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Prevention of respiratory diseases of pigs of viral-bacterial etiology in conditions of import substitution

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ABSTRACT

Introduction. Pig farming, as a fast-growing branch of animal husbandry, is capable of prompt achieving a significant increase in the production of pork with high nutritional properties and biological value. One of the acute problems of pig farming is respiratory diseases of viral and bacterial etiology. In the current economic conditions, reducing the dependence of the Russian pig farming on technological imports is of particular significance. Production of domestically manufactured feeds and veterinary drugs should be considered as the most important condition for achieving the technological sovereignty of the Russian Federation.

Objective. To analyze the provision of pig farming with domestic vaccines against such significant porcine respiratory diseases as swine influenza, porcine enzootic (mycoplasmal pneumonia), porcine reproductive and respiratory syndrome and circovirus infection as well as to identify factors that hinder the development of immunobiological drugs against these diseases.

Materials and methods. The information base of the research included data from pig-breeding organizations of the Russian Federation, the Rosselkhoznadzor's state register of veterinary medicinal products, reference and special literature, publications of research institutions.

Results. Agents of swine influenza, porcine enzootic (mycoplasmal) pneumonia, porcine reproductive and respiratory syndrome, porcine circovirus infection are the most prevalent pathogens that cause respiratory diseases in pigs on the pig farms. Over the past few years, Russian biofactories have been developing import substitution programs for the necessary immunobiological drugs. By the end of 2023, the domestic establishments manufactured 19.3 billion doses of veterinary vaccines, which is 3 billion doses more than in 2022.

Conclusion. Vaccination is the most efficient and cost-effective way to prevent viral infections. However, domestic immunological drugs against swine influenza have not yet been developed in our country, and vaccines against porcine enzootic (mycoplasmal) pneumonia, porcine reproductive and respiratory syndrome, porcine circovirus infection require modification due to high variability of the agents.

Keywords: review, vaccines, import substitution, pig farming, porcine respiratory diseases, national security

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Профилактика респираторных болезней свиней вирусно-бактериальной этиологии в условиях импортозамещения

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РЕЗЮМЕ

Введение. Свиноводство, как скороспелая отрасль животноводства, способно в короткие сроки добиться существенного увеличения производства свинины с высокими пищевыми свойствами и биологической полноценностью. Одной из острых проблем отрасли являются респираторные болезни вирусно-бактериальной этиологии. В сложившихся экономических условиях особое значение приобретает снижение технологической импортозависимости

российского свиноводства, поэтому выпуск кормовых и ветеринарных препаратов отечественного производства необходимо рассматривать как важнейшее условие достижения технологического суверенитета Российской Федерации.

Цель исследования. Анализ обеспеченности свиноводства отечественными вакцинами против таких значимых респираторных болезней свиней, как грипп, энзоотическая (микоплазменная) пневмония, репродуктивно-респираторный синдром, цирковирусная инфекция, а также выявление факторов, которые препятствуют разработке иммунобиологических лекарственных препаратов против указанных заболеваний.

Материалы и методы. Информационной базой исследований являлись данные свиноводческих организаций Российской Федерации, государственный реестр лекарственных средств для ветеринарного применения Россельхознадзора, нормативно-справочная и специальная литература, публикации научно-исследовательских учреждений.

Результаты. Возбудители гриппа, энзоотической (микоплазменной) пневмонии, репродуктивно-респираторного синдрома, цирковирусной инфекции являются наиболее распространенными патогенами, которые вызывают респираторные болезни свиней на свиноводческих комплексах. На протяжении последних лет российские биофабрики разрабатывают программы импортозамещения необходимых иммунобиологических лекарственных препаратов. По итогам 2023 г. отечественные предприятия выпустили 19,3 млрд доз вакцин для ветеринарного применения, что на 3 млрд доз больше по сравнению с 2022 г.

Заключение. Вакцинация является наиболее эффективным и экономичным способом профилактики вирусных инфекций. Однако отечественные иммунологические лекарственные препараты против гриппа свиней еще не разработаны в нашей стране, а вакцины против энзоотической (микоплазменной) пневмонии, репродуктивно-респираторного синдрома, цирковирусной инфекции свиней требуют доработки в связи с высокой изменчивостью возбудителей.

Ключевые слова: обзор, вакцины, импортозамещение, свиноводство, респираторные болезни свиней, национальная безопасность

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INTRODUCTION

According to the Food Security Doctrine approved by the President of the Russian Federation in 2010, the food security of the Russian Federation is a state of the economy that ensures the country's food independence and guarantees physical and economic availability of food products compliant with the legislative requirements of the Russian Federation.

Pork, along with poultry meat, is the most affordable type of meat for the population and the key raw material for the meat processing industry, whereas pig farming, as a fast-growing branch of animal husbandry, is capable of prompt achieving a significant increase in production of pork, characterized by high nutritional properties and biological value [1]. According to the National Union of Pig Breeders, the total volume of industrial pork production in 2023 amounted to 5,627.2 thousand tons of live weight, which is 352.1 thousand tons more than in 2022, and in the past decade this value has been annually increasing by at least 3–4%.

