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Global Trends in Veterinary Vaccine Development for Emerging Pathogens

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Abstract The development of veterinary vaccines for emerging pathogens is a critical area of research that addresses both animal and public health concerns. This study explores global trends in veterinary vaccine development, focusing on innovative technologies and methodologies that have emerged in recent years. Traditional vaccines, while effective, have limitations such as variable efficacy and adverse effects. Recent advancements in nanotechnology, mRNA vaccines, and viral vector platforms offer promising alternatives to overcome these challenges. Nanovaccines, for instance, utilize nanoparticles to enhance antigen delivery and immune response, providing a novel approach to combat persistent and rapidly evolving pathogens. The "One Health" approach emphasizes the interconnectedness of human and animal health, advocating for cross-species vaccination strategies to control zoonotic diseases. Additionally, the integration of socio-economic data into vaccine development can improve resource allocation and disease management, drawing lessons from human vaccinology. This study highlights the importance of continuous innovation and interdisciplinary collaboration in developing effective veterinary vaccines to safeguard both animal and human health.

Keywords Veterinary vaccines; Emerging pathogens; Nanotechnology; mRNA vaccines; One Health

1 Introduction

Emerging pathogens pose significant threats to both human and animal health, often originating from wildlife and spreading through zoonotic transmission. Notable examples include Ebola, Marburg hemorrhagic fevers, Lassa fever, Dengue fever, Yellow fever, West Nile fever, Zika, and Chikungunya, which have had profound impacts on global health and economies (Trovato et al., 2020). The emergence and re-emergence of these pathogens are often driven by factors such as climate change, socioeconomic shifts, and increased human-animal interactions, which facilitate the spread of viruses to new geographical areas (Marchi et al., 2018). In veterinary medicine, the emergence of numerous animal viruses has highlighted the necessity for effective disease control measures, including the development of vaccines (Allam et al., 2023).

Vaccination remains one of the most effective tools for preventing infectious diseases, significantly reducing morbidity and mortality rates (Trovato et al., 2020). The rapid development of vaccines, as demonstrated during the COVID-19 pandemic, underscores the critical role of vaccines in managing disease outbreaks and curtailing epidemic spread (Warimwe et al., 2021). Traditional vaccine technologies, while successful in many cases, face limitations when dealing with rapidly evolving pathogens, complex viral antigens, and emerging diseases (Gebre et al., 2021). Therefore, novel vaccine technologies, such as nucleic acid and viral vector vaccines, are being explored to address these challenges and improve vaccine efficacy and production speed (Brisse et al., 2020; Gebre et al., 2021). In veterinary medicine, the development of vaccines is crucial for controlling diseases that affect both animals and humans, thereby protecting public health and ensuring food security (Vrba et al., 2020; Allam et al., 2023).

This study aims to provide a comprehensive overview of global trends in veterinary vaccine development for emerging pathogens. This study examines the current state of vaccine development for emerging and re-emerging pathogens in veterinary medicine, identifies the challenges and hurdles in developing effective vaccines for these pathogens, explores novel vaccine technologies and their potential applications in veterinary medicine, and

highlights the importance of a One Health approach in accelerating vaccine development for shared health threats between humans and animals. Additionally, this study provides insights into future directions and priorities for research and development in veterinary vaccinology. By addressing these objectives, this study seeks to contribute to the ongoing efforts to develop effective vaccines that can mitigate the impact of emerging pathogens on global health.

2 Overview of Emerging Pathogens

2.1 Definition and characteristics of emerging pathogens

Emerging pathogens are microorganisms, such as viruses, bacteria, fungi, or parasites, that have recently increased in incidence or geographic range, or have the potential to do so. These pathogens often arise due to changes in the environment, human behavior, or pathogen evolution. They can cause new or previously unrecognized diseases and are often characterized by their ability to infect multiple species, including humans and animals, leading to zoonotic diseases (Trovato et al., 2020; Tse et al., 2020; Warimwe et al., 2021).

2.2 Examples of notable emerging pathogens in animals

Several emerging pathogens have been identified in animals, posing significant threats to both animal and public health. Notable examples include:

Coronaviruses: Emerging coronaviruses such as SARS-CoV, MERS-CoV, and SARS-CoV-2 have caused significant outbreaks in humans and animals. These viruses are known for their ability to jump species barriers, leading to zoonotic transmission (Trovato et al., 2020; Tse et al., 2020).

