



World Association for the Advancement of Veterinary Parasitology (WAAVP) concept paper on the efficacy evaluation of parasite vaccines

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ABSTRACT

Vaccination is considered a promising complementary tool to control parasitic infections in domestic animals. However, in many cases, limited insight is available on the level and duration of vaccine efficacy that is required to protect vaccinated animals against parasitic diseases and against the associated reductions in animal welfare, health and productivity, or the level of protection that is needed to be used in a complementary approach with drug treatments. In this concept paper, issued by the World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines subcommittee, potential efficacy claims and associated thresholds for parasite vaccines are discussed.

1. Introduction

Vaccination of animals is considered a promising parasite control measure for the coming decades, especially in view of increasing resistance to existing drug treatments (e.g., Charlier et al., 2022; Krämer et al., 2025; Rojas-Cabeza et al., 2025), concerns around drug withdrawal times for meat and milk products, and environmental safety concerns around antiparasitic drug residues (McKellar, 1997; Joachim et al., 2025). Indirectly, there are also concerns around co-selection by antiparasitic drug treatments for antibiotic resistance (Naemi et al., 2020). Although parasite vaccines could potentially be an alternative for, or complementary to, antiparasitic drugs, relatively few antiparasitic vaccines are on the market today (Lightowlers, 2021) (Table 1).

There is an urgent need for more vaccines, particularly for those parasites that are of greatest importance from human medical, veterinary and economic perspectives.

The development of parasite vaccines is hampered by several issues, (i) the complex structure and genome of parasites, which complicates the identification and recombinant expression of protective antigens (e.g., Geldhof et al., 2007); (ii) the complexity of the host's immune response, shaped by host-parasite co-evolution, which makes it difficult to identify the protective immune mechanisms that should be targeted by vaccination (Mitchell, 1991) and (iii) the ability of many parasites to suppress effective host immune responses (Schmid-Hempel, 2008). The external or primarily environmental lifecycles of many parasites add further challenges. In addition, in many cases, little insight is available

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on the level and duration of vaccine efficacy that is required to protect vaccinated (groups of) animals against parasitic diseases and the associated reductions in animal welfare, health and productivity, or the level of protection that is required under different management and epidemiological situations.

The objective of this World Association for the Advancement of Veterinary Parasitology (WAAVP) concept paper is to discuss which efficacy claims and associated thresholds could be considered for parasite vaccines. Better guidance on expected parasite vaccine efficacy would assist researchers in the design of their studies and the assessment of study outcomes and the regulatory authorities in the approval process of potential new parasite vaccines. The current paper aims to put forward concepts for efficacy claims and to discuss potential efficacy thresholds that should be considered by stakeholders while agreeing on

specific guidelines for parasite vaccine efficacy evaluations. It should be noted that this concept paper reflects the opinion of the contributing scientists and that (the conditions for) the successful registration and use of a parasite vaccine in the field will be further defined by additional stakeholders, i.e. regulatory authorities, pharmaceutical companies, veterinarians, farmers and animal owners. It is acknowledged that the success of a vaccine in the field will also depend on the degree of vaccine acceptance by the end-user, from cost and/or user-friendliness perspectives, and that these drivers should be considered in the decision-making process to develop a vaccination approach. However, a discussion around cost-effectiveness and user-friendliness is not within the scope of this WAAVP concept paper.

Table 1
Registered antiparasitic vaccines in domestic animals.

