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QUALITY CONTROL OF INACTIVATED ASSOCIATED VACCINES AGAINST NEWCASTLE DISEASE AND BIRD FLU

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Abstract. The work contains the results of quality control of an experimental series of inactivated associated vaccine against Newcastle disease (ND) and avian influenza (AI) produced at the Research Institute for Biological Safety Problems of the Ministry of Health of the Republic of Kazakhstan. The purpose of the study was to test to determine the main indicators - the physicochemical properties of an experimental series of inactivated associated vaccine against BN and AI. The results of the experimental series showed that the vaccine is without contaminants, the concentration of hydrogen ions (pH) is 7.29 ± 0.0002137, the kinematic viscosity of the emulsion is 35.37 ± 0.00944, the vaccine is immunogenic for 12 month old chickens and harmless for chickens 30 days old . The average titers of antibodies to the virus on the 28th day after vaccination averaged 1:24.5 against the HP virus and 1:27.3 against the ND virus 1:24.5 in the hemagglutination inhibition test (HAI). The vaccine meets all the requirements in its physical and biological properties and is suitable for an associated vaccine against ND and AI.

The vaccine meets all quality requirements according to the scientific and technical documentation of the manufacturer.

Keywords: avian influenza virus; Newcastle disease virus; associated vaccine.

Introduction

Avian influenza (AI) and Newcastle disease (ND) are particularly dangerous infectious diseases of birds, causing enormous economic damage to the global poultry industry [7]. When these diseases occur, it is necessary to urgently notify the World Organization for Animal Health (OIE) about their occurrence. A set of anti-epizootic measures is also carried out, which include: quarantine, depopulation, zoning, disinfection, control of the movement of poultry and poultry products within the country, and surveillance of wild avifauna [10]. The avian influenza virus is a member of the Orthomyxoviridae family, genus Influenza A virus. There are 18 known HA subtypes (H1-H18) and 11 known NA subtypes (N1-N11) [5]. According to the OIE classification, notifiable avian influenza, depending on the degree of pathogenicity, is divided into highly pathogenic influenza (HPI), which includes any subtype of the AP virus characterized as highly pathogenic, and low pathogenic avian influenza (LPI) of the H5 and H7 subtypes [10]. Highly pathogenic AP A/H5N1 was widespread among wild and domestic birds in Southeast Asia in 1999-2006, then in Western Siberia (including Kazakhstan), Europe, East Africa, and caused numerous outbreaks that were accompanied by illness and death of domestic and wild birds, as well as people [6].

ND is a highly contagious viral disease mainly affecting the order Galliformes. ND virus belongs to the avian paramyxovirus type 1, which is a representative of the genus Avulavirus of the family Paramyxoviridae [1]. ND is as important as AI due to its highly contagious nature and worldwide distribution [2]. It is characterized by rapid spread of a large number of birds, high mortality, pneumonia, encephalitis and manifestation of hemorrhagic syndrome in the form of multiple point hemorrhages in internal organs, causes enormous economic losses and is considered a particularly dangerous infection of birds. The disease is endemic in many countries [3]. According to the OIE, in recent years outbreaks of ND have been noted in various countries, including industrialized ones. In November 2010, a mass death of 30-40-day-old broiler chickens from ND occurred at the Allel Agro poultry farm (Iliysky district, Almaty region). The farm had a well-established preventive vaccination program; all birds were vaccinated with a live vaccine (Nobilis ND Clone 30, Intervet international B.V., Netherlands). In October 2012, ND outbreaks were registered in private farmsteads in the Timiryazevsky district, North Kazakhstan region – more than 900 individuals died. In June 2013, a mass death of poultry was also observed in private farmsteads in the village of Otar (Kordai district, Zhambyl region) and the village of Matybulak (Zhambyl district, Almaty region) [7]. Thus, in 2021, the disease was registered in Israel, Bolivia, Russia, Romania, Turkey, Sweden [4].