Newcastle Disease Virus (NDV): This virus affects poultry and has significant economic impacts, particularly in regions like Sub-Saharan Africa. The development of adenovirus-vectored vaccines is a promising approach to control NDV outbreaks (Farnós et al., 2020).

Rabies Virus: Although rabies is a well-known disease, it remains a significant emerging threat in certain regions due to its high mortality rate and the challenges in controlling its spread among wildlife and domestic animals (Le et al., 2022).

Zika Virus: Initially identified in monkeys, Zika virus has emerged as a significant pathogen affecting both humans and animals, with severe implications for public health (Le et al., 2022).

2.3 Impact on animal health and public health

Emerging pathogens have profound impacts on both animal and public health. In animals, these pathogens can lead to severe diseases, reduced productivity, and economic losses. For instance, outbreaks of diseases like Newcastle Disease in poultry can devastate local economies and food security (Farnós et al., 2020; Shuja et al., 2022).

From a public health perspective, zoonotic pathogens pose a significant risk as they can be transmitted from animals to humans, leading to outbreaks and pandemics. The COVID-19 pandemic is a stark reminder of the potential impact of zoonotic diseases on global health. More than 70% of emerging infectious diseases in humans are zoonotic, highlighting the critical need for a One Health approach that integrates human, animal, and environmental health to effectively manage these threats (Trovato et al., 2020; Tse et al., 2020; Warimwe et al., 2021).

In conclusion, the emergence of new pathogens necessitates continuous monitoring, research, and the development of innovative vaccines and therapeutic strategies to mitigate their impact on both animal and public health. The integration of advanced technologies, such as mRNA vaccines and nanovaccines, holds promise for addressing these challenges and improving global health outcomes (Celis-Giraldo et al., 2021; Gebre et al., 2021; Le et al., 2022).

3 Current Trends in Veterinary Vaccine Development

3.1 Traditional vaccine approaches

Traditional veterinary vaccines, such as inactivated and live-attenuated vaccines, have been instrumental in controlling numerous viral diseases in livestock and poultry. These vaccines have significantly contributed to livestock productivity, food security, and the reduction of morbidity and mortality associated with various zoonotic diseases (Aida et al., 2021; Fawzy et al., 2021). However, traditional vaccines often require high doses and multiple immunizations to achieve effective immune responses, as seen with inactivated influenza vaccines for H5N1 (Nicolodi et al., 2019). Additionally, live-attenuated vaccines, while effective, pose safety concerns due to the potential for reversion to virulence (Damme et al., 2019).

3.2 Advances in vaccine technologies

Recent advancements in vaccine technologies have led to the development of third-generation vaccines, including DNA, RNA, and recombinant viral-vector vaccines. These novel vaccines offer several advantages over traditional approaches, such as the ability to induce both humoral and cellular immune responses, economic manufacturing, and enhanced safety profiles (Figure 1) (Brisse et al., 2020; Aida et al., 2021). For instance, nanoparticle-based vaccines have emerged as a promising platform, providing improved antigen presentation and the potential for rapid deployment in response to emerging infectious diseases (Fawzy et al., 2021; Files et al., 2022). Additionally, chimeric hemagglutinin-based vaccines have shown the potential to induce broad and long-lasting immunity against influenza viruses, suggesting their utility in developing universal vaccines (Bernstein et al., 2019; Nachbagauer et al., 2020).