In the current economic environment, reduction of the Russian pig industry dependence on the imports is of particular importance. The predominance of foreign-made technological equipment, feed additives and veterinary drugs in the domestic market may make the industry dependent on the international situation. Therefore, an increase in the level of technical equipment of facilities, modernization of manufacturing equipment, domestic manufacture of feed and veterinary drugs should be considered as the most essential for improving the industry's effectiveness and sustainable development [2].

The subprogram "Development of technologies for the production of veterinary medicinal products" will be one of the priorities of the "Federal Research and Technology Program for Agriculture Development in 2017–2030", approved by Decree of the Government of the Russian Federation of 25 August 2017 No. 996. The comprehensive research plan of the subprogram includes, *inter alia*, development of scientific foundations for the production of new domestic vaccines for the prevention of porcine infectious diseases, thus contributing to animal health protection, as well as animal livability and improvement of their performance for the purpose of import substitution.

One of the acute problems of pig farming that slow down the pork production growth rate are respiratory diseases of viral and bacterial etiology, such as swine influenza, porcine enzootic (mycoplasmal) pneumonia, porcine reproductive and respiratory syndrome (PRRS), and porcine circovirus infection, which cause significant economic damage to pig farms in the Russian Federation [3].

The purpose of the study is to analyze the availability of domestic vaccines against viral and bacterial respiratory diseases of pigs in the Russian Federation, as well as to identify factors that hinder the development of immunobiological drugs against these diseases.

MATERIALS AND METHODS

The information base of the research included data from pig-breeding organizations of the Russian Federation, the Rosselkhoznadzor's state register of veterinary medicinal products, reference and special literature, publications of research institutions. The range of vaccines was

analyzed basing on the data from domestic biofactories and manufacturers of diagnostic, preventive and therapeutic products against infectious animal diseases.

RESULTS AND DISCUSSION

Over the past few years, Russian biofactories and specialized research institutions have been developing programs targeted at the substitution of the imports of the relevant and promising immunobiological medicinal products. Guided by the goal of achieving technological sovereignty of the Russian Federation, the key players are filling scarcity niches and investing in the development of new medicinal products.

According to the National Veterinary Association (NVA), which includes such leading manufacturers of veterinary pharmaceutical and immunological products as VIC Group of Companies, AVZ, NITA-FARM, Apicenna, Vetbiochem LLC, Avivac, etc., in 2023, the total veterinary medicinal product market in Russia amounted to 97.7 billion rubles, VAT included. A significant contribution to the growth was made by domestic manufacturers – NVA members, who collectively increased production by more than 25% in 2023. By the end of the year, domestic establishments produced 19.3 billion doses of vaccines for veterinary use, which is 3 billion doses more than in 2022. Positive dynamics is also observed in the extension of the product range by the domestic establishments: in 2023, about 100 new medicinal products were developed and authorized, which is 70% more than in 2022.

Porcine respiratory disease complex (PRDC) is a serious challenge for pig farming as it causes devastating economic losses due to lower growth rates of young animals, increased mortality and high cost of treatment. PRDC is a multifactorial disease, the development of which depends on the combination of infectious pathogens, exposure to environmental stressors and defects in the animal breeding system [4]. The diseases included in this complex, together with swine influenza, are present in all major countries – global pork manufacturers, and *Mycoplasma hyopneumoniae*, PRRS virus and porcine circovirus type 2 (PCV-2) triad are the most common pathogens causing PRDC in Asian countries. These etiological agents suppress the host's immune system and amplify the replication of each other and other pathogens. This results in the weakening of the animal population, high mortality of young animals, degradation of the boar semen performance, as well as additional costs associated with diagnostic, quarantine and therapeutic measures.

Swine influenza is an acute respiratory disease of pigs caused by type A influenza virus belonging to the family *Orthomyxoviridae*. The disease is accompanied by high morbidity (up to 100%) and low mortality (10–15%). Fever, apathy, anorexia, serous nasal discharge and upper respiratory tract lesions are typical for it [5, 6].

The swine influenza transmission patterns vary between and within the countries due to such factors as climate, pig population and farming methods. The main vehicles of the virus transmission are airborne and contact ones, as well as with personnel and care products. Humans and pigs have the same set of receptors in the respiratory cells, so interspecific transmission of influenza A viruses occurs in both directions. Introduction of effective measures for influenza control and prevention will, therefore, help to maintain the health of not only pigs, but also humans [7].

Upon contact with the respiratory mucous membrane, which is, as a rule, the portal of the infection entry, the influenza virus starts its replication thus leading to the necrosis of the affected tracheal and bronchial cells, impaired blood circulation, damage to the vascular system and further, in complex cases, to hemorrhages on the skin and mucous membranes as well as hemorrhages in internal organs.