Host species	Parasite	Vaccine	Vaccine type	Company
Dog	<i>Giardia duodenalis</i>	Giardia Vax®	Inactivated trophozoites	Zoetis
	<i>Leishmania infantum</i>	Leish-Tec®	Recombinant protein	Ceva
	<i>Leishmania infantum</i>	Letifend®	Recombinant protein	LetiPharma
	<i>Leishmania infantum</i>	Neoleish™	Plasmid DNA	Zendal
Cattle	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	Trivalent Tick Fever Vaccine	Live attenuated vaccine	Department of Agriculture and Fisheries, Biosecurity Queensland
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	Anabasan®	Live attenuated vaccine	Limor
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	HemoVac C	Live attenuated vaccine	König
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	Vacuna contra la anaplasmosis y la babesiosis bovina	Live attenuated vaccine	National Institute of Agricultural Technology (INTA)
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	Vacuna contra la anaplasmosis y la babesiosis bovina	Live attenuated vaccine	División de Laboratorios Veterinarios (DILAVE)
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>	Biojaja®	Live attenuated vaccine	Litoral Biologicos
	<i>Babesia bovis</i> , <i>B. bigemina</i> , <i>Anaplasma marginale</i>		Live attenuated vaccine	Kimron Veterinary Institute
	<i>Babesia bigemina</i>	Redwater African	Live attenuated vaccine	Onderstepoort Biological Products Soc Ltd
	<i>Babesia bovis</i>	Redwater Asiatic	Live attenuated vaccine	Onderstepoort Biological Products Soc Ltd
	<i>Neospora caninum</i>	Bovilis Neoguard®	Inactivated tachyzoites	MSD/Merck
	<i>Cryptosporidium parvum</i>	Bovilis Cryptium®	Recombinant protein	MSD/Merck
	<i>Trichostrongylus axei</i>	TrichGuard®	Inactivated trophozoites	Boehringer Ingelheim
	<i>Trichostrongylus axei</i>	Trichobovis®	Inactivated trophozoites	CZ Vaccines S.A.U.
	<i>Trichostrongylus axei</i>	Tricovac	Inactivated trophozoites	Laboratorio Biológico de Tandil
	<i>Dictyocaulus viviparus</i>	Bovilis Huskvac®	Irradiated larvae	MSD/Merck
	<i>Rhipicephalus microplus</i>	Gavac	Recombinant protein	Heber Biotec S.A.
	<i>Rhipicephalus microplus</i>	Bovimune Ixovac®	Recombinant protein	Lapisa
	<i>Rhipicephalus microplus</i>	Tick-Vac®; Go-Tick®	Recombinant protein	Limor
	<i>Haemonchus contortus</i>	Barbervax®	Purified proteins	Wormvax Australia Pty Ltd
	<i>Haemonchus contortus</i>	Wirevax®	Purified proteins	Afrivet Business Management Pty Ltd
Sheep	<i>Toxoplasma gondii</i>	Toxovax®	Inactivated tachyzoites	MSD/Merck
	<i>Echinococcus granulosus</i>	Hydatid vaccine	Recombinant protein	Chongqing Auleon Biologicals Co
	<i>Echinococcus granulosus</i>	Combivax EG95	Recombinant protein	MCI Santé Animale
	<i>Echinococcus granulosus</i>	Providean Hidatil EG95®	Recombinant protein	Tecnovax
Sheep/Goats				
Poultry	<i>Eimeria</i> spp.	Paracox-5®	Live attenuated vaccine (oocysts)	MSD/Merck
	<i>Eimeria</i> spp.	Paracox-8®	Live attenuated vaccine (oocysts)	Biopharm
	<i>Eimeria</i> spp.	Livacox® Q and T	Live attenuated vaccine (oocysts)	Biopharm
	<i>Eimeria</i> spp.	Hipracox®; Evalon®; Evant®; Evanovo®	Live attenuated vaccine (oocysts)	Hipra
	<i>Eimeria</i> spp.	Huveguard MMAT; Huveguard NB;	Live attenuated vaccine (oocysts)	Huvepharma
	<i>Eimeria</i> spp.	Advent™; Inovocox™	Live non-attenuated vaccine (oocysts)	Huvepharma
	<i>Eimeria</i> spp.	Immucox® range	Live non-attenuated vaccine (oocysts)	Ceva
	<i>Eimeria</i> spp.	Vaxxilive Cocci 3™	Live attenuated vaccine (oocysts)	Boehringer Ingelheim
	<i>Eimeria</i> spp.	Vaxxon Coccivet™	Live attenuated vaccine (oocysts)	Vaxxinova
	<i>Eimeria maxima</i>	CoxAbic®	Purified protein	Abic Ltd.
Pigs	<i>Taenia solium</i>	Cysvax®	Recombinant protein TSOL18	Indian Immunologicals Limited

2. Potential efficacy claims for parasite vaccines

Vaccine efficacy can be defined either as a direct lethal effect of vaccination against the parasite, as an effect on parasite development, reproduction, and excretion of transmissible (environmental) stages or as an effect on the health or productivity of vaccinated animals. All these outcomes of vaccination have potential value from an economic, veterinary or medical point of view and are discussed in more detail below. While the below paragraphs discuss the benefits of parasite vaccines, there are only limited data around the potential risks, such as the selection of more pathogenic parasite subpopulations.

2.1. Vaccination leads to a decreased parasite burden in the vaccinated animal(s)

A primary efficacy claim of parasite vaccines could be a reduction in the number of immature and/or mature parasites in the vaccinated animals. Most ‘macroparasites’ (e.g., gastrointestinal nematodes, lungworms, sea lice or ticks) can be quantified directly (i.e., through parasite counts) or indirectly (e.g., through faecal antigen detection for *Fasciola hepatica*).

In the case of ‘microparasites’ (May and Anderson, 1979), which multiply within the final host, quantification might also be possible in some cases, for example in the case of *Babesia* parasitaemia or *Giardia* trophozoite or cyst counts. Molecular tools such as quantitative polymerase chain reaction (qPCR) can also be useful, assessing replication in terms of genome copy number in absolute terms or normalising relative to host cell genome number (e.g., Nolan et al., 2015).

Instead of quantifying the effect of vaccination on the parasite burden in individual animals, a population-level qualitative approach could be used, in which the host is considered either infected/infested or not, without quantification of the parasites. The reduction of the number of infected/infested animals is thus considered as an efficacy read-out. While this approach eliminates the need for parasite quantification, it does imply a 100% efficacy in a large proportion of the vaccinated animals, which may be difficult to achieve.

2.2. Vaccination aids in the prevention or reduction of clinical disease or production losses associated with parasite infection

2.2.1. Prevention of disease, pathologic changes and mortality

According to the World Health Organisation (WHO, 2021), the overall objective of vaccination is to protect the vaccinated animal(s) against disease. The vaccine’s efficacy should therefore be evaluated based on how many vaccinated subjects developed the ‘outcome of interest’ (in this case disease) compared with non-vaccinated subjects. In this claim structure, a vaccine efficacy of 80% means that those subjects who received the vaccine were at an 80% lower risk of developing disease than those non-vaccinated subjects.