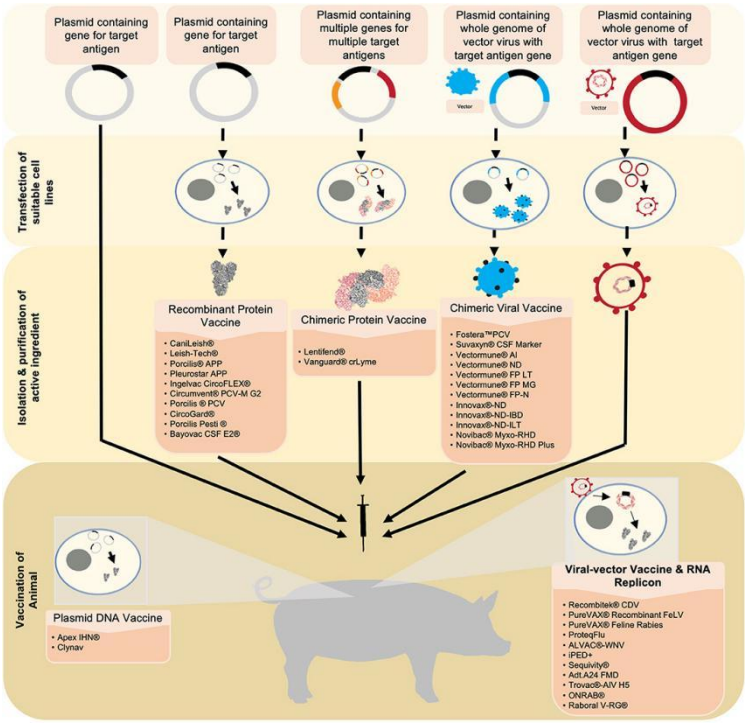

Figure 1 Overview of six novel vaccine technologies (Adapted from Aida et al., 2021)

Image caption: A simplified summary of six innovative vaccine technologies, from antigen generation to vaccination. Plasmid-DNA vaccines start with inserting the target antigen gene into a plasmid, which, upon vaccination, translates into the desired protein within the recipient's cells, eliciting an immune response. Recombinant and chimeric protein vaccines also use transfected cell lines to express antigens, which are then purified and formulated into vaccines. Chimeric viral vaccines employ plasmids containing the whole virus genome and target antigen gene to produce viruses expressing these antigens. Viral vector vaccines use engineered viruses to deliver genes into host cells, where they are transcribed into target antigens. RNA replicon vaccines utilize RNA segments encoding antigens within vesicle carriers, leading to direct antigen translation in host cells and triggering an immune response (Adapted from Aida et al., 2021)

3.3 Role of biotechnology in vaccine development

Biotechnology plays a crucial role in the advancement of veterinary vaccine development. Techniques such as genetic engineering and rational vaccine design have enabled the creation of vaccines that are more effective and safer than traditional methods. For example, live attenuated vaccines that lack specific viral proteins, such as the NS1 protein in H5N1 influenza vaccines, have demonstrated significant immunogenicity and safety in clinical trials (Nicolodi et al., 2019). Furthermore, the use of viral-like particles and nanoparticle-based platforms has revolutionized the field, offering innovative solutions to address the challenges of vaccine development for both viral and bacterial pathogens (Brisse et al., 2020; Files et al., 2022). These biotechnological advancements not only enhance our understanding of vaccine immunology but also pave the way for the development of vaccines against rapidly emerging infectious diseases and other health threats.

In summary, the field of veterinary vaccine development is witnessing significant progress through the integration of traditional approaches with cutting-edge technologies and biotechnological innovations. These advancements hold promise for more effective and safer vaccines, capable of addressing the evolving landscape of emerging pathogens.

4 Challenges in Developing Vaccines for Emerging Pathogens

4.1 Scientific and technical challenges

Developing vaccines for emerging pathogens presents numerous scientific and technical challenges. One significant issue is the high variability and rapid evolution of pathogens, which can lead to persistent infections and reduce vaccine efficacy (Celis-Giraldo et al., 2021; Gebre et al., 2021). Traditional vaccine technologies, such as inactivated and live-attenuated vaccines, often fall short in addressing these challenges due to their inherent limitations, including variable efficacy and safety concerns (Aida et al., 2021).

Moreover, the development of vaccines for Risk Group 3 (RG-3) and Risk Group 4 (RG-4) pathogens, which include many zoonotic diseases, requires high and maximum biocontainment facilities. These facilities are essential for safely handling and studying highly infectious agents, but they also add complexity and cost to the vaccine development process (Brake et al., 2021).

Emerging technologies, such as nanovaccines and viral vector vaccines, offer promising solutions by providing more effective antigen delivery and immunostimulatory properties. These technologies can potentially overcome some of the limitations of traditional vaccines, but they also require significant research and development to ensure their safety and efficacy (Brisse et al., 2020; Celis-Giraldo et al., 2021; Gebre et al., 2021).

