DIVA STRATEGY IN ANIMAL DISEASE CONTROL AND ERADICATION: A REVIEW

Nirali Khunt[1]*, Kathiriya J B[1], Barad D B[2], Patel S S[2], Niranchaana S[2], Babariya H B[2]

[1]*Department of Veterinary Microbiology, College of Veterinary Science & Animal Husbandry, Kamdhenu University, Junagadh,[2]Department of Veterinary Microbiology, College of Veterinary Science & Animal Husbandry, Kamdhenu University, Junagadh

Corresponding author: khuntnirali6@gmail.com*

Abstract

Conventional vaccines are important for controlling infectious diseases in livestock but have a major limitation, they cannot differentiate between animals that are vaccinated and those that are naturally infected. This diagnostic gap complicates disease monitoring, slows down eradication programs, and disrupts international trade. To address this challenge, the concept of DIVA (Differentiating Infected from Vaccinated Animals), also referred to as marker vaccination, was introduced by Van Oirschot in 1999. DIVA vaccines are specially designed either by removing certain antigens (negative markers) or by adding foreign antigens (positive markers), creating a unique immunological signature in vaccinated animals that can be distinguished from the immune response in naturally infected animals. When used in combination with specific companion diagnostic tests such as ELISA, this strategy enables clear identification of infected animals within vaccinated populations. This review describes the fundamental principles, types, and mechanisms of DIVA vaccines including deletion mutants, subunit vaccines, live attenuated, inactivated, recombinant, and DNA/vector based platforms and their applications in controlling major diseases such as Pseudorabies, Foot and Mouth Disease, Infectious Bovine Rhinotracheitis, Classical Swine Fever, Avian Influenza, Lumpy Skin Disease, Brucellosis, and Rabies. The review also highlights the benefits of DIVA in supporting disease control and trade facilitation, discusses current limitations, and outlines future prospects for advancing this strategy in global veterinary medicine.

Keywords: DIVA strategy, marker vaccines, companion diagnostic tests, ELISA, veterinary vaccinology

INTRODUCTION

Infectious diseases in livestock continue to pose significant challenges to global food security, animal health, and agricultural economies. These diseases reduce productivity through decreased growth, milk yield, and fertility, while imposing substantial economic burdens due to treatment costs, trade restrictions, and control measures. A particularly critical group known as transboundary animal diseases (TADs) can spread rapidly across national borders, causing devastating outbreaks affecting entire livestock populations and disrupting international trade. Important TADs include foot and mouth disease (FMD), peste des petits ruminants (PPR), and classical swine fever (CSF), each requiring well-coordinated control strategies beyond conventional approaches. Vaccination is the most effective and economical tool for preventing and controlling infectious diseases in animals. However, conventional vaccines whether live attenuated or inactivated induce immune responses that closely resemble those generated during natural infection. As a result, standard serological tests cannot distinguish vaccinated animals from naturally infected ones (Van Oirschot, 1999), creating a major barrier for disease surveillance, trade certification, and eradication programs. To

overcome this fundamental limitation, the concept of Differentiating Infected from Vaccinated Animals (DIVA), also referred to as marker vaccination, was formally introduced by J.T. Van Oirschot of the Central Veterinary Institute, Netherlands, in 1999. The DIVA strategy uses specially designed marker vaccines combined with companion diagnostic tests to create a clear, exploitable immunological difference between vaccinated and infected animals. This integration of vaccination and precise diagnostics represents a major advancement in veterinary disease control, enabling continuous surveillance even during active vaccination campaigns (Pasick, 2004). In today's era of intensified global trade, climate change influenced disease dynamics, and growing societal concerns about mass culling of healthy animals, DIVA based strategies have become increasingly critical for achieving sustainable, scientifically robust disease control and eradication.