When applied to parasite vaccines and depending on the parasite and animal species, ‘protection against disease’ could mean preventing mortality (including abortion in pregnant animals), the reduction or absence of clinical signs or the reduction in pathologic changes.

The prevention of clinical disease is likely to be a consequence of the successful prevention of parasite infections. This is, for example, the case in the poultry coccidiosis vaccines developed for the active immunisation of chickens to reduce parasite replication and associated clinical signs caused by *Eimeria* spp. (Mathis et al., 2025), or for GiardiaVax® which has been proven to prevent clinical disease caused by *Giardia duodenalis* infection in dogs and to significantly reduce the incidence, intensity and duration of cyst shedding (Payne et al., 2002).

This direct correlation between infection and clinical disease does not always need to be demonstrated, as is the case for the *Cryptosporidium parvum* vaccine (Bovilis Cryptium®) in cattle that was recently approved in the EU. It is based on the active immunisation of pregnant heifers and cows, inducing antibodies against the *C. parvum* protein

Gp40, which are transferred to newborn calves via colostrum from vaccinated pregnant heifers or cows, significantly reducing clinical signs (i.e. diarrhoea) caused by *C. parvum* in the calves (Reijnders et al., 2025). For this vaccine it was not required to demonstrate a direct effect against the parasite. The antibodies lead to passive immunisation of calves and were demonstrated to reduce clinical signs. The efficacy of active immunization of grazing cattle with Bovilis Huskvac®, a vaccine containing *Dictyocaulus viviparus* 3rd stage irradiated larvae, has also been evaluated based on the reduction of clinical signs and lesions of parasitic bronchitis attributable to the bovine lungworm *D. viviparus* (McKeand, 2000).

In chickens, qualitative assessment of pathology (e.g. intestinal lesion scores) is used to evaluate vaccine or drug efficacy against *Eimeria* spp., which frequently does not equate to ‘disease’ severity since many modern broilers have been bred to continue to eat and grow, even in the face of apparently severe pathology (tolerance/susceptibility).

Examples of vaccines preventing mortality are the vaccines containing inactivated/attenuated tachyzoites of *Neospora caninum* (Imhof et al., 2024) or *Toxoplasma gondii* (Hasan, Nishikawa, 2022) that are used to prevent abortion caused by *N. caninum* and *T. gondii* infection in cattle and sheep, respectively.

Although effective vaccination typically results in fewer clinical signs and decreased disease severity, sometimes vaccines that reduce pathogen replication may select for more virulent pathogens, as observed in rodent malaria (Mackinnon et al., 2008).

2.2.2. Prevention of production losses

Parasites often have a negative impact on animal productivity without causing clinical signs of disease, which poses a significant economic burden on livestock farming (Charlier et al., 2020; Soutter et al., 2020; Parker et al., 2021). Next to the effect on clinical disease, vaccination might have a positive outcome on the occurrence of negative subclinical impacts of infection, including production loss. These might include effects on growth, feed conversion, reproduction, egg production or milk yield. For example, vaccination against *Trichostrongylus axei* in cattle does not completely prevent infection, but still results in shorter mean calving intervals and calving rates (Ortega-Mora et al., 2022). Likewise, the poultry coccidiosis vaccines (e.g. Paracox 5®) do not prevent infection but claim to reduce loss in weight gain caused by infections with *E. acervulina*, *E. maxima*, *E. mitis* and *E. tenella* and to improve feed conversion ratios in vaccinated broilers (Crouch et al., 2003). In other cases, reduced production losses after vaccination can be directly linked to an effect of vaccination on the parasite burden. For example, vaccination with Barbevax®, a subunit vaccine against the barber’s pole worm, *Haemonchus contortus*, reduces adult worm burden and the clinical signs related to heavy worm burden in sheep (Bassetto et al., 2020).

2.3. Vaccination leads to the prevention or reduction of parasite transmission

Effectively reducing the transmission of a parasite will decrease the environmental infection pressure, resulting in lower levels of infection of all co-grazing or co-housed animals, while also reducing the re-infection risk for the vaccinated animals.

For example, anticoccidial vaccines in poultry reduce oocyst shedding and provide time for immunity to develop against local strains (Chapman et al., 2002; Crouch et al., 2003). In cattle, vaccines against *Trichostrongylus axei* improve genital clearance of *T. axei* organisms, thereby helping to reduce the spread of infection throughout the herd (Ortega-Mora et al., 2022). GiardiaVax® claims to significantly reduce the incidence, intensity and duration of *Giardia* cyst shedding, as such lowering infection risk for other, especially co-housed dogs, but potentially also reducing zoonotic transmission.

The recombinant antigen vaccines against *Echinococcus granulosus* in sheep and *Taenia solium* in pigs, which are registered and in practical use

in various countries, are used to reduce transmission of parasites because of their potential to cause zoonotic disease in humans, rather than primarily for the protection of the animal hosts *per se* (Lightowlers et al. 2021).

In the case of helminth infections in grazing animals, it is expected that by reducing the number of excreted eggs or larvae the pasture contamination will decrease, leading to a decreased infection level in grazing animals, and potentially a decreased worm burden later in the grazing season (Vercruyse and Claerebout, 2003; Claerebout and Geldhof, 2020). Barbervax® for example controls disease caused by Barber's pole worm (*H. contortus*) by reducing worm egg excretion and preventing the build-up of infection on pasture (Broomfield et al., 2020). In addition to, or as an alternative mechanism to, reduced egg excretion, decreased egg viability following vaccination, as observed in *F. hepatica* (Dalton et al., 1996) may also contribute to lower environmental contamination and reduced parasite transmission.