4.2 Regulatory and approval processes

The regulatory and approval processes for veterinary vaccines are stringent and complex, often requiring extensive data to meet the licencing requirements of global regulatory bodies (Francis, 2022). This process can be particularly challenging for novel vaccine platforms, which may not fit neatly into existing regulatory frameworks. The rapid development and approval of COVID-19 vaccines have highlighted the potential for accelerated regulatory pathways, but these are not yet standard practice for veterinary vaccines (Excler et al., 2021; Francis, 2022).

Additionally, the development of vaccines for emerging pathogens often involves navigating different regulatory environments across countries, which can further complicate the approval process. Harmonizing these regulations and creating more flexible frameworks could facilitate the faster development and deployment of vaccines for emerging threats (Excler et al., 2021; Francis, 2022).

4.3 Economic and market considerations

Economic and market considerations play a crucial role in the development of veterinary vaccines. The cost of developing and manufacturing vaccines, particularly for emerging pathogens, can be prohibitively high. This is

especially true for vaccines requiring high biocontainment facilities and advanced technologies (Farnós et al., 2020; Brake et al., 2021).

Moreover, the market for veterinary vaccines is influenced by various factors, including the economic burden of the targeted disease, the feasibility of large-scale vaccine production, and the socio-economic context in which the vaccines will be used (Thomas et al., 2019). In low- and middle-income countries, where the burden of zoonotic diseases is often highest, the financial feasibility of vaccine development and deployment can be a significant barrier (Farnós et al., 2020; Excler et al., 2021).

Public-private partnerships and investment in novel vaccine technologies can help address some of these economic challenges. By leveraging advances in human vaccine development and integrating socio-economic data into the decision-making process, the veterinary vaccine industry can improve resource allocation and enhance the impact of vaccination programs (Thomas et al., 2019; Aida et al., 2021; Brake et al., 2021).

5 Case Studies of Successful Veterinary Vaccines

5.1 Case study 1: vaccine for a specific emerging pathogen

One notable example of a successful veterinary vaccine is the development of a vaccine for the COVID-19 virus in animals. The rapid development and deployment of COVID-19 vaccines for humans provided a framework that was adapted for veterinary use. The COVID-19 pandemic response leveraged innovations in vaccine technology, such as mRNA vaccines, which were quickly adapted to create effective vaccines for animals susceptible to the virus. This case highlights the importance of cross-species vaccination approaches and the potential for rapid vaccine development using advanced technologies (Figure 2) (Excler et al., 2021; Warimwe et al., 2021; Francis, 2022).