Currently, at least three different subtypes of influenza A virus (H1N1, H1N2 and H3N2) are jointly circulating all over the world, *inter alia* in the Russian Federation. Herewith, pigs can act as a "mixing vessel" in which influenza viruses of various origins can reassort (including with avian and human influenza pathogens), creating new progeny viruses capable of replicating and spreading in humans [7].

Vaccination is the main tool for swine influenza control. However, despite the large number of vaccines, the disease still cannot be effectively controlled, as the pathogen strains are very diverse and prone to mutations. Therefore, development of the vaccines capable of providing broad heterologous protection against antigenically diverse virus strains is crucial for the effective disease control [8, 9, 10].

The majority of globally used modern vaccines against swine influenza contain inactivated whole viruses with an adjuvant for intramuscular injection and are used either in sows for protection during pregnancy and in piglets during suckling, or in repair young animals to make their clinical signs milder. These products are targeted at the induction of the serum antibodies that neutralize the influenza virus on the respiratory mucous membranes. In the foreign countries, the inactivated vaccines are manufactured locally and contain various antigenic and genetic virus strains circulating in the relevant region, which is indicative of high evolutionary capacities of the virus [7]. For example, about half of the vaccines used in the United States are customized and herd-specific. One of the solutions to this problem could be an approach to constructing vaccines involving cocktail of numerous immunologically promising amino acid sequences of various strains of swine influenza virus [11].

Only foreign immunological medicinal products for swine influenza prevention are currently listed in the Rosselkhoznadzor's register of the veterinary medicinal products. All vaccines are inactivated and contain type A swine influenza virus of subtypes H1N1 and H3N2 (Italy, Spain) and subtypes H1N1, H1N2 and H3N2 (Germany), Table 1. Thus, despite a fairly wide range of products available on the Russian market, it is necessary to develop a domestic inactivated vaccine against swine influenza comprising those virus strains that circulate in the Russian Federation.

Porcine enzootic (mycoplasmal) pneumonia is a chronic infectious disease caused by the bacterium *Mycoplasma hyopneumoniae*, which is accompanied by cough, catarrhal bronchopneumonia and a decrease in such performance parameters such as survival rate, average daily weight gain, feed conversion rate [12]. The infection is mainly spread via airborne route, indirect transmission and infection through contact with wild boars are also possible [13].

The disease pathogenesis is very complex and has not been fully examined. The agent attaches to the ciliated epithelium of the trachea, bronchi, and bronchioles, causing damage to the mucosal mucociliary clearance system (ciliostasis), which interferes with the normal functioning of the cilia, leads to a delayed and ineffective immune

response, and contributes to a higher susceptibility of animals to other respiratory infections [14].

Mycoplasma hyopneumoniae is able to enhance replication of PRRS virus and PCV-2, increasing severity of pneumonia in pigs. Practicing pig breeders most often use vaccination rather than antibiotic treatment and prefer combined vaccines to effectively control the entire range of porcine respiratory diseases. Immunization against *M. hyopneumoniae* is usually carried out at the age of 21 days. If the pathogen is detected in swabs from the larynx of suckling piglets, vaccination can be carried out at 7 days of age to avoid *M. hyopneumoniae* transmission in weaning piglets and to control enzootic pneumonia during fattening on the farms [15, 16]. As for breeding sows, in some herds pigs are immunized against *M. hyopneumoniae* during the quarantine, before they are delivered to the breeding sow premises. Such practice allows to avoid immunity upset in breeding population by reducing the bacterial load and severity of clinical signs in vaccinated pigs in *M. hyopneumoniae*-positive herds [17].

The majority of the commercially available bacterin vaccines are adjuvanted whole-cell preparations of the inactivated cultured *M. hyopneumoniae* [18]. For the prevention of porcine enzootic pneumonia, a domestic VERRES-M.hyo (Vetbiochem LLC, Moscow) inactivated vaccine has been enlisted in the Rosselkhoznadzor register of veterinary medicinal products, as well as a number of foreign-made vaccines that can be used in the disease-affected breeding and commercial pig holdings (Table 2).

The main advantages of the vaccination involve an increase in the daily weight gain of piglets (2–8%) and feed conversion rate (2–5%), as well as a reduction in animal mortality. Moreover, the period of reaching the slaughter weight is shortened, the clinical signs of lung lesions and their treatment costs are reduced [19]. However, the disadvantage of these vaccines is that protection against the onset of *M. hyopneumoniae*-caused clinical signs and lesions is often incomplete, and vaccination leads to only a slight decrease in the transmission rate. There is, therefore, a need to develop new vaccines capable of providing more efficient protection. New vaccines are currently being actively tested, including aerosol and feed-based vaccines, as well as subunit and DNA vaccines. Feed-based vaccines or aerosol vaccines could significantly facilitate the operational procedure of the mass immunization of pigs, and would also create immunity at the infection entrance gate, i.e. in the respiratory tract. However, as a result of the experiments, it was found that even triple aerosol immunization was less effective than intramuscular administration, so this method still needs to be improved [12, 14, 19].