The currently available vaccines for ticks in cattle do not have a direct acaricidal effect resulting in reducing tick numbers, but rather impact on the reproductive capacity of the female ticks. This causes a partial and progressive reduction in the level of larval infestation on pastures (Bishop et al., 2023). Tick vaccines under development aim to affect all or different stages of the tick life cycle including the reduction in the number of adult female ticks, reduction in egg laying and/or decreased larval emergence, which has been proven to be effective against one-host ticks. Thus, when testing tick vaccine efficacy, adult female ticks are collected from vaccinated animals and transferred to the laboratory to monitor a direct effect as well as the effect on the subsequent stages. Efficacy measurements for tick vaccines have been reviewed by Cunha et al. (2013) who recommended assessing the following variables between vaccinated and control groups to calculate vaccine efficacy: tick numbers, weight of eggs/tick, and percentage larval emergence.

Recently, the WAAVP published guidelines for studies evaluating the efficacy of parasiticides in reducing the risk of vector-borne pathogen transmission in dogs and cats (Otranto et al., 2021). These guidelines defined a benefit of acaricide preventive treatments as the reduction of the risk of infection (i.e. disease transmission). This concept can also be applied for parasite vaccine efficacy claims, especially since most parasite vaccines are not likely to yield a 100% reduction of disease transmission, due to the many variables defining a successful outcome of vaccination. Specifically for parasite vaccines, the concept of efficacy claims regarding the prevention or reduction of disease transmission as a direct efficacy outcome has the potential to aid in the decreased use and reliance on preventive treatment programs using antiparasitic drugs, and thus may decrease the selection for drug resistance development.

3. How to define thresholds for different efficacy claims for parasite vaccines?

Given the multitude of variables impacting the nature of vaccine efficacy, parasite vaccines can be evaluated using a multitude of parameters including parasite burden, mortality, morbidity, lesions, productivity and epizootiological impact, as well as through biomarkers (e.g. serological response, liver enzyme levels, faecal egg counts, faecal antigen levels). For a biomarker to be acceptable as a correlate of vaccine efficacy, it must be shown that a sufficient qualitative and quantitative correlation exists between the indicator measured and the claimed protection in the target species, or the efficacy claim should be based on the biomarker itself, e.g. a reduction of faecal egg counts. Although, in many cases, vaccination leads to a measurable serum antibody response, that response is not necessarily protective and antibody levels alone should not be relied upon as the sole indicator of vaccine efficacy. The use of biomarkers for parasite infection as an indicator of antiparasitic efficacy is discussed in detail in Geurden et al. (2022).

When new products are evaluated for regulatory approval an important evaluation criterion is the benefit versus the risk of the new

vaccine. Each of the above discussed efficacy claims have the potential to yield a benefit either for individual animals or at the herd or flock level. Additionally, since a given vaccine can produce efficacy in several different ways, combinations of the efficacy claims described above are possible. For example, reduced faecal egg excretion in cattle vaccinated against gastro-intestinal nematodes may reduce the number of infective larvae on pasture, thereby reducing the number of worms later in the grazing season, leading to a reduction in morbidity and production losses caused by the parasites (Claerebout and Geldhof, 2020).

An important consideration is that efficacy claims and thresholds for parasite vaccines may be different for different parasite-host systems and, within a given parasite and animal species, for different climate, epidemiological and management settings. Moreover, vaccine efficacy can be affected by breed, genetic background, age and physiological status of the host. As such it needs to be considered whether vaccination of a group of animals should result in a benefit for each individual animal or in a group effect only. For example, given that a certain group effect is obtained (e.g., a set threshold for a mean reduction in parasite load or a mean growth effect), a wider, pre-set efficacy range could be acceptable at individual animal level. Alternatively, vaccine efficacy could be considered at the group level only (e.g., Turner et al., 2016), which is also the case for most anthelmintic drug efficacy assessments (Geurden et al., 2022).

3.1. Vaccination leads to a decreased parasite burden in the vaccinated animal(s)

Efficacy as defined in the WAAVP anthelmintic guidelines (Geurden et al., 2022) and in the ecto-parasiticide guidelines (Marchiondo et al., 2013; Holdsworth et al., 2022), as well as in regulatory guidelines for antiparasitic drugs, typically require the drugs to have a high efficacy (>90%). Some vaccines, such as the vaccines against taeniid cestode infections, do have efficacies of > 90%, demonstrated both experimentally and during practical use in the field (Lightowlers et al. 2021). However, applying these high efficacy thresholds for parasite vaccines may hamper the development or approval of many other vaccines. For example, in some jurisdictions it is expected that anti tick vaccines need to compete with the high efficacy of acaricides. The problems of tick vaccines to be approved under this regulatory framework (for example, the efficacy of Bm86 vaccines against *Rhipicephalus microplus* is much lower than 90%) have become a restriction for their adoption in most countries (de la Fuente et al., 1999; Bishop et al., 2023).