Currently, vaccination of domestic and wild birds is an effective way to prevent these diseases. However, currently available vaccines against these diseases are unsatisfactory. Inactivated vaccines against AI are mainly used for poultry (95%) [8]. In addition, currently available inactivated vaccines are costly and labor-intensive both in production and during vaccine administration. Also, these vaccines provide suboptimal protection in vaccinated birds [9]. In addition, inactivated vaccines can be effective when birds are immunologically mature (birds >3 weeks old) [10].

In this regard, the urgent issue is the search for effective vaccines for immunization of poultry. Among such analogues, associated vaccines show efficiency in the prevention of various infectious diseases, since one vaccine contains antigens of two or more pathogens. Thus, the use of such vaccines reduces the cost of production and additional preventive measures for each disease separately, reducing the stress of poultry. Based on the above, the purpose of this work is to conduct quality control of the experimental series of inactivated associated vaccine against AI and ND according to scientific and technical documentation (NTD).

Materials and methods

Objects of research

The object of the study in this work is an inactivated associated vaccine against AI and NV from the recombinant strain A/Gyrfalcon/Washington/41088/6/2014 (H5N8) of the influenza virus and from the La Sota strain of the Newcastle disease virus.

The composition of the inactivated associated vaccine consists of an inactivated suspension of the AI and ND viruses with the addition of the oil adjuvant Montanide ISA-70 in a ratio to the antigen of 70:30. The combination of semi-finished products and emulsification, as well as the packaging of the vaccine, were carried out in accordance with the NTD [20].

Research methods

Quality control of the associated emulsified vaccine against ND and AI was carried out in accordance with the NTD. The control was carried out according to the following parameters:

determination of sterility (bacterial and fungal contamination), physicochemical properties and concentration of hydrogen ions (pH), control of vaccine stability, kinematic viscosity, assessment of harmlessness and determination of immunogenicity.

Determination of the appearance of the vaccine

The work was carried out in accordance with the State Pharmacopoeia of the Republic of Kazakhstan I, v. 1, 2.6.14. Determination of the appearance of the vaccine, the presence of foreign impurities, mold.

Determination of hydrogen ion concentration (pH)

Determination of hydrogen ions (pH). Determination of hydrogen ion concentration (pH) was carried out in three replicates using a pH meter according to the State Pharmacopoeia of the Republic of Kazakhstan I, v. 1, 2.2.3.

Sterility control

Determination of hydrogen ion concentration (pH) was carried out according to the State Pharmacopoeia of the Republic of Kazakhstan I, v. 1, 2.6.14. Sowing was carried out on seven media (Sabouraud solid, Sabouraud liquid, meat-peptone agar (MPA), meat-peptone broth (MPB), Kita-Tarotsii, Edward liquid, Edward semi-liquid).

Determination of kinematic viscosity

Viscosity was determined by three-fold measurement using a VPZh-2 capillary viscometer. The work was carried out in accordance with the State Pharmacopoeia of the Republic of Kazakhstan I, v. 1, 2.6.14.

Determination of immunogenicity

The immunogenicity of the vaccine is determined by the level of formation of antihemagglutinins in the blood serum of vaccinated birds using the hemagglutination inhibition reaction (HIR) according to the generally accepted method. The work was carried out in accordance with the State Pharmacopoeia of the Republic of Kazakhstan I, v. 1, 2.6.14.

Determination of harmlessness

The safety of vaccines was tested on 10 month-old chickens. The chickens were vaccinated intramuscularly in the chest area with a five-fold higher dose of vaccines in a volume of 2.5 cm3. The clinical observation period for the vaccinated chickens was 14 days [15].

Emulsion stability control

Emulsion stability control was carried out by centrifuging the vaccine and thermostatting at 37.0±0.5 °C [20].

Centrifugation method

From three vials with the vaccine, after vigorous shaking, 12 ml of emulsion were taken and transferred into three glass centrifuge tubes. The tubes with the emulsion were centrifuged at 3000 rpm for 30 min, after which the height of the column of the transparent fraction in the upper part of the tube was measured with a ruler [20].