2. THE DIVA CONCEPT: PRINCIPLES AND IMMUNOLOGICAL BASIS

The DIVA principle relies on engineering a clear immunological distinction between the vaccine and the natural infection. Although vaccinated animals are protected by marker vaccines, their immune response differs fundamentally from that of naturally infected animals. This distinction is achieved either by removing a specific antigen from the vaccine (negative marker) or by incorporating a foreign antigen absent from the natural pathogen (positive marker) (Clavijo *et al.,* 2004; Van Oirschot, 1999). The selected marker antigen is typically a non-protective, non-essential protein whose replacement or deletion does not affect vaccine efficacy. Animals in a vaccinated population remain seronegative for the marker protein but develop antibodies against all shared antigens. In contrast, naturally infected animals develop antibodies against all pathogen proteins, including the marker antigen. A highly specific companion diagnostic test usually a marker-specific ELISA detects this binary antibody response (Paton *et al.,* 2006). A DIVA strategy is not just a vaccine but a complete system. It has two important parts that must work together: (i) a marker vaccine, which is specially designed to produce a unique immune response, and (ii) a companion diagnostic test, which helps detect or differentiate infected animals from vaccinated ones. If either of these components is missing, the DIVA approach cannot work properly. In addition, the diagnostic test must be highly accurate, with good sensitivity and specificity, because any error may result in missing infected animals or wrongly culling healthy ones (Uttenthal *et al.,* 2010).

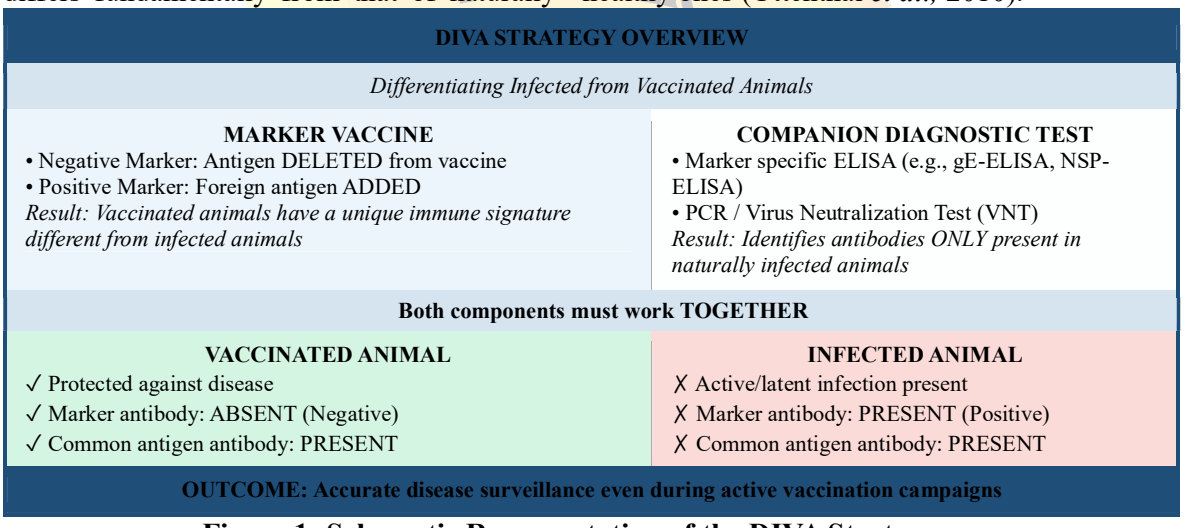

Figure 1: Schematic Representation of the DIVA Strategy

3. TYPES OF DIVA VACCINES

3.1 Negative Marker Vaccines (Gene Deletion Vaccines)

Negative marker vaccines represent the most extensively developed and field validated DIVA vaccine category. In this approach, genes encoding immunologically accessible but non protective antigens are precisely deleted from the pathogen genome using recombinant DNA technology. Vaccinated animals seroconvert against all retained antigens while remaining seronegative for the deleted marker protein (Van Oirschot, 1999). The classical example is the gE (glycoprotein E)-deleted vaccine for Bovine Herpesvirus 1 (BoHV-1), causative agent of Infectious Bovine Rhinotracheitis (IBR). Since the gE protein is immunogenic but dispensable for protective immunity, its deletion creates a clear serological window exploited by a paired gE-ELISA. Similarly, gE-deleted marker vaccines were pivotal in eradicating Pseudorabies Virus (PRV) from domestic pig populations across Europe and North America (Kaashoek *et al.,* 1998; Van Oirschot, 2001).