A > 90% reduction of parasite burden in all vaccinated animals might not be achievable in most situations, because vaccine efficacy depends on the host's immune response, which is imperfect and varies between genetically diverse individuals and over time, as well as between animals living in different epidemiological circumstances. However, lower efficacy thresholds might still provide substantial benefits to vaccinated animals, as described above and in Paragraph 3.2. Lower efficacy thresholds might therefore be agreed upon for parasite vaccines, and any other efficacy claim could thus be defined as appropriate, e.g. in regions where GI nematodes show multidrug resistance the use of even a partially efficacious vaccine (such as Barbervax®) may still be useful to producers.

Another important difference between the efficacy evaluation of vaccines and antiparasitic drugs relative to measurements of parasite burden, is the timing of the efficacy evaluation after vaccination/treatment. For anthelmintic drugs, efficacy is usually evaluated quite shortly after treatment or infection, whereas the efficacy of parasite vaccines might only be measurable after multiple weeks or even months. Some vaccines rely on natural exposure to boost efficacy, imposing a longer timescale, e.g., the lungworm vaccine in cattle. Still others require multiple doses of vaccine over multiple weeks to produce the desired effect.

3.2. Vaccination aids in the prevention or reduction of clinical disease and mortality, or production losses associated with parasite infection

When considering prevention or reduction of clinical disease as the main parameter for vaccine efficacy, different outcomes can be taken into account:

- (i) What proportion of the vaccinated animals should remain free of disease when exposed to the parasite infection? This proportion will be defined by the severity of the disease as well as the clinical and commercial realities for the specific parasite. For example, the reported efficacy of commercially available anti-*Leishmania* vaccines in the prevention of active infection in vaccinated dogs ranges from 68.4% to 80%, yet the protection against clinical disease is 92.7–95% (Velez and Gallego, 2020). The high protection against clinical disease seems appropriate given the severity of the disease. In this case a high protection against clinical disease, despite a < 90% efficacy in prevention of infection, was adequate to support the development of the vaccine.
- (ii) Should vaccinated animals remain healthy or is it acceptable that the severity of the disease is reduced and/or that a higher proportion of vaccinated animals survive the infection? For example, the new vaccine against *C. parvum* in cattle is licenced for passive immunisation of calves to reduce the severity and duration of clinical signs (i.e., diarrhoea), provided that the calf receives sufficient colostrum from its vaccinated dam.

3.3. Vaccination leads to the prevention or reduction of parasite transmission

When prevention or reduction of parasite transmission is intended, thresholds could be set for the reduction in egg/larval shedding as well as for the duration of this reduction (area under the curve). For example, a vaccine that reduces faecal egg output in grazing ruminants by 60% during several months could have a greater impact on the pasture infection level and parasite transmission than a vaccine exhibiting 90% reduction in egg output for only a few weeks. In parasite genera where host immunity primarily affects worm fecundity (e.g., *Ostertagia* and *Cooperia* in cattle) reduced faecal egg output can be obtained with a vaccine that has no direct impact on the number of parasites in the vaccinated hosts (Vercruysse and Claerebout, 2003). In other cases, when increased parasite density leads to lower fecundity per parasite (density dependent effect), alleviating the crowding effect can complicate interpretation of transmission thresholds when individual parasite fecundity increases as population density decreases (e.g. *Eimeria* in chickens; Williams, 2001).

For vector-borne diseases, setting a threshold for vaccine efficacy can be complicated by multiplication of the parasite in the vector, e.g., *Babesia* in ticks or *Fasciola hepatica* in the vector snail. Results from a mathematical model to assess the efficacy of a partially effective (43% efficacy) vaccine for control of liver fluke infection indicated that protective immunity must be maintained in at least 90% of the animals for the whole grazing season for a vaccine to be effective (Turner et al., 2016).

3.4. Efficacy of vaccine in complementary management approaches

If a vaccine could be registered to be used as part of an integrated control strategy (e.g., BM86 vaccine against *R. microplus*), the required efficacy levels may be lower than for a vaccine that is registered as a stand-alone solution. Immunological control through vaccination against ticks may become instrumental in complementing the use of synthetic drugs when multi-drug-resistant parasites prevail. A similar approach could be used in the management of sea lice in salmon farming (Raynard et al., 2002). The promotion of the use of vaccines should be accompanied by precise information for users regarding their mode of

action and the type of efficacy to be expected. A combination strategy involving vaccination and simultaneous anthelmintic medication has been found to be exceptionally effective for prevention of porcine cysticercosis (Lightowlers et al. 2021). The Cysvax® vaccine protects vaccinated pigs against *T. solium* infection, but does not cure an infection that may already exist at the time of vaccination. Combining vaccination with a single treatment with oxfendazole eliminates any potentially preexisting infection and provides protection against subsequent exposure to infection through until the animals reach slaughter age. In poultry, sequential 'bioshuttle' prophylaxis using non-attenuated anti-coccidial vaccines followed by an in-feed anticoccidial drug supports development of immunity while minimising spread in individuals that missed vaccination and reducing the risk of necrotic enteritis.

4. Conclusions

In this paper we provide evidence supporting the concept that a uniform vaccine efficacy threshold for parasite vaccines in animals cannot be defined. The appropriate threshold for a given vaccine will depend on the intended claim of the vaccine (reduced morbidity/mortality, increased productivity and/or reduced transmission), on the pathogenicity and/or fecundity of the parasite and, within a specific host-pathogen model, on the local husbandry and epidemiological situation. Therefore, it is essential that the intended claim is clearly and explicitly defined and that the benefit of the intended claim clearly outweighs any risks associated with vaccination.