Thermostat method

From three vials with the vaccine, after vigorous shaking, 10 ml of emulsion were taken and transferred into three glass test tubes, closed with rubber stoppers, placed in a rack and placed in a thermostat with a heating temperature of 37.0 ± 0.5 ° C, then for 14 days the appearance of a transparent fraction in the upper part of the test tube and the separation of the emulsion were observed [20].

Results of the study and their discussion

Vaccination has become one of the most important strategies for disease prevention and control in poultry farms. Immunity through the use of associated vaccines is easy to apply, time- and cost-effective, and widely applicable to ensure the safety of birds. In this study, we share the results of quality control of the finished associated vaccine against AI and ND, produced at the Research Institute of Bacterial and Biological Safety of the Ministry of Health of the Republic of Kazakhstan. The results showed that the prepared vaccine fully complies with the requirements of the NTD.

Quality control experiments were conducted on one batch of inactivated associated vaccine against AI and ND from the recombinant strain AI A/Gyrfalcon/Washington/41088/6/2014 (H5N8) and from the La Sota ND strain. The first stage was to determine the external parameters of the vaccine. The external appearance of the vials with the vaccine complies with the requirements of the NTD. No mold or foreign impurities were found in the vials with the vaccine.

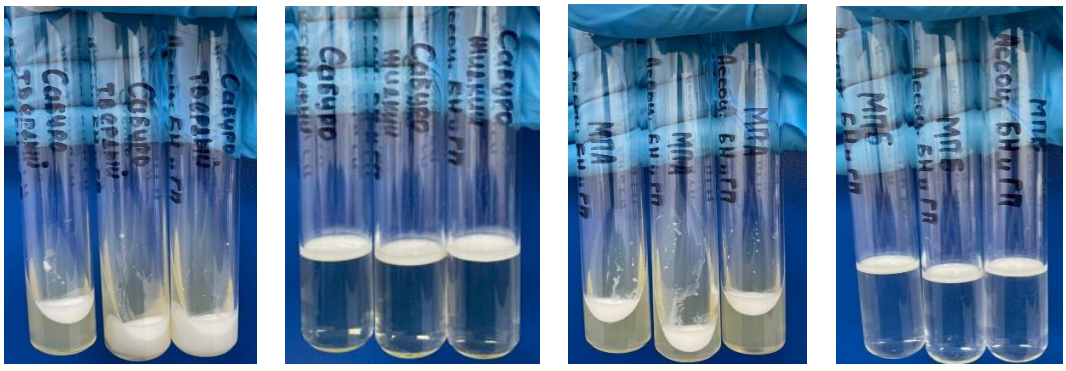
The results of hydrogen ion (pH) measurements of the associated vaccine against ND and AI are presented in Table 1.

Table 1. Results of pH control of the associated inactivated vaccine against ND and AI.

Names of the material	Repeatability of tests	Average pH value	pH	Uncertainty of experience
Inactivated associated vaccines against AI and NV from the A/Gyrfalcon/Washington/41088/6/ 2014 (H5N8) strain of the AI virus and from the La Sota strain of the NV virus	1	7,30	7,293	± 0,0002137
	2	7,29		
	3	7,29		

The concentration of hydrogen ions (pH) of the associated inactivated vaccine against ND and AI at a temperature of (2-8) ºC was that, with an experimental uncertainty of ±0.0002137, the average value was 7.29.

As a result of sterility determination, all media remained clean during the observation period from bacterial and fungal contamination, the sterility of the associated inactivated vaccine against Newcastle disease and bird flu complies with the requirement of the State Pharmacopoeia of the Republic of Kazakhstan. This control was carried out for 14 days (Figure 1).



