < 0.001$) and SD 22 ($p = 0.026$). The CVP group exhibited higher body weights than the IVP 2 group on SD 8 ($p < 0.001$), SD 15 ($p < 0.001$), SD 22 ($p = 0.018$) and SD 29 ($p < 0.001$). No statistical differences in body weights were observed on SD 36. The performance index was 386.15 for group 1, 375.22 for group 2 and 356.44 for the controls.
Conclusion	Overall clinical and production results were comparable between groups. Avishield IB QX was shown to be safe when given by spray in the hatchery to day-old chickens, simultaneously with Avishield IB H120 and Avishield IB GI-13, according to the results in this field trial.

3.D. 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. The assessment concluded that since the IBV QX 1285 strain does not revert to virulence and does not cause clinical IB and because the excipients are non-toxic, while the risk of exposure to the hazard is high, the consequences are negligible and the risk can be evaluated as effectively zero. Standard warnings on disposal of unused medicines are considered adequate to limit the environmental exposure. Warnings and precautions as listed in the product literature are adequate to ensure safety to the environment when the product is used as directed.

3.E. Assessment required for veterinary medicinal products containing or consisting of genetically modified organisms

Not applicable.

3.F. Residue tests to be included in the pre-clinical studies

Maximum Residue Levels

The active substance, live IBV QX 1285 strain, is an immumological for which no residue studies are required in accordance with Reg 2021/805 (IIIb.3F). Excipients are either on the list of EU approved additives or on the out of scope list. Therefore, no study of residues was performed, which is accepted.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days was accepted.

4. EFFICACY DOCUMENTATION

4.A. General requirements

Efficacy studies were performed generally in accordance with Ph.Eur. 0442, with observation of mortality, clinical signs and post-mortem ciliostasis scores.

Initially, onset and duration of immunity studies were performed to investigate the efficacy of the vaccine with a minimum dose of 3.9 $\log_{10}$ $TCID_{50}$.However, considering the results of the long term stability that became available later, a lower minimum dose was required and studies were performed in SPF and MDA+ broiler to test efficacy of a minimum dose of 3.7 $\log_{10}$ EID_{50}.
The passage level of the vaccine batches was MSV+3 which is one passage further that what is planned to be routinely use for manufacturing of vaccine.

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.

Two studies were performed to determine the onset of immunity after vaccination with a minimum dose of 3.7 $\log_{10}$ EID_{50}. In the first study, day-old SPF chicks were vaccinated via spray and challenged at 14 and 21 days post vaccination. Protection as determined by ciliostasis scores was 50% at 14 days and 80% at 21 days post vaccination. In the second study, SPF birds were vaccinated via eye-nose drop at day-old or via oral route at 7 days old. Protection as determined by ciliostasis scores at day 21 post vaccination was 85% in the oculo-nasally vaccinated group and 80% in the orally vaccinated group.

The Ph.Eur. 0442 requirement of 80% protection was met for all administration routes at the claimed onset of immunity of 21 days post vaccination.

One study was performed to determine the duration of immunity. Day-old SPF chicks were vaccinated by spray at one day of age or by oral route at 7 days of age or left untreated. Challenge was performed at 9 and at 10 weeks post vaccination. 80% protection was found at 9 weeks in both groups. At 10 weeks the protection had decreased to 60% in the spray vaccinated birds and 70% in the orally vaccinated birds. However, protection from clinical signs was 100% at 10 weeks post vaccination and the results are considered to support the claimed duration of immunity of 10 weeks.

Protection was investigated in commercial broilers with maternal antibodies. Three studies were performed, with different administration routes and similar set up. In the first study, birds were vaccinated at day-of-age with a minimum dose of vaccine via spray and challenged at 21 days. Protection, based on ciliostasis scores, was 70%. In the second study, birds were vaccinated at day-of-age with a minimum dose of vaccine via eye-nose drop and challenged at 21 days. Protection based on ciliostasis scores was 80%. In the third study, in birds vaccinated at 7 days of age via the oral route, a protection of 85% was found.

Five studies were performed to test compatibility of the Avishield IB QX 1285 vaccine with Avishield IB GI-3 and Avishield IB H120, when applied mixed. The Avishield IB QX 1285 vaccine dose used in two studies was the higher 3.9 $\log_{10}$ $TCID_{50}$. In the first study, 3 groups of birds were vaccinated with the three vaccines on Day 0 via spray, three groups remained unvaccinated and one group was vaccinated on Day 0 via spray with Avishield IB GI-3 and Avishield IB H120 mixed. A challenge was performed at 10 days to test protection against IB 793B. Birds vaccinated with two vaccines were 90% protected, birds vaccinated with the three vaccines were 65% protected at day 10. Challenges were performed at day 21 against either IB M41 or IB QX, protection was 95% against IB M41 and 100% against IB QX.

A second study with a similar set up was performed to study the duration of immunity after mixed use. The Avishield IB QX 1285 vaccine dose used was the higher 3.9 $\log_{10}$ $TCID_{50}$. Challenges were performed at 8 and at 9 weeks. At 8 weeks, birds vaccinated with two vaccines were 100% protected from IB 793B challenge and 90% protected from IB M41 challenge. At 8 weeks, birds vaccinated with the three vaccines were 100% protected from IB 793B and 85% protected from IB M41. At nine weeks birds were 100% protected from IB QX.

A third study investigated the protection achieved against IB QX at 21 days post vaccination with a minimum dose of vaccine, applied via spray to day old SPF birds. The protection achieved at 21 days was 80%.

Duration of immunity against IB QX was tested at 9 and 10 weeks post vaccination with a minimum dose of vaccine, applied via spray to day old SPF birds. The protection achieved was 85% both after 9 and 10 weeks.

Finally, the protection against IB 793B was tested at 21 days post vaccination with the three vaccines in day old SPF birds, albeit the onset of immunity for Avishield IB GI-13 is currently claimed at 10 days p.v.. The protection was 85%.

Together, the studies support the absence of significant interference of the three vaccines when applied simultaneously.

4.C. Clinical trials

Efficacy of vaccination was also demonstrated under field conditions in two controlled field trials.

In the first study (refer to part 3.C, study 1/2022) 20,033 vaccinated chicks and 25,024 control vaccinated animals (Poulvac IB QX) were included. Field infection was not confirmed during the trial. However, 25 vaccinated birds were taken to the laboratory at 15 days of age and 15 non-vaccinated broilers were included as controls. A challenge with IB QX was performed at 21 days of age, a protection of 70% against ciliostasis was achieved. The protection was significant and confirms the results of the laboratory studies.

In the second study (refer to part 3.C, study 1/2023) 19,519 vaccinated chicks and 22,896 control vaccinated animals (Avishield IB H120) were included. Field infection was not confirmed during the trial. However, 25 vaccinated birds were taken to the laboratory at 15 days of age and 15 non-vaccinated broilers were included as controls. A challenge with IB QX was performed at 21 days of age, a protection of 85% against ciliostasis was achieved. The protection was significant and confirms the results of the laboratory studies.

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.

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).

This section contains information on significant changes agreed after the original procedure, which are important for the quality, safety or efficacy of the product.

None.