CRediT authorship contribution statement

Spithill Terry: Writing – review & editing, Writing – original draft, Validation. **Santiago Nava:** Writing – review & editing, Writing – original draft, Validation. **Tabor Ala:** Writing – review & editing, Writing – original draft, Validation. **Anja Joachim:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Thomas Geurden:** Writing – review & editing, Writing – original draft, Validation, Supervision, Conceptualization. **Edwin Claerebout:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation, Conceptualization. **Blake Damer:** Writing – review & editing, Writing – original draft, Validation. **Lightowlers Marshall:** Writing – review & editing, Writing – original draft, Validation. **Kaplan Ray:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Silvina Fernandez:** Writing – review & editing, Writing – original draft, Validation, Conceptualization. **Livio Costa Junior:** Writing – review & editing, Writing – original draft, Validation, Conceptualization.

Declaration of Competing Interest

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References

- Bassetto, C.C., Almeida, F.A., Newlands, G.F.J., Smith, W.D., Amarante, A.F.T., 2020. Repeated vaccination against *Haemonchus contortus* provides continuous protection to young grazing sheep. *Vet. Parasitol.* 287, 109273. <https://doi.org/10.1016/j.vetpar.2020.109273>.
- Bishop, L.J., Stutzer, C., Maritz-Olivier, C., 2023. More than three decades of Bm86: what we know and where to go. *Pathogens* 12 (9), 1071. <https://doi.org/10.3390/pathogens12091071>.
- Broomfield, M.A., Doyle, E.K., Kahn, L.P., Smith, W.D., Walkden-Brown, S.W., 2020. A simplified Barbevax® vaccination regimen in lambs to evoke immunological protection to *Haemonchus contortus*. *Vet. Parasitol.* 287, 109243. <https://doi.org/10.1016/j.vetpar.2020.109243>.
- Chapman, H.D., Cherry, T.E., Danforth, H.D., Richards, G., Shirley, M.W., Williams, R.B., 2002. Sustainable coccidiosis control in poultry production: the role of live vaccines. *Int. J. Parasitol.* 32, 617–629. [https://doi.org/10.1016/S0020-7519\(01\)00362-9](https://doi.org/10.1016/S0020-7519(01)00362-9).
- Charlier, J., Bartley, D.J., Sotiraki, S., Martinez-Valladares, M., Claerebout, E., von Samson-Himmelstjerna, G., Thamsborg, S.M., Hoste, H., Morgan, E.R., Rinaldi, L., 2022. Anthelmintic resistance in ruminants: challenges and solutions. *Adv. Parasitol.* 115, 171–222. <https://doi.org/10.1016/bs.apar.2021.12.002>.
- Charlier, J., Rinaldi, L., Musella, V., Ploeger, H.W., Chartier, C., Vineer, H.R., Hinney, B., von Samson-Himmelstjerna, G., Băcescu, B., Mickiewicz, M., Mateus, T.L., Martinez-Valladares, M., Quealy, S., Azaiz, H., Sekovska, B., Akkari, H., Petkevicius, S., Hektoen, L., Höglund, J., Morgan, E.R., Bartley, D.J., Claerebout, E., 2020. Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. *Prev. Vet. Med.* 182, 105103. <https://doi.org/10.1016/j.prevetmed.2020.105103>.
- Claerebout, E., Geldhof, P., 2020. Helminth vaccines in ruminants: from development to application. *Vet. Clin. North Am. Food Anim. Pr.* 36, 159–171. <https://doi.org/10.1016/j.cvfa.2019.10.001>.
- Crouch, C.F., Andrews, S.J., Ward, R.G., Francis, M.J., 2003. Protective efficacy of a live attenuated anti-coccidial vaccine administered to 1-day-old chickens. *Avian Pathol.* 32, 297–304. <https://doi.org/10.1080/10307945031000097912>.
- Cunha, R.C., Andreotti, R., Garcia, M.V., de Abreu Rangel Aguirre, A., Leitao, A., 2013. Calculation of the efficacy of vaccines against tick infestations on cattle. *Rev. Bras. Parasitol.* 107, 571–578. <https://doi.org/10.1590/S1984-29612013000400019>.
- Dalton, J.P., McGonigle, S., Rolph, T.P., Andrews, S.J., 1996. Induction of protective immunity in cattle against infection with *Fasciola hepatica* by vaccination with cathepsin L proteinases and with hemoglobin. *Infect. Immun.* 64, 5066–5074. <https://doi.org/10.1128/iai.64.12.5066-5074.1996>.
- de la Fuente, J., Rodríguez, M., Montero, C., Redondo, M., García-García, J.C., Méndez, L., Serrano, E., Valdés, M., Enríquez, A., Canales, M., Ramos, E., Boué, O., Machado, H., Leonart, R., 1999. Vaccination against ticks (*Boophilus* spp.): the experience with the Bm86-based vaccine Gvac. *Genet. Anal.* 15, 143–148. [https://doi.org/10.1016/S1050-3862\(99\)00018-2](https://doi.org/10.1016/S1050-3862(99)00018-2).