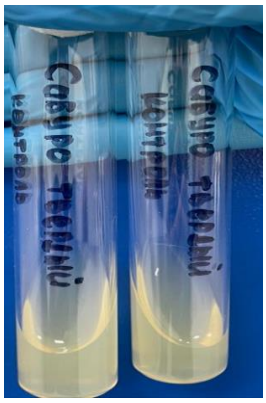
Saburo solid Saburo liquid MPA MPB

Kita-Tarotsiya

Edwarda liquid

Edwarda semi liquid

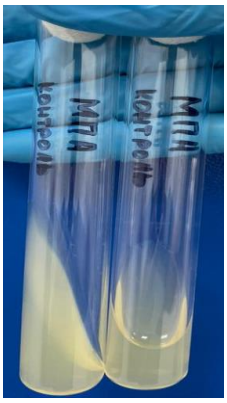
Control



Saburo solid

Saburo liquid

MPA



MPB

Kita-Tarotsiya

Edwarda liquid

Edwarda semi liquid

Figure 1 - Results of seeding the test vaccine associated with AI and NV from the A/Gyrfalcon/Washington/41088/6/2014 (H5N8) strain of the AI virus and from the La Sota strain of the NV virus. The following results were obtained (Figure 1).

In vaccines containing oil adjuvants, the kinematic viscosity of the emulsion is estimated. Viscosity is understood as the properties of a liquid, which determines the resistance of the liquid to external influences. Viscosity can be represented as internal friction between individual layers of liquid types when they are shifted relative to each other. According to regulatory documents for the production of immunobiological preparations in different countries, kinematic viscosity is measured using a viscometer (capillary, rotational, vibration, microfluidic and non-contact rheology). Determination of kinematic viscosity is carried out, according to using a capillary viscometer [22]. The method is based on determining the time of flow through a capillary of a certain volume of liquid from a measuring reservoir. The results are presented in Table 2.

Table 2 – Results of monitoring the kinematic viscosity of the emulsion of the inactivated emulsified associated vaccine against AI and ND from the A/Gyrfalcon/Washington/41088/6/2014 (H5N8) strain of the AI virus and from the La Sota strain of the ND virus

Name of the vaccine	**Repeatability of tests**	**Time t, s**	**t, averages**	**Viscosity, V**	**Uncertainty of experience**
Inactivated emulsified associated vaccines against GP and BN from the A/Gyrfalcon/ Washington/41088/6/ 2014 (H5N8) strain of the GP virus and from the La Sota strain of the BN virus	1	36	36,0	35,37	±0,00944
	2	36,5			
	3	35,5			

When studying the kinematic viscosity of the inactivated emulsified associated vaccine against AI and ND from the A/Gyrfalcon/Washington/41088/6/2014 (H5N8) strain of the AI virus and from the La Sota strain of the ND virus, it was determined that the kinematic viscosity of the tested vaccines against AI at a storage temperature of (2-8) °C was that, with an experimental uncertainty of ±0.00944, the viscosity indices were equal to 35.37 mm2/s.

The main factor of the quality of immunobiological preparations is their stability, i.e. the ability to maintain the physicochemical properties and pharmacological activity stipulated by the requirements of regulatory documentation during the established shelf life. The main criterion of vaccine stability is the preservation of its quality, i.e. appearance, emulsion stability, pH, kinematic viscosity, safety and other standardized indicators [27]. Also, the stability of the immunobiological preparation is significantly affected by the conditions of production, storage and transportation. As a result of violation of the storage conditions of the vaccine, its immunobiological properties are lost, such as the ability to induce active specific immunity. Thus, it is very important to comply with the conditions of the technological process, which ensures compliance with the specification requirements and the stability of the final product.

As a result of the work carried out to determine the stability control of vaccines by the centrifugation method, in each of the three test tubes with the tested vaccines, no changes in the

contents were detected during visual control and the height of the column of the transparent fraction formed in the upper part of the test tube did not exceed 30 mm.

According to the results of vaccine stability control by thermostatting during the entire observation period, no transparent water fraction was detected at the bottom of the test tube in each of the three test tubes with the tested vaccines during visual control, and no complete stratification of the emulsion into its constituent components was observed. During the tests, there was a minor appearance of a transparent or yellowish oil fraction at the top of the test tube, which was easily eliminated by shaking, which is not a sign of stratification (Figure 2).

As a result of the work carried out to determine the stability control of vaccines by the centrifugation method, no changes in the contents were detected in each of the three test tubes with the tested vaccines during visual control, and the height of the column of the transparent fraction formed in the upper part of the test tube did not exceed 30 mm, easily removed by shaking, which is not a sign of stratification (Figure 2).