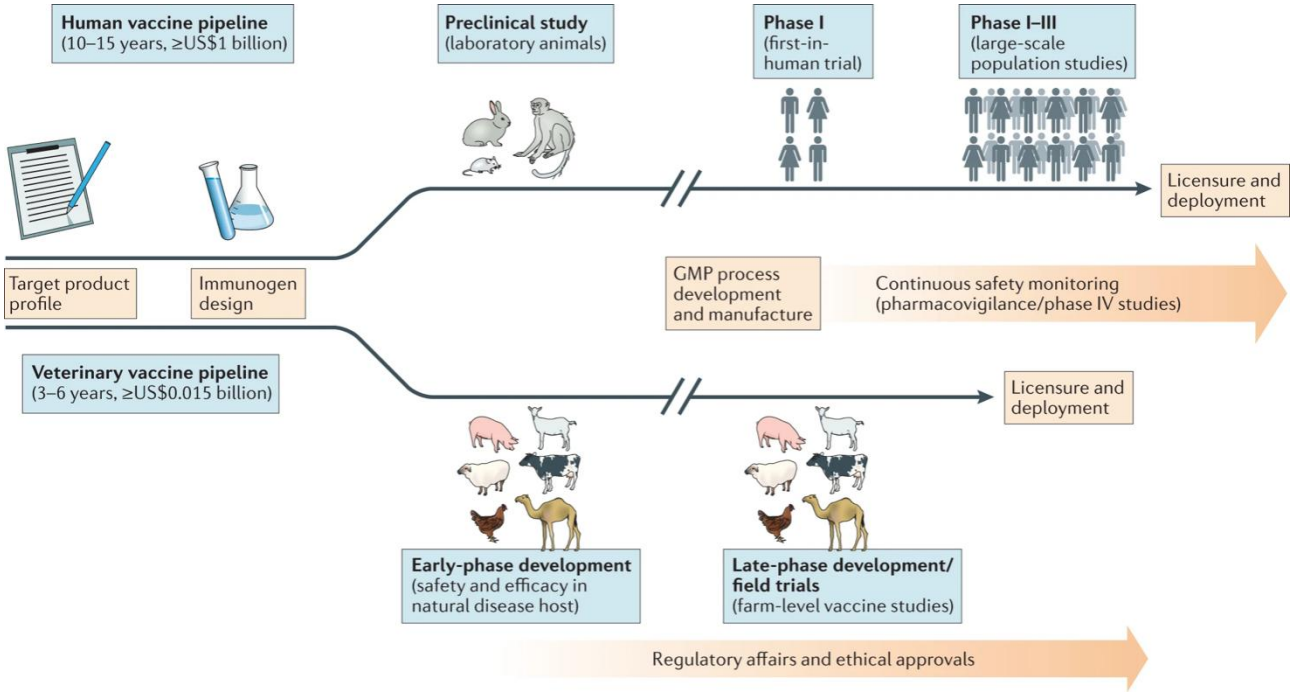

Figure 2 Vaccine development pipeline (Adopted from Warimwe et al., 2021)

Image caption: The typical vaccine development pipeline, beginning with target product profiling and culminating in licensure and deployment. It outlines the stages and estimated costs for both veterinary and human vaccines. While the process is depicted linearly, certain stages for a 'multispecies' vaccine may proceed concurrently. For example, the ChAdOx1 RVF vaccine for Rift Valley fever is set to be evaluated in human clinical trials simultaneously with veterinary development, utilizing the same initial manufacturing material. GMP stands for good manufacturing practice (Adapted from Warimwe et al., 2021)

Warimwe et al. (2021) highlight that the development pipelines for human and veterinary vaccines share structural similarities, starting with target product profiling and immunogen design, followed by preclinical studies. Human vaccines undergo extensive phase I-III trials, while veterinary vaccines are tested for safety and efficacy in natural disease hosts and later in field trials. Despite differing regulatory requirements and clinical data needs, common challenges like optimizing immunogenicity are addressed similarly in both pipelines. Human vaccine development is notably more time-consuming and costly compared to veterinary vaccines. The figure also highlights that certain stages, such as the development of the ChAdOx1 RVF vaccine, can be conducted in parallel for both human and veterinary applications, using the same manufacturing starting material.

5.2 Case study 2: overcoming development challenges

The development of vaccines for rapidly evolving pathogens, such as the African Swine Fever (ASF) virus, presents significant challenges. Traditional vaccine technologies often fall short due to the high variability and complexity of such pathogens. However, novel approaches, including the use of nanoparticle-based vaccines, have shown promise in overcoming these hurdles. Nanovaccines, which utilize self-assembling proteins, virus-like particles, and other nanomaterials, offer enhanced efficacy and safety. These technologies have been pivotal in developing vaccines that can adapt to the rapid evolution of pathogens, ensuring timely and effective responses to outbreaks (Aida et al., 2021; Celis-Giraldo et al., 2021; Gebre et al., 2021).

5.3 Lessons learned from case studies

Several key lessons can be drawn from these case studies:

Rapid Adaptation of Human Vaccine Technologies: The swift adaptation of human vaccine technologies, such as mRNA vaccines, for veterinary use underscores the importance of a One Health approach. This strategy facilitates the sharing of knowledge and resources across human and veterinary medicine, accelerating the development of effective vaccines for emerging pathogens (Excler et al., 2021; Warimwe et al., 2021; Francis, 2022).

Innovative Vaccine Platforms: The use of novel vaccine platforms, including nanoparticle-based vaccines, has proven essential in addressing the limitations of traditional vaccines. These platforms offer greater flexibility and efficacy, particularly for pathogens with high genetic variability and complex antigens (Aida et al., 2021; Celis-Giraldo et al., 2021; Gebre et al., 2021).

Regulatory and Manufacturing Considerations: The success of rapid vaccine development also hinges on understanding and navigating regulatory requirements. Streamlined processes and clear guidelines from regulatory bodies can significantly expedite the development and licensure of new vaccines, ensuring timely responses to emerging threats (Thomas et al., 2019; Francis, 2022).