3.2 Positive Marker Vaccines

Positive marker vaccines incorporate a heterologous antigen absent from the wild type pathogen directly into the vaccine construct. This foreign protein acts as a unique serological tag: animals encountering only the field virus lack antibodies to the introduced marker, while vaccinated animals carry them exclusively (Van Oirschot, 1999). Although conceptually elegant, positive marker vaccines have seen limited commercial uptake, partly because the immune response to the marker antigen can sometimes interfere with responses to protective antigens. Experimental applications include recombinant poxvirus and adenovirus vectored vaccines encoding reporter antigens (Clavijo *et al.,* 2004).

3.3 Subunit Marker Vaccines

Subunit marker vaccines present only defined, purified protective antigens, naturally excluding non-structural and accessory proteins produced during active viral replication. Since these excluded proteins are generated during natural infection but absent in the vaccine, detection of antibodies directed against them forms the basis for DIVA differentiation (Paton *et al.,* 2006). The FMD purified inactivated vaccine is the archetype: highly purified vaccines contain exclusively viral capsid proteins, while non-structural proteins (NSPs) such as the 3ABC polyprotein are rigorously removed. Animals recovering from natural infection invariably develop anti NSP antibodies, while properly vaccinated animals do not (Clavijo *et al.,* 2004; Lubroth and Brown, 1996). E2 subunit vaccines for Classical Swine Fever (CSF) follow analogous logic, with the companion E-rns-ELISA distinguishing vaccinated from infected animals (Moormann *et al.,* 2000).

3.4 Live Attenuated Marker Vaccines

When combined with gene deletion, live attenuated vaccines become a powerful DIVA platform, retaining the immunological potency of replication competent strains inducing robust humoral and cellular immunity while carrying a defined molecular deletion that enables serological differentiation. The gE-deleted attenuated BoHV-1 and PRV vaccines exemplify this category and have demonstrated outstanding field performance in national eradication campaigns (Kaashoek *et al.,* 1998).

3.5 Inactivated Marker Vaccines

Inactivated marker vaccines combine the high safety profile of killed preparations with engineered antigen exclusion. Because inactivated organisms cannot replicate, no post vaccination amplification of non-structural proteins occurs, underpinning the FMD inactivated DIVA platform. Their main limitations include the need for adjuvantation, multiple booster doses, and rigorous cold chain compliance. They are the preferred choice for disease-free zones and for susceptible animal groups where live vaccines are contraindicated (Van Oirschot, 2001; WOAH, 2021).

3.6 Recombinant and Vector Based Marker Vaccines

Advances in molecular biology have enabled the design of recombinant marker vaccines in which selected protective antigens are expressed within heterologous viral or bacterial vectors, offering precise control over antigen composition. The recombinant Vaccinia-Rabies Glycoprotein (V-RG) vaccine for oral wildlife rabies control is the most prominent field deployed example: it expresses only the rabies surface glycoprotein G while completely lacking the nucleoprotein N present in wild type virus, enabling DIVA discrimination by N-ELISA (Maki *et al.,* 2017). DNA vaccine platforms, encoding only selected antigens, similarly offer inherent DIVA properties through restricted antigen expression profiles, though most remain in preclinical or early evaluation phases (Blome *et al.,* 2020; Li *et al.,* 2023).

4. MECHANISMS OF ACTION IN SPECIFIC DIVA SYSTEMS

4.1 Gene Deletion Strategy (Pseudorabies / IBR Model)

The deletion mutant approach exploits the fact that many enveloped herpesviruses encode glycoproteins that, while highly immunogenic, are dispensable for viral replication and for eliciting neutralizing immunity. For PRV, gE-deficient strains were demonstrated to be avirulent yet immunologically competent. Animals vaccinated with gE-deleted vaccines produce gE-negative serological profiles detectable by commercially validated gE-ELISAs, while naturally exposed animals uniformly develop gE antibodies (Van Oirschot *et al.,* 1990). This clean binary output simplified herd classification and enabled systematic test and removal programs.