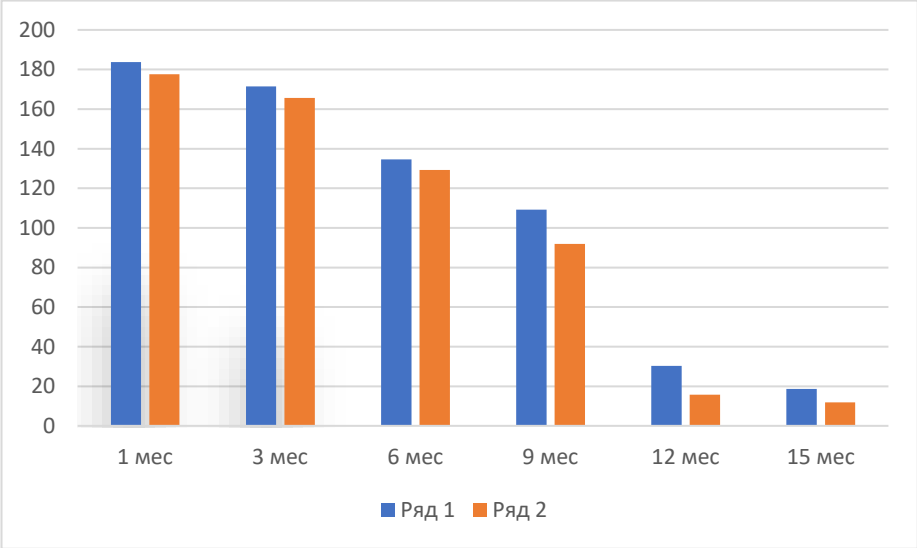


Figure 2 - Stability control of the inactivated emulsified associated vaccine against AI and ND

When testing the serum of birds vaccinated against AI and ND in HAI, after vaccination the birds had 100% antibodies to the AI and ND virus, but after 15 months it decreased to 16.5% antibodies to the AI virus and 6.7% antibodies to the ND virus, therefore after 12 months the birds should be vaccinated again.

One of the most important indicators of vaccines, along with antigenic activity, is their harmlessness and reactogenicity.

The safety of the tested associated inactivated vaccine against ND and AI was tested on 30-day-old chickens weighing at least 100 g from farms free of acute infectious diseases and sero-negative to the avian influenza virus type A. The results are presented in Table 3.

Table 3 – Results of determining the safety of vaccines against AI and ND in chickens

Name of the vaccines being tested	**Number of birds in the experiment, heads**	**Bird Observation Results (Local Response)**	**Tissue reaction at the injection site**
Inactivated emulsified vaccine associated against avian influenza from the strain A/Gyrfalcon/Washington/41088/6/2014 (H5N8) AI and from the La Sota strain of the ND virus	10	- - - -	- - - -
Notes 1 "+" reaction is insignificant (single discrete growth of fibrous connective tissue of white color, 2.0-2.5 mm in diameter 2 "-" no reaction			

According to the obtained data (Table 3) of the control of the test vaccine against AI and ND, it was revealed that the studied vaccine preparation is harmless/reactogenic and avirulent.

In order to confirm the immunogenicity of the vaccine we tested, studies were conducted to determine the antigenic activity of the experimental sample of the associated inactivated vaccine against AI and ND in birds.

After immunization, blood serum samples were taken from the birds to check for the presence of antibodies against the AI and ND viruses in the HAI. The results are presented in Tables 4 and 5.