Porcine reproductive and respiratory syndrome (PRRS) is a quarantinable contagious viral disease that is manifested in reproductive dysfunction in sows and boars and severe pneumonia in newborn piglets and weaned piglets during fattening.

The PRRS etiological agent is an RNA-genome arterivirus (genus *Betaarterivirus*, family *Arteriviridae*) capable of replication in the pig macrophages, thus resulting in the increased animal susceptibility to primary and secondary infections, decreased animal growth as well as morbidity and mortality development and increase [20].

The virus transmission can be both horizontal and vertical. The infection mostly occurs through the contact with the diseased animals, as well as through vehicles, clothing and footwear of the personnel, through blood-sucking insects and birds. In addition, the infection is possible through boar semen, where the pathogen remains active for up to 2 weeks. The virus can cross the placental barrier in the second half of pregnancy and infect the fetus, and the surviving piglets become the virus carriers. There is also some evidence of the infectious agent airborne (aerosol) transmission [21].

Table 1
Register of main vaccines against swine influenza registered in the Russian Federation

Vaccine	Vaccine type	Influenza virus strain used	Manufacturer
Bayovac® Influ	inactivated	X53a (H1N1), MRC 11 (H3N2)	Fatro S.p.A., Italy
GRIPORK	inactivated	A(H1N1)OLL, A(H3N2)GHA	Laboratorios Hipra, S.A., Spain
Respiporc FLU 3	inactivated	Haselünne/IDT2617/2003 (H1N1), Bakum/1832/2000 (H1N2), Bakum/IDTI769/2003 (H3N2)	IDT Biologika GmbH, Germany

Table 2
Register of main vaccines against porcine enzootic (mycoplasmal) pneumonia registered in the Russian Federation

Vaccine	Vaccine type	Influenza virus strain	Manufacturer
VERRES-M.hyo	inactivated	*Mycoplasma hyopneumoniae*	Vetbiochem LLC, Russia
Ingelvac MycoFLEX®	inactivated	*Mycoplasma hyopneumoniae* (strain J)	Boehringer Ingelheim Vetmedica GmbH, Germany
Porcilis® M Hyo ID Once	inactivated	*Mycoplasma hyopneumoniae* (strain 11)	Intervet International B.V., Netherlands
Suvaccin MN-One	inactivated	*Mycoplasma hyopneumoniae* (strain P-5722-3)	Zoetis Inc., USA
Hyogen	inactivated	*Mycoplasma hyopneumoniae* (strain 2940)	Ceva Sante Animale, Hungary

The disease economic damage involves losses due to reproductive dysfunction of sows (abortions, stillbirth, death of 80–100% of newborn piglets) and the cost of diagnostic and quarantine measures, especially during acute and massive outbreaks, when 1–3% of adult breeding stock may die [22, 23, 24, 25].

Vaccination is the main tool for PRRS prevention, however, genetic studies demonstrated that the virus genome has one of the highest mutation rates among the RNA viruses, which contributes to its extensive antigenic and genetic variability [26]. There are at least three subtypes of the PRRS type 1 virus, differentiated based on ORF-5 gene analysis [27]. The reported genetic diversity of the field virus isolates is the main obstacle to the disease control [28].

A number of both domestic and foreign manufactured vaccines have been currently authorized in the Russian Federation, which can be subdivided into two large groups: live attenuated vaccines and inactivated vaccines. The range of the key Russian vaccines against PRRS is presented in Table 3.

Table 3
Register of main vaccines against porcine reproductive and respiratory syndrome registered in the Russian Federation

Vaccine	Vaccine type	PRRS virus strain used	Manufacturer
VERRES-PRRS	inactivated	domestic author's strain OB	Vetbiochem LLC, Russia
ARRIAH-PRRS inact	inactivated	production strain KPR-96, European genotype	Federal Centre for Animal Health, Russia
ARRIAH-RePovac	inactivated combined	production strain KPR-96, European genotype	Federal Centre for Animal Health, Russia
ARRIAH-Aujeszky+PRRS	inactivated combined	production strain KPR-96, European genotype	Federal Centre for Animal Health, Russia
Resvac	live dry	strain PRRS-1SBC, genotype 1	Shchelkovo biocombinat, Russia

Taking into account both safety aspects and wide variety of PRRS virus strains, the inactivated vaccines are preferable to attenuated ones, but despite these advantages, they are not effective enough. The inactivated products induce a lower immune response than the attenuated live ones, since the vaccine virus strains do not replicate in the vaccinated animals. The inactivated vaccines are not recommended to be used for immunization of seronegative animals. Vaccination of seropositive animals (due to natural infection or immunization with live vaccines) with inactivated products, nevertheless, causes a pronounced secondary humoral and cellular immune response, which allows them to be used in combined vaccination programs [29].