4.2 Non Structural Protein Differentiation (FMD Model)

During productive FMD virus replication, the genomic polyprotein is processed to yield not only structural capsid proteins but also non structural enzymes including the 3ABC precursor polyprotein. Animals recovering from natural infection invariably develop antibodies against 3ABC, while animals vaccinated with sufficiently pure vaccines do not. The 3ABC ELISA exploits this immunological distinction, with vaccine purity being the critical quality control parameter. Even residual NSP contamination from inadequate purification can yield false positive ELISA results in vaccinated animals, undermining the surveillance framework (Paton *et al.,* 2006; Uttenthal *et al.,* 2010; EFSA, 2022).

4.3 Heterologous Neuraminidase Strategy (Avian Influenza)

For Avian Influenza (AI), the DIVA mechanism operates at the level of the neuraminidase (NA) surface glycoprotein. Vaccine strains are engineered to share the same hemagglutinin (HA) type as the circulating field virus while carrying a different NA subtype. For example, an H5N2 vaccine used against an H5N1 outbreak ensures that all vaccinated birds develop anti-H5 antibodies, but only naturally infected birds acquire anti-N1 antibodies. Detection of N1-specific antibodies in a vaccinated flock thus serves as a reliable indicator of field virus circulation (Capua and Marangon, 2003; Suarez, 2005).

5. DIAGNOSTIC TESTS IN THE DIVA FRAMEWORK

The companion diagnostic test is the operational core of any DIVA program. Multiple test formats have been developed and validated for different diseases:

- Marker specific ELISAs (e.g., gE-ELISA for IBR/PRV, NSP-ELISA for FMD, E-rns-ELISA for CSF, NA-ELISA for AI) offer high throughput, quantitative results, and suitability for large scale population screening. They are internationally recognized by WOAH and incorporated into official disease control protocols.
- Virus Neutralization Tests (VNT) measure functional antibody activity against the pathogen and are used as confirmatory assays in reference

laboratory settings when marker specific ELISA results require verification (Van Oirschot, 1999).

- Molecular diagnostics, including conventional and real time quantitative PCR, detect pathogen nucleic acids in clinical samples and serve a complementary role during the pre seroconversion window after infection, when antibody based DIVA tests may yield false negative results (Pasick, 2004; WOAH, 2021).
- Next Generation Sequencing (NGS) is increasingly being explored to support DIVA surveillance by enabling full genome characterization of field strains and ensuring that marker antigens remain conserved and diagnostic integrity is maintained (Li *et al.,* 2023).

6. APPLICATIONS IN DISEASE ERADICATION PROGRAMS

6.1 Pseudorabies (Aujeszky's Disease)

The eradication of PRV from commercial pig industries in the United States and multiple European Union member states during the 1990s and early 2000s remains the definitive benchmark for DIVA strategy efficacy (Mettenleiter *et al.,* 1985; Pasick, 2004). Regulatory authorities mandated exclusive use of gE deleted vaccines, and the highly sensitive gE-ELISA enabled consistent identification of gE-seropositive animals within vaccinated populations. Countries including Germany, the Netherlands, Belgium, Denmark, and the United States achieved official PRV free status through this approach (Muller *et al.,* 2003; Stegeman *et al.,* 1994).

6.2 Infectious Bovine Rhinotracheitis (IBR)

IBR eradication programs across Austria, Scandinavia, and several other European nations have employed gE-deleted BoHV-1 marker vaccines in conjunction with gE-ELISA surveillance. Austria and Finland achieved IBR free status by mandating marker vaccines followed by systematic elimination of all gE seropositive cattle. The gE-ELISA proved sufficiently robust to support both on farm herd certification and national eradication programs (Ackermann and Engels, 2006; Nuotio *et al.,* 2007).