Economic and Social Data Integration: Incorporating economic and social data into the vaccine development process can enhance decision-making and resource allocation. This approach, already common in human vaccinology, can provide valuable insights for prioritizing and implementing veterinary vaccines, ultimately improving animal health outcomes (Thomas et al., 2019).

By learning from these case studies, the veterinary field can continue to advance vaccine development, ensuring preparedness for future emerging pathogens and safeguarding both animal and human health.

6 Global Collaboration and Initiatives

6.1 International partnerships and networks

International partnerships and networks play a crucial role in the development and distribution of veterinary vaccines for emerging pathogens. The Developing Countries Vaccine Manufacturers Network (DCVMN) has been instrumental in fostering international cooperation, bringing together vaccine manufacturing experts and leaders from both local and global public health organizations. These collaborations have facilitated the sharing of best practices, quality control measures, and the development of harmonized standards, which are essential for

accelerating vaccine access globally (Pagliusi et al., 2019). Additionally, the Coalition for Epidemic Preparedness Innovations (CEPI) and the International Vaccine Institute (IVI) have reported on new strategies to ensure rapid progress in the development of innovative vaccines for emerging diseases such as MERS and Zika (Pagliusi et al., 2018).

The COVID-19 pandemic has further highlighted the importance of international partnerships. The Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership, spearheaded by the U.S. National Institutes of Health (NIH), exemplifies how collaboration among industry, government, and academia can accelerate vaccine development and distribution Corey (Corey et al., 2020). Similarly, nearly one-third of COVID-19 vaccine candidates were developed through partnerships, emphasizing the critical role of collaborative efforts in leveraging next-generation vaccine platforms (Druedahl et al., 2021).

6.2 Role of government and non-governmental organizations

Governments and non-governmental organizations (NGOs) have been pivotal in supporting vaccine development initiatives. The UK Government, for instance, established the UK Vaccine Network to address emerging disease threats and streamline the vaccine development process. This initiative led to the creation of a Veterinary Vaccine Development Process Map, which outlines the steps from target product profile generation to product development and registration, thereby identifying potential bottlenecks and facilitating a rapid response to pandemics (Francis, 2020).

Organizations such as Gavi, the Vaccine Alliance, have also contributed significantly by improving the supply base from manufacturers in developing countries and enhancing global vaccine access and immunization coverage (Pagliusi et al., 2018). The World Health Organization (WHO) has been actively involved in regulatory convergence initiatives, such as the WHO Collaborative Registration Procedure, which aims to accelerate vaccine registration and access in developing countries (Pagliusi et al., 2019).

6.3 Global funding and support programs

Global funding and support programs are essential for sustaining vaccine development efforts. The success of the US government-led operation to accelerate COVID-19 vaccine development underscores the importance of substantial financial investment and the mobilization of public and private sector resources (Bok et al., 2021). Funding mechanisms have been crucial in supporting the rapid development and deployment of vaccines, as seen with the adenovirus-vectored vaccine technology platform proposed for controlling Newcastle Disease Virus infections in Sub-Saharan Africa (Farnós et al., 2020).

Moreover, the integration of economic and social data into vaccine development processes can enhance resource allocation and disease management. By learning from human vaccinology, the veterinary field can better utilize socio-economic data to prioritize vaccine development and implementation, ultimately improving the effectiveness and reach of vaccination programs (Thomas et al., 2019).

In conclusion, global collaboration, the active involvement of governments and NGOs, and robust funding mechanisms are vital components in the development and distribution of veterinary vaccines for emerging pathogens. These efforts ensure that vaccines are developed efficiently, distributed equitably, and accessible to all regions, thereby enhancing global health security.

7 Future Directions in Veterinary Vaccine Development

7.1 Emerging technologies and innovations

The landscape of veterinary vaccine development is rapidly evolving with the advent of new technologies and innovative approaches. Nanotechnology, for instance, is playing a pivotal role in the creation of nanovaccines, which utilize nanoparticles such as self-assembling proteins, virus-like particles, liposomes, virosomes, and polymeric nanoparticles. These nanovaccines offer enhanced antigen delivery and immunostimulatory properties,

making them highly effective against a range of animal pathogens (Celis-Giraldo et al., 2021). Additionally, the development of DNA, RNA, and recombinant viral-vector vaccines has shown promise in inducing both humoral and cellular immune responses, which are crucial for effective immunization (Aida et al., 2021). These third-generation vaccines are not only safe and economically viable but also allow for the differentiation between infected and vaccinated animals, a feature that is particularly useful in managing disease outbreaks (Aida et al., 2021).