The effectiveness of the attenuated live vaccines is due to the fact that they ensure the development of not only humoral, but also cellular immune response against the PRRS virus. However, live vaccines have significant disadvantages. The protective immune response caused by the attenuated PRRS vaccines depends on the genetic diversity of the field virus strains circulating in a given region. The greatest effect of immunization is assumed to be achieved when the vaccine virus is antigenically similar to the field one. Moreover, there are serious concerns about the safety of the attenuated vaccines, since viremia develops after immunization of pigs with live products and a vaccine virus is shed during a few weeks, which can be directly or indirectly transmitted to the unvaccinated susceptible animals [30].

Circovirus infection in pigs is a viral disease, mainly of weaning piglets [31]. The causative agent is PCV-2, which belongs to the *Circovirus* genus of the *Circoviridae* family, which includes small single-stranded non-enveloped DNA viruses with an unsegmented circular genome [32]. The mechanisms of PCV-2 recognition, attachment and penetration into the body are currently not fully understood. The virus is believed to use a relatively common cellular receptor, since the virus replication and PCV-2 antigen were reported in many different cell types [33]. After entering the host's body and completing the 2–4-week incubation period, PCV-2 replicates in the lymph nodes, infects B cells and spreads throughout the body through the lymphatic system. Viremia in pigs is detected between days 7 and 14 after the virus inoculation. PCV-2 is capable of causing long-term infection and the viral DNA is detected in pigs for up to 125 days after experimental infection [34].

Porcine circovirus type 2 can be transmitted by several routes. The main route is with infected excretions (including urine, saliva, semen) or through the direct contact with the infected pigs. The virus can also be transmitted placentally, although this transmission route is less frequent [35, 36]. Experiments in piglets also demonstrated that some slaughter products (lymphoid tissue, skeletal muscles, and bone marrow) can be a source of infection in pigs and, when fed to experimental animals for 3 days they can lead to viremia and seroconversion in all animals [37, 38].

The causative agent of circovirus infection in pigs is widespread in many countries of the world with developed industrial pig breeding and it causes significant economic damage due to high morbidity and mortality, decreased performance and reproductive capacities of the animals [38].

There are currently four types of porcine circoviruses globally identified: PCV-1, PCV-2, PCV-3 and PCV-4 [39]. PCV-2 plays an important role in the pathologies of piglets of 6–16 weeks of age. It causes damage to various systems, but the disease clinical signs develop only in young animals with compromised immune system. When replicating in the cells of the piglets' immune system, PCV-2 causes immunodeficiency disorders, which increase the susceptibility to other infectious agents, reduce the immune response to vaccination, and result in the animal death [40].

Specific prevention of circovirus infection is successfully carried out with inactivated and recombinant subunit vaccines, which significantly reduce the piglets' morbidity and mortality during finishing and fattening [38].

The viral subunit vaccine is formulated with the components of the main viral immunogen by means of genetic engineering. The commercial subunit vaccines against porcine circovirus infection have been developed and manufactured primarily based on the expression of the recombinant capsid protein ORF-2 in the baculovirus expression system.

To prepare an inactivated vaccine, the PCV-2-infected cells are inactivated by a physical or chemical method, as a result of which the virus loses its infectious capacities, but at the same time retains its immunogenicity [40]. To date, several domestic vaccines against circovirus infection have been registered and certified in Russia, which contain the recombinant capsid protein ORF-2 of porcine circovirus type 2 (Table 4).

The technology of manufacturing vaccines against porcine circovirus infection is constantly being updated due to high frequency of mutations in the HCV-2 genome and emergence of new virus subtypes. Currently, nine PCV-2 genotypes are known (from PCV-2a to PCV-2i). Circovirus genotypes 2a, 2b, and 2d are widespread worldwide, while other genotypes are detected sporadically [41]. The emergence of new virus genotypes leads to ineffective vaccination, which dramatically increases the spread of circovirus infection outbreaks. To date, PCV-2d is the most common and dominant genotype, it has a higher virulence, causes more serious clinical signs and pathological lesions as compared to classical genotypes 2a and 2b. The majority of

the commercially available vaccines against porcine circovirus infection are based on capsid proteins of PCV-2a and PCV-2b viruses and they are often ineffective against PCV-2d. In this regard, there is a need to develop new effective vaccines to protect against the most clinically significant PCV-2 genotypes [42].

CONCLUSION

Porcine respiratory diseases are a serious problem causing devastating economic losses in the pig industry due to decreased animal growth rate, as well as increased livestock mortality and cost of treatment. Among the multiple etiological agents such pathogens as *Mycoplasma hyopneumoniae*, porcine reproductive and respiratory syndrome virus and porcine circovirus type 2 remain the most prevalent PRDC-causing ones in the Russian Federation. Swine influenza also causes great economic damage to production, being at the same time a potentially dangerous agent for humans.

Vaccination is one of the most efficient and cost-effective means to prevent the viral infections. However, domestic immunological medicinal products against swine influenza have not yet been developed, and vaccines against enzootic (mycoplasmal) pneumonia, porcine reproductive and respiratory syndrome, and porcine circovirus infection require further development due to high variability of the pathogens, which hinders the development of a universal vaccine product.