- Geldhof, P., De Maere, V., Vercruysse, J., Claerebout, E., 2007. Recombinant expression systems: the obstacle to helminth vaccines? *Trends Parasitol.* 23, 527–532. <https://doi.org/10.1016/j.pt.2007.08.012>.
- Geurden, T., Smith, E.R., Vercruysse, J., Yazwinski, T., Rehbein, S., Nielsen, M.K., 2022. Reflections and future directions for continued development and refinement of guidelines for anthelmintic efficacy studies. *Vet. Parasitol.* 307–308, 109741. <https://doi.org/10.1016/j.vetpar.2022.109741>.
- Hasan, T., Nishikawa, Y., 2022. Advances in vaccine development and the immune response against toxoplasmosis in sheep and goats. *Front. Vet. Sci.* 9, 951584. <https://doi.org/10.3389/fvets.2022.951584>.
- Holdsworth, P., Rehbein, S., Jonsson, N.N., Peter, R., Vercruysse, J., Fourie, J., 2022. World Association for the Advancement of Veterinary Parasitology (WAAVP) second edition: guideline for evaluating the efficacy of parasiticides against ectoparasites of ruminants. *Vet. Parasitol.* 302, 109613. <https://doi.org/10.1016/j.vetpar.2021.109613>.
- Imhof, D., Hänggeli, K.P.A., De Sousa, M.C.F., Vigneswaran, A., Hofmann, L., Amdouni, Y., Boubaker, G., Müller, J., Hemphill, A., 2024. Working towards the development of vaccines and chemotherapeutics against neosporosis-With all of its ups and downs-Looking ahead. *Adv. Parasitol.* 124, 91–154. <https://doi.org/10.1016/bs.apar.2024.01.001>.
- Joachim, A., Robertson, L.J., Ferroglio, E., Bäumer, W., Leschnik, M., 2025. Antiparasitics against ectoparasites in small animals – important pharmaceutical substances or underestimated environmental hazards? *Vet. Parasitol.* 339, 110557. <https://doi.org/10.1016/j.vetpar.2025.110557>.
- Krämer, F., Baneth, G., Dantas-Torres, F., Hamer, S., Lappin, M.R., Otranto, D., Roura, X., Sager, H., Schunack, B., Scorza, V., Traub, R., Geary, T.G., 2025. Resistance of companion animal parasites to antiparasitic drugs. *Adv. Parasitol.* 128, 35–157. <https://doi.org/10.1016/bs.apar.2025.07.002>.
- Lightowlers, M.W., 2021. Antiparasitic vaccines. In: Bowman, D.D. (Ed.), *Georgis' parasitology for veterinarians*, 11th ed. Elsevier Saunders, St. Louis, Missouri, pp. 479–500.
- Lightowlers, M.W., Gasser, R.B., Hemphill, A., Romig, T., Tamarozzi, F., Deplazes, P., Torgerson, P.R., Garcia, H.H., Kern, P., 2021. Advances in the treatment, diagnosis, control and scientific understanding of taeniid cestode parasite infections over the past 50 years. *Int. J. Parasitol.* 51, 1167–1192. <https://doi.org/10.1016/j.ijpara.2021.10.003>.
- Mackinnon, M.J., Gandon, S., Read, A.F., 2008. Virulence evolution in response to vaccination: the case of malaria. *Vaccine* 26, C42–C52. <https://doi.org/10.1016/j.vaccine.2008.04.012>.
- Marchiondo, A.A., Holdsworth, P.A., Fourie, L.J., Rugg, D., Hellman, K., Snyder, D.A., Dryden, M.W., 2013. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) second edition: guidelines for evaluating the efficacy of parasiticides for the treatment, prevention and control of flea and tick infestations on dogs and cats. *Vet. Parasitol.* 194, 84–97. <https://doi.org/10.1016/j.vetpar.2013.02.003>.
- Mathis, G.F., Lumpkins, B., Cervantes, H.M., Fitz-Coy, S.H., Jenkins, M.C., Jones, M.K., Price, K.R., Dalloul, R.A., 2025. Coccidiosis in poultry: Disease mechanisms, control strategies, and future directions. *Poult. Sci.* 104, 104663. <https://doi.org/10.1016/j.psj.2024.104663>.
- May, R.M., Anderson, R.M., 1979. Population biology of infectious diseases: Part II. *Nature* 280, 455–461. <https://doi.org/10.1038/280455a0>.
- McKeand, J.B., 2000. Vaccine development and diagnostics of *Dictyocaulus viviparus*. *Suppl. S17 Parasitology* 120, 23. <https://doi.org/10.1017/s003182099005727>.
- McKellar, Q.A., 1997. Ecotoxicology and residues of anthelmintic compounds. *Vet. Parasitol.* 72, 413–426. [https://doi.org/10.1016/s0304-4017\(97\)00108-8](https://doi.org/10.1016/s0304-4017(97)00108-8).
- Mitchell, G.F., 1991. Co-evolution of parasites and adaptive immune responses. *Immunol. Today* 12, A2–A5. [https://doi.org/10.1016/S0167-5699\(05\)80002-7](https://doi.org/10.1016/S0167-5699(05)80002-7).
- Naemi, A., Dey, H., Kiran, N., Sandvik, S.T., Slettemeas, J.S., Nesse, L.L., Simm, R., 2020. NarAB is an ABC-type transporter that confers resistance to the polyether ionophores narasin, salinomycin, and maduramycin, but not monensin. *Front. Microbiol.* 11, 104. <https://doi.org/10.3389/fmicb.2020.00104>.