6.3 Foot and Mouth Disease (FMD)

FMD control through DIVA vaccination is arguably the most economically consequential application of the marker vaccine paradigm globally. Highly purified inactivated FMD vaccines paired with 3ABC NSP ELISAs allow endemic countries to maintain vaccination coverage while demonstrating freedom from active viral circulation. The ability to achieve WOAH recognized 'FMD Free with Vaccination' status has enormous trade implications for major livestock exporting economies (Bergevoet and Van Asseldonk, 2009; Paton *et al.,* 2006; Paton and Reeve, 2022; EFSA, 2022). A persistent challenge is the carrier state in cattle, where the virus may persist in the pharynx for months despite vaccination. Recent work has focused on improving NSP-ELISA sensitivity for carrier detection and enhancing vaccine purity standards (Paton and Reeve, 2022).

6.4 Classical Swine Fever (CSF)

E2 subunit vaccines for CSF, commercially available for decades in Europe and Asia, are paired with E-rns-ELISA to distinguish vaccinated from field infected animals. Implementation has supported CSF eradication campaigns in several EU member states. Recent developments in CSF DIVA marker vaccination have included improved live attenuated deletion mutants that combine faster onset of immunity with reliable DIVA discrimination, addressing a key limitation of early E2 subunit vaccines (Beer *et al.,* 2007; Blome *et al.,* 2017; Moormann *et al.,* 2000; Blome *et al.,* 2020).

6.5 Avian Influenza (AI)

The heterologous neuraminidase DIVA strategy for AI has been most extensively applied in Italy during H7N1 outbreaks (1999-2000) and in Southeast Asia and China for various H5 subtypes. Vaccination with heterologous NA vaccines significantly reduced clinical disease and

mortality while allowing surveillance systems to detect field virus circulation through NA-ELISA monitoring of sentinel flocks. This approach enabled targeted depopulation only of infected flocks, avoiding the catastrophic economic impact of blanket stamping-out policies (Capua *et al.,* 2003; Suarez, 2005).

6.6 Lumpy Skin Disease (LSD)

A DIVA compatible vaccine for Lumpy Skin Disease, BIOLUMPIVAXIN, based on a live attenuated LSDV strain Ranchi/2019, has been developed through collaboration between Biovet (a Bharat Biotech subsidiary), ICAR-NRCE, and IVRI. This vaccine enables differentiation between vaccinated cattle and buffaloes and those naturally infected with field strains, strengthening the surveillance and eradication framework for this economically important disease in the Indian subcontinent (Kumar *et al.,* 2025). Recent studies have confirmed its field performance and safety profile (Kumar *et al.,* 2025; Mohan *et al.,* 2023).

6.7 Brucellosis

The RB51 live attenuated rough strain of Brucella abortus serves as a DIVA vaccine by lacking the O-polysaccharide side chain on its lipopolysaccharide. Standard brucellosis serological tests primarily detect antibodies to the O-chain; RB51-vaccinated animals do not generate O-chain antibodies and therefore test negative on these assays, whereas naturally infected animals are seropositive. This property facilitates surveillance of brucellosis in vaccinated herds, overcoming a key limitation of the traditional smooth S19 vaccine (Schurig *et al.,* 2002,Blasko *et al*.,2023).

6.8 Rabies (Wildlife Reservoir Control)

The V-RG recombinant vaccine, distributed via oral baiting in wildlife reservoirs, has been employed across Europe and North America to eliminate sylvatic rabies from fox and raccoon populations. The DIVA property arises from the vaccine's exclusive expression of the rabies G protein, with complete absence of the N protein. Anti-N antibody ELISA surveys can identify animals with prior wild type virus exposure, guiding adaptive management of ongoing oral vaccination campaigns (Maki *et al.,* 2017).

6.9 DIVA Strategy in India

In India, the DIVA strategy is actively strengthening disease surveillance and control frameworks for several economically significant livestock diseases. The development of BIOLUMPIVAXIN for LSD represents a notable indigenous achievement. India also utilizes DIVA vaccines for IBR (Raksha IBR), Bovine Brucellosis (Brucella abortus RB51 and S19DELTA), FMD (purified inactivated NSP free vaccines), and Pseudorabies. DIVA vaccines for Classical Swine Fever, Avian Influenza, Newcastle Disease, and Rabies are currently not commercially available within the country, highlighting the need for further research and regulatory development (Mohan *et al.,* 2023).