In the current economic conditions, it is of particular importance to reduce the use of foreign immunobiological drugs and to accelerate domestic vaccine production in order to achieve technological sovereignty of the Russian Federation. In this regard, manufacturers of veterinary medicinal products are actively developing new vaccines and improving existing ones, and they are working to expand the collection of pathogens that can later become the basis for the development of new medicinal products. However, the full cycle of the development of a single vaccine takes from three to five years, and the domestic manufacturers cannot fully cover the needs of the industry so far.

Government support provided to the manufacturers of the veterinary medicinal products as regards to the accelerated registration of the medicinal products contributes to the introduction of new capital-intensive projects, and creation of new production facilities will allow for the significant increase in the volume of the manufactured products in the coming years.

Table 4
Register of main vaccines against porcine circovirus infection registered in the Russian Federation

Vaccine	Vaccine type	PCV-2 strain used	Manufacturer
VERRES-CIRCO	recombinant	recombinant viral capsid protein ORF-2	Vetbiochem LLC, Russia
ReCircoVac	recombinant	recombinant viral capsid protein ORF-2 (PCV2b)	Armavir Biofactory, Russia
Circostop	inactivated	strain PCV2/SHBC	Shchelkovo biocombinat, Russia

REFERENCES

1. VanderWaal K., Deen J. Global trends in infectious diseases of swine. *Proceedings of the National Academy of Sciences*. 2018; 115 (45): 11495–11500. https://doi.org/10.1073/pnas.1806068115

2. Tikhomirov A. I. The state of pig breeding technological and product import substitution in Russia. *Bulletin of Altai State Agricultural University.* 2015; (1): 159–165. https://elibrary.ru/tbdcxv (in Russ.)

3. Polishchuk S. V., Belyavtseva E. A. Diagnosis enzootic pneumonia pigs at farm "Veles-Crimea". *Transactions of Taurida Agricultural Science*. 2015; (1): 164–171. https://elibrary.ru/wfdujf (in Russ.)

4. Chae C. Porcine respiratory disease complex: Interaction of vaccination and porcine circovirus type 2, porcine reproductive and respiratory syndrome virus, and *Mycoplasma hyopneumoniae*. *The Veterinary Journal*. 2016; 212: 1–6. https://doi.org/10.1016/j.tvjl.2015.10.030

5. Rajao D. S., Anderson T. K., Gauger P. C., Vincent A. L. Pathogenesis and vaccination of influenza A virus in swine. *In: Influenza Pathogenesis and Control – Vol. I. Eds. R. Compans, M. Oldstone. Current Topics in Microbiology and Immunology.* Springer; 2014; 385: 307–326. https://doi.org/10.1007/82_2014_391

6. Chauhan R. P., Gordon M. L. A systematic review analyzing the prevalence and circulation of influenza viruses in swine population worldwide. *Pathogens.* 2020; 9 (5):355. https://doi.org/10.3390/pathogens9050355

7. Mancera Gracia J. C., Pearce D. S., Masic A., Balasch M. Influenza A virus in swine: epidemiology, challenges and vaccination strategies. *Frontiers in Veterinary Science*. 2020; 7:647. https://doi.org/10.3389/fvets.2020.00647

8. Ma W. Swine influenza virus: Current status and challenge. *Virus Research.* 2020; 288:198118. https://doi.org/10.1016/j.virusres.2020.198118

9. Sandbulte M. R., Spickler A. R., Zaabel P. K., Roth J. A. Optimal use of vaccines for control of influenza A virus in swine. *Vaccines*. 2015; 3 (1): 22–73. https://doi.org/10.3390/vaccines3010022

10. Pliasas V. C., Neasham P. J., Naskou M. C., Neto R., Strate P. G., North J. F., et al. Heterologous prime-boost H1N1 vaccination exacerbates disease following challenge with a mismatched H1N2 influenza virus in the swine model. *Frontiers in Immunology*. 2023; 14:1253626. https://doi.org/10.3389/fimmu.2023.1253626

11. Bullard B. L., Corder B. N., DeBeauchamp J., Rubrum A., Korber B., Webby R. J., Weaver E. A. Epigraph hemagglutinin vaccine induces broad cross-reactive immunity against swine H3 influenza virus. *Nature Communications*. 2021; 12:1203. https://doi.org/10.1038/s41467-021-21508-6

12. Raev S. A., Aliper T. I. Diagnosis and prevention enzootic pneumonia pigs. *Veterinariya*. 2014; (10): 15–21. https://elibrary.ru/sxsylf (in Russ.)

13. Ovsukhno T. V., Terentiev S. S., Yashin I. V., Blokhin A. A. *Mycoplasma hyopneumoniae* infection in pigs. *Pigbreeding*. 2023; (5): 44–49. https://doi.org/10.37925/0039-713X-2023-5-44-49 (in Russ.)