- Nolan, M.J., Tomley, F.M., Kaiser, P., Blake, D.P., 2015. Quantitative real-time PCR (qPCR) for *Eimeria tenella* replication-Implications for experimental refinement and animal welfare. *Parasitol. Int.* 64, 464–470. <https://doi.org/10.1016/j.parint.2015.06.010>.
- Ortega-Mora, L.M., Sánchez-Sánchez, R., Rojo-Montejo, S., Román-Trufero, A., Montenegro-Gregorio, D., Puentes-Colorado, E., Parra-Romero, A., Regidor-Cerrillo, J., Osoro, K., Collantes-Fernández, E., 2022. A new inactivated *Trichomonas foetus* vaccine that improves general clearance of the infection and calving intervals in cattle. *Front. Vet. Sci.* 6, 1005556. <https://doi.org/10.3389/fvets.2022.1005556>.
- Otranto, D., Dantas-Torres, F., Fourie, J.J., Lorusso, V., Varloud, M., Gradoni, L., Drake, J., Geurden, T., Kaminsky, R., Heckeroth, A.R., Schunack, B., Pollmeier, M., Beugnet, F., Holdsworth, P., 2021. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) guidelines for studies evaluating the efficacy of parasiticides in reducing the risk of vector-borne pathogen transmission in dogs and cats. *Vet. Parasitol.* 290, 109369. <https://doi.org/10.1016/j.vetpar.2021.109369>.
- Parker, C.D., Lister, S.A., Gittins, J., 2021. Impact assessment of the reduction or removal of ionophores used for controlling coccidiosis in the UK broiler industry. *Vet. Rec.* 189, e513. <https://doi.org/10.1002/vetr.513>.
- Payne, P.A., Ridley, R.K., Dryden, M.W., Bathgate, C., Milliken, G.A., Stewart, P.W., 2002. Efficacy of a combination febantel-praziquantel-pyrantel product, with or without vaccination with a commercial *Giardia* vaccine, for treatment of dogs with naturally occurring giardiasis. *J. Am. Vet. Med. Assoc.* 220, 330–333. <https://doi.org/10.2460/javma.2002.220.330>.
- Raynard, R.S., Bricknell, I.R., Billingsley, P.F., Nisbet, A.J., Vigneau, A., Sommerville, C., 2002. Development of vaccines against sea lice. *Pest Manag. Sci.* 58, 569–575. <https://doi.org/10.1002/ps.474>.
- Reijnders, M., van Roosmalen, M., Holtslag, H., Arts, S., Pel, S., Dufé, D., Kaashoek, M., Vertenten, G., van Werven, T., Sietsma, S., Roy, C., Herman, N., 2025. The evaluation of the efficacy of a novel subunit vaccine in the prevention of *Cryptosporidium parvum*-caused diarrhoea in neonatal calves. *Animals* 15, 132. <https://doi.org/10.3390/ani15020132>.
- Rojas-Cabeza, J.F., Moreno-Cordova, E.N., Ayala-Zavala, F.F., Ochoa-Teran, A., Sonenshine, D.E., Valenzuela, J.G., Sotelo-Mundo, R.R., 2025. A review of acaricides and their resistance mechanisms in hard ticks and control alternatives with synergistic agents. *Acta Trop.* 261, 107519. <https://doi.org/10.1016/j.actatropica.2024.107519>.
- Schmid-Hempel, P., 2008. Immune defence, parasite evasion strategies and their relevance for 'macroscopic phenomena' such as virulence. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 364, 85–98. <https://doi.org/10.1098/rstb.2008.0157>.
- Soutter, F., Werling, D., Tomley, F.M., Blake, D.P., 2020. Poultry coccidiosis: design and interpretation of vaccine studies. *Front. Vet. Sci.* 7, 101. <https://doi.org/10.3389/fvets.2020.00101>.
- Turner, J., Howell, A., McCann, C., Caminade, C., Bowers, R.G., Williams, D., Baylis, M., 2016. A model to assess the efficacy of vaccines for control of liver fluke infection. *Sci. Rep.* 6, 23345. <https://doi.org/10.1038/srep23345>.
- Velez, R., Gallego, M., 2020. Commercially approved vaccines for canine leishmaniasis: a review of available data on their safety and efficacy. *Trop. Med. Int. Health* 25, 540–557. <https://doi.org/10.1111/tmi.13382>.
- Vercruysse, J., Claerebout, E., 2003. Assessment of the efficacy of helminth vaccines. *J. Parasitol.* 89, S202–S209 (Suppl.).
- WHO, 2021. <https://www.who.int/news-room/feature-stories/detail/vaccine-efficacy-effectiveness-and-protection> (Accessed 28 March 2024).
- Williams, R.B., 2001. Quantification of the crowding effect during infections with the seven *Eimeria* species of the domesticated fowl: its importance for experimental designs and the production of oocyst stocks. *Int. J. Parasitol.* 31, 1056–1069. [https://doi.org/10.1016/S0020-7519\(01\)00235-1](https://doi.org/10.1016/S0020-7519(01)00235-1).