7.2 Potential for personalized veterinary vaccines

The concept of personalized veterinary vaccines is gaining traction, driven by advances in omics technologies and vaccinomics. These approaches enable the characterization of host-vector-pathogen molecular interactions and the identification of candidate protective antigens (Fuente and Contreras, 2021). By leveraging these insights, it is possible to develop vaccines tailored to the specific immunological needs of individual animals or groups of animals, thereby enhancing vaccine efficacy and safety (Fuente and Contreras, 2021). This personalized approach could be particularly beneficial in managing diseases that exhibit high variability or in animals with compromised immune systems (Brisse et al., 2020).

7.3 Strategies for rapid response to emerging pathogens

The rapid development and deployment of vaccines are critical in responding to emerging pathogens. The COVID-19 pandemic has underscored the importance of having robust systems in place for the swift creation and distribution of vaccines. Lessons learned from the pandemic highlight the potential of platform technologies, such as mRNA vaccines, which can be rapidly adapted to new pathogens (Gershwin and Woolums, 2020). Additionally, the integration of molecular techniques in virology has facilitated the development of replicating, attenuated, and non-replicating virus vector vaccines, which can be quickly mobilized in response to emerging viral threats (Afrough et al., 2019). Regulatory frameworks also play a crucial role in this context, as streamlined processes for emergency use authorization and licensure can significantly expedite vaccine availability.

In summary, the future of veterinary vaccine development lies in the adoption of emerging technologies, the potential for personalized vaccines, and the implementation of rapid response strategies. These advancements will not only enhance the efficacy and safety of vaccines but also ensure timely intervention in the face of emerging infectious diseases.

8 Concluding Remarks

The development of veterinary vaccines for emerging pathogens has seen significant advancements in recent years, driven by the urgent need to control outbreaks and improve animal health. Traditional vaccine technologies, while effective for many pathogens, face limitations when dealing with persistent infections, rapidly evolving pathogens, and complex viral antigens. Novel approaches such as nucleic acid vaccines, viral vector vaccines, and nanotechnology-based vaccines have shown promise in overcoming these challenges. The integration of omics technologies and the concept of vaccinomics have further enhanced our understanding of host-pathogen interactions, leading to the identification of new vaccine candidates and improved vaccine efficacy. The COVID-19 pandemic has underscored the importance of rapid vaccine development and the potential of new vaccine technologies to address emerging infectious diseases.

Continued research and development in veterinary vaccine technologies are crucial for several reasons. First, the increasing global demand for food and the rise of intensive farming practices have led to more frequent outbreaks of zoonotic diseases, necessitating the development of new and more effective vaccines. Second, the rapid evolution of pathogens and the emergence of antibiotic-resistant bacteria require innovative approaches to vaccine development to ensure global health security. Third, the shared experiences and technologies between human and veterinary medicine, as highlighted by the One Health approach, can accelerate progress in both fields and lead to more effective vaccines for both humans and animals. Finally, the ongoing advancements in nanotechnology, viral

vectors, and nucleic acid vaccines hold great potential for creating vaccines that are not only effective but also safe and easy to produce and distribute.

For researchers and developers, it is essential to continue exploring and integrating novel vaccine technologies, such as nanoparticle-based vaccines, viral vectors, and nucleic acid vaccines, to address the limitations of traditional vaccines. Collaboration between human and veterinary medicine should be encouraged to leverage the One Health approach, which can lead to more comprehensive and effective vaccine solutions. Policymakers and funding agencies should prioritize investment in vaccine research and development, particularly for emerging and re-emerging pathogens, to ensure preparedness for future outbreaks. Additionally, efforts should be made to improve vaccine accessibility and distribution, especially in low- and middle-income countries, to achieve global health equity. Finally, continuous monitoring and evaluation of vaccine safety and efficacy are necessary to maintain public trust and ensure the long-term success of vaccination programs.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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