14. Maes D., Boyen F., Devriendt B., Kuhnert P., Summerfield A., Haesebrouck F. Perspectives for improvement of *Mycoplasma hyopneumoniae* vaccines in pigs. *Veterinary Research*. 2021; 52:67. https://doi.org/10.1186/s13567-021-00941-x

15. Yang S., Oh T., Mago J., Iwakuma A., Chae C. Optimal vaccination strategy against *Mycoplasma hyopneumoniae*,

porcine reproductive and respiratory syndrome virus, and porcine circovirus type 2 in case of early *M. hyopneumoniae* infection. *Veterinary Medicine and Science*. 2020; 6 (4): 860–874. https://doi.org/10.1002/vms3.284

16. Tassis P. D., Tsakmakidis I., Papatsiros V. G., Koulialis D., Nell T., Brellou G., Tzika E. D. A randomized controlled study on the efficacy of a novel combination vaccine against enzootic pneumonia (*Mycoplasma hyopneumoniae*) and porcine Circovirus type 2 (PCV2) in the presence of strong maternally derived PCV2 immunity in pigs. *BMC Veterinary Research*. 2017; 13:91. https://doi.org/10.1186/s12917-017-1014-7

17. Arsenakis I., Michiels A., Schagemann G., Gomez-Duran C. O., Boyen F., Haesebrouck F., et al. Effects of pre-farrowing sow vaccination against *Mycoplasma hyopneumoniae* on offspring colonisation and lung lesions. *Veterinary Research*. 2019; 184 (7):222. https://doi.org/10.1136/vr.104972

18. Michiels A., Arsenakis I., Boyen F., Krejci R., Haesebrouck F., Maes D. Efficacy of one dose vaccination against experimental infection with two *Mycoplasma hyopneumoniae* strains. *BMC Veterinary Research*. 2017; 13:274. https://doi.org/10.1186/s12917-017-1195-0

19. Maes D., Segales J., Meyns T., Sibila M., Pieters M., Haesebrouck F. Control of *Mycoplasma hyopneumoniae* infections in pigs. *Veterinary Microbiology*. 2008; 126 (4): 297–309. https://doi.org/10.1016/j.vetmic.2007.09.008

20. Niederwerder M. C., Jaing C. J., Thissen J. B., Cino-Ozuna A. G., McLoughlin K. S., Rowland R. R. R. Microbiome associations in pigs with the best and worst clinical outcomes following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2). *Veterinary Microbiology*. 2016; 188: 1–11. https://doi.org/10.1016/j.vetmic.2016.03.008

21. Arruda A. G., Tousignant S., Sanhueza J., Vilalta C., Poljak Z., Torremorell M., et al. Aerosol detection and transmission of porcine reproductive and respiratory syndrome virus (PRRSV): What is the evidence, and what are the knowledge gaps? *Viruses*. 2019; 11 (8):712. https://doi.org/10.3390/v11080712

22. Renken C., Nathues C., Swam H., Fiebig K., Weiss C., Eddicks M., et al. Application of an economic calculator to determine the cost of porcine reproductive and respiratory syndrome at farm-level in 21 pig herds in Germany. *Porcine Health Management*. 2021; 7:3. https://doi.org/10.1186/s40813-020-00183-x

23. Calderón Díaz J. A., Fitzgerald R. M., Shalloo L., Rodrigues da Costa M., Niemi J., Leonard F. C., et al. Financial analysis of herd status and vaccination practices for porcine reproductive and respiratory syndrome virus, swine influenza virus, and *Mycoplasma hyopneumoniae* in farrow-to-finish pig farms using a bio-economic simulation model. *Frontiers in Veterinary Science*. 2020; 7:556674. https://doi.org/10.3389/fvets.2020.556674

24. Boeters M., Garcia-Morante B., van Schaik G., Segalés J., Rushton J., Steeneveld W. The economic impact of endemic respiratory disease in pigs and related interventions – a systematic review. *Porcine Health Management*. 2023; 9:45. https://doi.org/10.1186/s40813-023-00342-w

25. Ruedas-Torres I., Rodríguez-Gómez I. M., Sánchez-Carvajal J. M., Larenas-Muñoz F., Pallarés F. J., Carrasco L., Gómez-Laguna J. The jigsaw of PRRSV virulence. *Veterinary Microbiology*. 2021; 260:109168. https://doi.org/10.1016/j.vetmic.2021.109168

26. Renukaradhya G. J., Meng X.-J., Calvert J. G., Roof M., Lager K. M. Inactivated and subunit vaccines against porcine reproductive and respiratory syndrome: Current status and future direction. *Vaccine*. 2015; 33 (27): 3065–3072. https://doi.org/10.1016/j.vaccine.2015.04.102

27. Stadejek T., Stankevicius A., Murtaugh M. P., Oleksiewicz M. B. Molecular evolution of PRRSV in Europe: Current state of play. *Veterinary Microbiology*. 2013; 165 (1–2): 21–28. https://doi.org/10.1016/j.vetmic.2013.02.029

28. Huang Y. W., Meng X. J. Novel strategies and approaches to develop the next generation of vaccines against porcine reproductive and respiratory syndrome virus (PRRSV). *Virus Research*. 2010; 154 (1–2): 141–149. https://doi.org/10.1016/j.virusres.2010.07.020

29. Mateu E., Prieto C. Tipy dostupnykh vaktsin protiv reproduktivno-respiratornogo sindroma svinei i ozhidaemye rezul'taty ikh primeneniya = Types of available vaccines against porcine reproductive and respiratory syndrome and expected results of their use. *Effectivnoe zhivotnovodstvo*. 2022; (1): 24–25. https://elibrary.ru/ufidwc (in Russ.)