Table 4 – Level of antibodies against the AI virus in the blood serum of birds after immunization in the HAI

Name of the vaccine	Bird No.	титр	№ птицы	titer
Ассоциированная инактивированная против болезни Ньюкасла и гриппа птиц	1	1:20	11	1:20
	2	1:40	12	1:40
	3	1:40	13	1:20
	4	1:10	14	1:40
	5	1:20	15	1:20
	6	1:40	16	1:40
	7	1:20	17	1:20
	8	1:10	18	1:40
	9	1:20	19	1:20
	10	0	20	1:10
Average titer: 24,5				

Table 5 – Level of antibodies against the NDV in the blood serum of birds after immunization in the HAI

Name of the vaccine	Bird No.	titer	Bird No.	titer
Ассоциированная инактивированная против болезни Ньюкасла и гриппа птиц	1	1:40	11	1:40
	2	1:80	12	1:20
	3	1:40	13	1:80
	4	1:20	14	1:40
	5	1:20	15	1:20
	6	1:80	16	1:10
	7	1:20	17	1:20
	8	1:10	18	1:20
	9	1:20	19	1:40
	10	1:10	20	1:40
Average titer: 27,3				

The results of the study showed that the intensity of immunity on the 28th day after a single administration of the studied vaccine associated inactivated against ND and AI, the level of antibodies in the blood of vaccinated birds in the HAI was on average 1:24.5 against the AI virus and 1:27.3 against the ND virus.

Conclusion

1. The experimental series of inactivated associated vaccine against Newcastle disease and avian influenza manufactured at the «RIBSP» of the Ministry of Health Republic of Kazakhstan showed full compliance of physical and biological parameters with the requirements of the approved regulatory and technical documentation.
2. The concentration of hydrogen ions (pH) of the preparation is 7.29±0.0002137. Kinematic viscosity is 35.39±0.00944.
3. The vaccine is harmless to 30-day-old chickens when administered intranasally with a 10-fold immunizing dose.
4. Immunogen vaccine for 30-day-old chickens. Average antibody titers to the ND virus 28 days after vaccination average 1:24.5 against the AI virus and 1:27.3 against the ND virus.
5. All associated vaccines against ND and AI carried out comply with the requirements of the NTD.

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Conflict of Interest: The authors have no potential conflicts of interest.

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Literature

1. Aulicino F.A., Marranzano M., Mauro L. Surface water pollution and microbiological indicators // Ann Ist Super Sanita. – 2005. – V. 41(3). – P. 359-70. PMID: 16552127.

2. Kolpin D.W., Furlong E.T., Meyer M.T., Thurman E.M., Zaugg S.D., Barber L.B. Buxton H.T. Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in US // Environmental Science and Technology. – 2002. – V. 36. – P. 1202-1211. http://dx.doi.org/10.1021/es011055j.

3. Sandle T. An approach for the reporting of microbiological results from water systems // PDA J Pharm Sci. Technol. – 2004. – V. 58(4). – P. 231-237.

4. Jimenez L. (Ed.). (2004). Microbial Contamination Control in the Pharmaceutical Industry (1st ed.) // CRC Press. https://doi.org/10.1201/9780203026267.

5. Traeger H. Pharmaceuticals, The Presence of Bacteria, Endotoxins, and Biofilms in Pharmaceutical Water, Ultrapure Water // International Journal of Veterinary Sciences and Animal Husbandry. – 2018. – V. 3(4). – P. 24-29. doi: 10.1016/j.biologicals.2020.07.001

6. Abdul M.M., Qunxing X.D., Kelly G.P., Erin N.H., Andrew J. Direct injection analysis of per and polyfluoroalkyl substances in surface and drinking water by sample filtration and liquid chromatography-tandem mass spectrometry // J Chromatogr A. – 2021. – V. 1653:462426.

7. Marine M., Frédéric V., Thierry B. Comparison of bacterial endotoxin testing methods in purified pharmaceutical water matrices // J Biologicals. – 2020. – V. 67. P. 49-55.

8. European medicines agency. Guideline on the quality of water for pharmaceutical use // 2019. P.10

9. Dang T.H., Vu T.C., Vu T.B., Dao T.T., Nguyen T.H., Nguyen P.T., Do T.T., Ta M.H., Chu M.L., Nguyen V.L. Evaluation of Drinking Water Quality in Schools in a District Area in Hanoi, Vietnam // Environ Health Insights. – 2020. – V. 14:1178630220959672. doi: 10.1177/1178630220959672.