TABLE 1: DIVA VACCINE APPLICATIONS ACROSS MAJOR ANIMAL DISEASES

Disease	DIVA Vaccine (Marker Type)	Companion Diagnostic Test	Availability
Lumpy Skin Disease	BIOLUMPIVAXIN (Live attenuated LSDV Ranchi/2019)	gE-ELISA / PCR	India
Infectious Bovine Rhinotracheitis (IBR)	Raksha-IBR (gE-deleted BoHV-1)	gE-ELISA	India & Worldwide
Bovine Brucellosis	Brucella abortus RB51 / S19DELTA per vaccine	Rose Bengal & CFT (O-chain negative)	India & Worldwide
Foot and Mouth Disease (FMD)	Purified Inactivated (NSP-free)	3ABC-NSP ELISA	India & Worldwide
Pseudorabies (Aujeszky's Disease)	Porcilis AD Begonia, Auskipra GN (gE-deleted PRV)	gE-ELISA	India & Worldwide

Classical Swine Fever (CSF)	Porcilis Pesti, Suvaxyn CSF Marker (E2 subunit)	E-rns-ELISA	Worldwide (Not India)
Avian Influenza (AI)	Vectormune HVT AIV (Heterologous NA)	NA-specific ELISA	Worldwide (Not India)
Newcastle Disease (ND)	Innovax-ND, Vectormune HVT NDV (Recombinant HVT)	VN antibody / ELISA	Worldwide (Not India)
Rabies	V-RG, ONRAB (Recombinant oral bait — G protein only)	Anti-N antibody ELISA	Worldwide (Not India)

7. ADVANTAGES AND LIMITATIONS

7.1 Advantages

- Trade facilitation and economic continuity: DIVA strategies decouple vaccination from trade restriction, enabling accelerated recovery of disease free certification and preventing prolonged trade embargoes after outbreaks of high consequence diseases such as FMD (Bird and Kitching, 2003; Thiermann, 2004).
- Precision eradication: Targeted test and removal policies replace economically devastating whole herd depopulation, identifying individual infected animals within immune populations while preserving vaccinated animals of high genetic and productive value (Muller *et al.,* 2003; Pasick, 2004).
- Ethical acceptability: DIVA vaccination enables a 'vaccinate to live' policy framework, reducing reliance on mass culling and aligning disease control with contemporary animal welfare expectations (Domenech *et al.,* 2006; Scudamore and Harris, 2002).
- One Health integration: Reducing pathogen load at the livestock wildlife human interface contributes to public health, as DIVA strategies enable sustained vaccination without compromising the surveillance needed to detect emerging zoonotic threats (OIE, 2019).

7.2 Limitations

- Diagnostic accuracy dependence: The DIVA strategy is only as robust as its companion diagnostic. Suboptimal sensitivity generates false negatives, allowing infected animals to remain in herds; suboptimal specificity generates false positives, eroding farmer confidence. A critical gap also exists immediately post infection before specific antibodies develop (Uttenthal *et al.,* 2010).
- Vaccine purity requirements: For subunit DIVA vaccines, the system's integrity depends entirely on the absence of diagnostic antigens from the final vaccine product. Even trace NSP contamination can render vaccinated cohorts serologically ambiguous, neutralizing the surveillance benefit (Lubroth and Brown, 1996; Paton *et al.,* 2006).
- Cost and infrastructure: Implementing a DIVA program demands sustained investment in serological surveillance, laboratory capacity, and data management systems, placing programs beyond the resource capacity of many developing nations (Bergevoet and Van Asseldonk, 2009; Domenech *et al.,* 2006).
- Antigenic drift and marker stability: Continuous mutation of field virus populations can alter or eliminate the antigenic marker relied upon for DIVA differentiation, requiring vigilant molecular surveillance of circulating strains (Mettenleiter, 2016).