30. Glazunova A. A., Korogodina E. V., Sevskikh T. A., Krasnova E. A., Kukushkin S. A., Blokhin A. A. Reproductive and respiratory syndrome of pigs in pig breeding enterprises (review). *Agricultural Science Euro-North-East*. 2022; 23 (5): 600–610. https://doi.org/10.30766/2072-9081.2022.23.5.600-610 (in Russ.)

31. Ouyang T., Zhang X., Liu X., Ren L. Co-infection of swine with porcine circovirus type 2 and other swine viruses. *Viruses*. 2019; 11 (2):185. https://doi.org/10.3390/v11020185

32. Gillespie J., Opriessnig T., Meng X. J., Pelzer K., Buechner-Maxwell V. Porcine circovirus type 2 and porcine circovirus-associated disease. *Journal of Veterinary Internal Medicine*. 2009; 23 (6): 1151–1163. https://doi.org/10.1111/j.1939-1676.2009.0389.x

33. Darwich L., Segalés J., Mateu E. Pathogenesis of postweaning multisystemic wasting syndrome caused by *Porcine circovirus* 2: An immune riddle. *Archives of Virology*. 2004; 149 (5): 857–874. https://doi.org/10.1007/s00705-003-0280-9

34. Pogranichnyy R. M., Yoon K.-J., Harms P. A., Swenson S. L., Zimmerman J. J., Sorden S. D. Characterization of immune response of young pigs to porcine circovirus type 2 infection. *Viral Immunology*. 2000; 13 (2): 143–153. https://doi.org/10.1089/vim.2000.13.143

35. Allan G. M., Kennedy S., McNeilly F., Foster J. C., Ellis J. A., Krakowka S. J., et al. Experimental reproduction of severe wasting disease by coinfection of pigs with porcine circovirus and porcine parvovirus. *Journal of Comparative Pathology*. 1999; 121 (1): 1–11. https://doi.org/10.1053/jcpa.1998.0295

36. Park J.-S., Kim J., Ha Y., Jung K., Choi C., Lim J.-K., et al. Birth abnormalities in pregnant sows infected intranasally with porcine circovirus 2. *Journal of Comparative Pathology*. 2005; 132 (2–3): 139–144. https://doi.org/10.1016/j.jcpa.2004.09.003

37. Opriessnig T., Patterson A. R., Meng X.-J., Halbur P. G. Porcine circovirus type 2 in muscle and bone marrow is infectious and transmissible to naive pigs by oral consumption. *Veterinary Microbiology*. 2009; 133 (1–2): 54–64. https://doi.org/10.1016/j.vetmic.2008.06.018

38. Green S. A., Matveeva I. N., Bogomolova O. A., Fedorov Yu. N., Popova V. M., Kryukova E. N., Litenkova I. Yu. Assessment of PCV2 circulation among pigs of

different ages and antigenic activity of a vaccine against this infection. *Veterinariya*. 2019; (12): 20–26. https://doi.org/10.30896/0042-4846.2019.22.12.20-26 (in Russ.)

39. Fehér E., Jakab F., Bányai K. Mechanisms of circovirus immunosuppression and pathogenesis with a focus on porcine circovirus 2: a review. *Veterinary Quarterly*. 2023; 43 (1): 1–18. https://doi.org/10.1080/01652176.2023.2234430

40. Guo J., Hou L., Zhou J., Wang D., Cui Y., Feng X., Liu J. Porcine circovirus type 2 vaccines: commercial application and research advances. *Viruses*. 2022; 14 (9):2005. https://doi.org/10.3390/v14092005

41. Pleguezuelos P., Sibila M., Cuadrado-Matías R., López-Jiménez R., Pérez D., Huerta E., et al. Efficacy studies of a trivalent vaccine containing PCV-2a, PCV-2b genotypes and *Mycoplasma hyopneumoniae* when administered at 3 days of age and 3 weeks later against porcine circovirus 2 (PCV-2) infection. *Vaccines*. 2022; 10 (8):1234. https://doi.org/10.3390/vaccines10081234

42. Lim J., Jin M., Yoon I., Yoo H. S. Efficacy of bivalent vaccines of porcine circovirus type 2 and *Mycoplasma hyopneumoniae* in specific pathogen-free pigs challenged with porcine circovirus type 2d. *Journal of Veterinary Science*. 2022; 23 (3):e49. https://doi.org/10.4142/jvs.21287

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