10. Mottaleb M.A., Ding Q.X., Pennell K.G., Haynes E.N., Morris A.J. Direct injection analysis of per and polyfluoroalkyl substances in surface and drinking water by sample filtration and liquid chromatography-tandem mass spectrometry // J Chromatogr A. Epub. – 2021. – V. 1653. doi: 10.1016/j.chroma.2021.462426.

11. Luis A.B., Manmohan S. Acceptable levels of endotoxin in vaccine formulations during preclinical research // J Pharm Sci. – 2011. – V. 100(1). – P. 34-37. doi: 10.1002/jps.22267.

КОНТРОЛЬ КАЧЕСТВА ИНАКТИВИРОВАННОЙ АССОЦИИРОВАННОЙ ВАКЦИНЫ ПРОТИВ БОЛЕЗНИ НЬЮКАСЛА И ГРИППА ПТИЦ

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Абстракт. В работе проведены результаты контроля качества экспериментальной серий инактивированной ассоциированной вакцины против болезни Ньюкасла (БН) и гриппа птиц (ГП) изготовленную в «Научно-исследовательском институте проблем биологической безопасности» МЗ РК. Целью исследования являлись испытаний по определению основных показателей - физико-химических свойств экспериментальной серий инактивированной ассоциированной вакцины против БН и ГП. Результаты экспериментальной серий показали, что вакцина без контаминантов, концентрации водородных ионов (pH) составляет 7,29± 0,0002137, кинематический вязкость эмульсии 35,37 ± 0,00944, вакцина иммуногенна для 12 месячных цыплят и безвредна для цыплят 30-суточного возраста. Средние титры антител к вирусу на 28 сутки после вакцинации составили в среднем 1:24,5 против вируса ГП и 1:27,3 против вируса БН 1:24,5 в реакции торможения гемагглютинации (РТГА). Вакцина соответствует по своим физико-биологическим свойствам всем предъявляемым требованиям и пригодна для ассоциированной вакцины против БН и ГП.

Вакцина соответствует всем требованиям качества согласно научно-технической документации изготовителя.

Ключевые слова: вирус гриппа птиц; вирус болезни Ньюкасла; ассоциированная вакцина.

НЬЮКАСЛ АУРУЫ МЕН ҚҰС ТҰМАУЫНА ҚАРСЫ БЕЛСЕНДІРІЛМЕГЕН ІЛЕСПЕ ВАКЦИНАНЫҢ САПАСЫН БАҚЫЛАУ

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Абстракт. Жұмыста Қазақстан Республикасы Денсаулық сақтау министрлігінің Биологиялық қауіпсіздік проблемалары ғылыми-зерттеу институтында өндірілген Ньюкасл ауруы (НА) мен құс тұмауына (ҚТ) қарсы белсендірілмеген ілеспе вакцинаның тәжірибелік сериясының сапасын бақылау нәтижелері қамтылған. Зерттеудің мақсаты негізгі

көрсеткіштерді – НА және ҚТ қарсы белсендірілмеген ілеспе вакцинаның тәжірибелік сериясының физика-химиялық қасиеттерін анықтау үшін тестілеу болды. Тәжірибе сериясының нәтижелері вакцинаның ластаушы заттарсыз екенін, сутегі иондарының концентрациясы (pH) 7,29 ± 0,0002137, эмульсияның кинематикалық тұтқырлығы 35,37 ± 0,00944, вакцина 12 айлық тауықтар үшін иммуногенді және 30 күндік тауықтар зиянсыз екенін көрсетті. Вакцинациядан кейінгі 28-ші күні вирусқа қарсы антиденелердің орташа титрлері гемагглютинацияның тежелу сынағы (ГАТР) кезінде НР вирусына қарсы орташа 1:24,5 және НА вирусына қарсы 1:27,3 1:24,5 құрады. Вакцина физикалық және биологиялық қасиеттері бойынша барлық талаптарға жауап береді және НА және ҚТ қарсы ілеспе вакцина үшін жарамды.

Вакцина өндірушінің ғылыми-техникалық құжаттамасына сәйкес барлық сапа талаптарына сәйкес келеді.

Түйін сөздер: құс тұмауының вирусы; Ньюкасл ауруының вирусы; ілеспе вакцина.