8. FUTURE PROSPECTS

The DIVA strategy is rapidly evolving with new technologies, and the coming years hold great promise for making it even more effective, affordable, and widely available. Below are some key areas where DIVA is likely to advance in simple terms:

8.1 Better and Faster Vaccines

Scientists are now using advanced platforms like mRNA vaccines and nanoparticle based delivery systems to create DIVA vaccines that work faster and last longer. Just like mRNA vaccines were used successfully in humans during the COVID 19 pandemic, similar approaches are being tested for animals. These next generation vaccines could provide protection within days and may need fewer booster doses, making vaccination programs easier to manage on farms.

8.2 Smarter and Cheaper Diagnostic Tests

New diagnostic tools such as rapid lateral flow tests (similar to home COVID test kits) are being developed for DIVA programs. These portable tests can be done directly on the farm without sending samples to a laboratory. This would make disease monitoring much faster, cheaper, and more accessible even in remote areas or in developing countries where laboratory infrastructure is limited.

8.3 Digital Technology and Artificial Intelligence (AI)

Modern data analytics and artificial intelligence can help analyze large numbers of test results quickly and accurately, identifying disease patterns before outbreaks spread. AI based tools can flag suspicious herds, predict outbreak risks, and guide farmers and veterinary officers to act early. In the future, DIVA test data may be directly linked to digital herd management platforms, making disease surveillance almost automatic.

8.4 DIVA Vaccines for New and Emerging Diseases

As new animal diseases emerge including African Swine Fever (ASF), which currently has no approved vaccine the DIVA concept is being applied in research on next generation ASF vaccines. Similarly, DIVA compatible vaccines are being explored for diseases like Peste des Petits Ruminants (PPR), Rift Valley Fever, and other transboundary diseases that are growing threats globally due to climate change and increased animal movement.

8.5 One Health Approach Protecting Animals, People, and the Environment Together

Many animal diseases can spread to humans (zoonoses). The DIVA strategy, by allowing continuous vaccination without losing surveillance ability, will play an increasingly important role in the 'One Health' framework. This means protecting animal health, human health, and the environment together, rather than separately. Global organizations like WOAH, FAO, and WHO are promoting DIVA based programs as an important part of this integrated approach.

8.6 Expanding DIVA Use in Developing Countries, Including India

Currently, DIVA programs are mainly used in high income countries with advanced laboratory systems. There is a strong need to make DIVA tools more affordable and simpler so that countries like India, which have large livestock populations and high disease burdens, can benefit from them. India has already made progress with indigenous DIVA vaccines for LSD (BIOLUMPIVAXIN) and IBR (Raksha-IBR), and future efforts should focus on developing DIVA tools for diseases like Classical Swine Fever and Avian Influenza within the country.

9. CONCLUSION

The DIVA strategy represents one of the most significant advances in veterinary vaccinology, transforming vaccination from a potential barrier to disease surveillance into a powerful tool that supports it. By using specially engineered marker vaccines combined with highly specific companion diagnostic tests, DIVA allows veterinarians and disease control authorities to accurately distinguish infected animals from vaccinated ones even during active vaccination campaigns. This capability has already led to the eradication of Pseudorabies in multiple countries and the successful control of Infectious Bovine Rhinotracheitis, Foot and Mouth Disease, Avian Influenza, Classical Swine Fever, Brucellosis, Lumpy Skin Disease, and Rabies in various parts of the

world. Despite remaining challenges including the need for high vaccine purity, accurate and affordable diagnostic tests, and the risk of antigenic drift in field virus populations the future of DIVA is bright. Emerging technologies such as mRNA vaccines, rapid on farm diagnostic kits, AI assisted disease surveillance, and digital data integration are poised to overcome current limitations and expand the reach of DIVA based programs globally. As international animal trade grows and zoonotic diseases become more frequent, and as society increasingly opposes the mass culling of healthy animals, the DIVA approach's 'vaccinate to live' philosophy offers the most scientifically sound, economically efficient, and ethically acceptable path forward for animal disease control and eradication worldwide.

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